



Therapy of Suppressing Yang and Astringing Yin for the Treatment of Cancer-Related Insomnia

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Abstract

Keywords

- cancer-related insomnia (CRI)
- suppressing yang and astringing yin
- Zhenjing Anshen Granules
- syndrome differentiation and treatment
- Yuling Zheng

The pathogenesis of cancer-related insomnia (CRI) mainly includes, first, the flow of cancerous toxin leading to the disorder of visceral qi; second, cancer-related radiotherapy and chemotherapy belonging to “exogenous pathogenic factors” to a certain extent, which can further aggravate visceral disorders. The therapeutic principle of Chinese medicine is to tranquilize the mind on the basis of regulating viscera, suppressing yang, and astringing yin. On this theoretical basis, Professor Zheng Yuling created a representative prescription of Zhenjing Anshen Granules (镇静安神颗粒) which can achieve the co-regulation of the heart, liver, and kidney, tranquilizing the mind and nourishing the blood. Clinically, the selection of prescriptions and medicines needs to be considered due to factors such as different treatment stages and differences in patients’ constitutions.

Introduction

Cancer-related insomnia (CRI) refers to insomnia due to tumor factors, with an incidence rate of 35 to 70%,¹ ranking second in cancer-related diseases.² Its clinical manifestations are short sleep time or poor sleeping quality of the patient, among which the main symptoms include difficulty in falling asleep, difficulty in falling asleep after waking up, waking up easily after sleep, fatigue after waking up, dreaminess, nightmares, etc.^{3,4} It can be seen that during the course of the malignant tumor each stage will not only hinder the treatment process but also affect the patients’ mental health and reduce their quality of life. Simultaneously, it often complicates with anxiety and depression of concurrent rate as high as 49 and 53%, respectively,⁵ causing great trouble to the patient’s family, work, and life.⁶ At present, CRI is mainly treated symptomatically with sedatives and hypnotic Western medicines, such as estazolam Tablets and diazepam. Although the effect is positive, it also has adverse

reactions such as cognitive decline, fatigue, lethargy, and listlessness, and long-time use will lead to dependence to some degree. Chinese medicine has achieved certain effects in the treatment of insomnia. However, due to the complexity of the cause of CRI, there are relatively few explorations of Chinese patent medicines for the treatment of CRI. At present, Chinese patent medicines of Jieyu Anshen Granules (解郁安神颗粒), Zaoren Anshen Capsules (枣仁安神胶囊), etc., for the treatment of insomnia are not very powerful for relaxing the mind. For more complex CRI, the clinical effect of these medicines is not satisfactory and it lacks high-quality methods and support by medical evidence.¹

Professor Zheng Yuling is the instructor of the sixth batch of national Chinese medicine experts in the succession of academic experience, Qihuang scholar, and an expert with special allowance of the State Council. Professor Zheng has long been engaged in medical treatment, teaching, and scientific research of malignant tumors with integrative

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medicine. With rich clinical experience and remarkable curative effects, she has gradually developed unique academic thoughts in clinical practice: taking traditional Chinese medicine thinking as the root, protecting healthy qi as the basis, and simultaneous purging and tonifying it as the principle with comprehensive syndrome differentiation and treatment as the purpose.

CRI belongs to the category of “insomnia” in Chinese medicine. In *Discussion on Great Perplexity of Spiritual Pivot* (*Ling Shu Da: Huo Lun*): “Defensive qi cannot flow into the yin phase...remains in the yang phase, then yang qi is full. When yang qi is full, the yin in the Yangqiao channel becomes excessive. Since the defensive qi cannot flow into the yin phase, yin qi is deficient. That is why the patient cannot sleep.” According to *Questions and Answers of Spiritual Pivot* (*Ling Shu: Kou Wen*), it records “When yang qi is exhausted, yin qi will be predominant and therefore people close their eyes to sleep. When yin qi is exhausted, yang qi will be predominant and therefore people keep awake.” The disease location of CRI is mainly in the heart and closely related to the kidney, liver, spleen, stomach, gallbladder, etc.^{7,8} The pathogenesis includes imbalance between the heart and the kidney, disharmony between the spleen and stomach, liver-qi stagnation, and deficiency of both the heart and spleen, etc.⁹ Professor Zheng Yuling believes that the pathogenesis of CRI is nothing more than the imbalance of yin and yang and visceral disorder, especially the heart, liver, and kidney. The core pathogenesis is the overflight of the mind and the imbalance between the liver and the kidney. If the heart fails to dominate the spirit, the mind will be uneasy and lead to insomnia. If the liver fails to store the soul, the soul will be restless. If the kidney fails to store will, the will may not hide but become uneasy. Professor Zheng Yuling holds that CRI is different from general insomnia. On the one hand, cancer patients suffer from the flow of cancerous toxin and disorder of visceral qi internally; on the other hand, cancer-related radiotherapy and chemotherapy belong to “exogenous pathogenic factors to a certain extent,” which can further aggravate visceral disorders. Therefore, Professor Zheng Yuling believes that the therapeutic principle of Chinese medicine is to tranquilize the mind on the basis of regulating viscera, suppressing yang and astringing yin. Based on this theoretical basis, she created the representative prescription of Zhenjing Anshen Granules (镇静安神颗粒) which has been applied clinically for many years and achieved good effects. Now, her experience in the clinical application of Zhenjing Anshen Granules (镇静安神颗粒) in the treatment of CRI is expounded as follows.

Interpretation of the Meaning of Zhenjing Anshen Granules ()

The composition of the Zhenjing Anshen Granules (镇静安神颗粒) includes Sheng Muli (unprocessed Concha Ostreae), Zhenzhumu (Concha Margaritiferae Usta), Chao Suanzaoren (fried Semen Ziziphi Spinosae), Zhi Yuanzhi (processed Radix Polygalae), Shouwuteng (Caulis Polygoni Multiflori), and Dengxincao (Medulla Junci). Sheng Muli

(unprocessed Concha Ostreae), the king medicine in the prescription, is salty in flavor and slightly cold in property, pertaining to the kidney, liver, and gallbladder meridians, with the effects of tranquilizing the mind, suppressing yang and astringing yin. Zhenzhumu (Concha Margaritiferae Usta) is salty in flavor and cold in nature, pertaining to the heart and liver meridians, with effects of calming the mind, soothing the liver and suppressing yang. Combined with Sheng Muli (unprocessed Concha Ostreae), it has stronger effects of tranquilizing the mind, suppressing yang and astringing yin. Chao Suanzaoren (fried Semen Ziziphi Spinosae) is sour and sweet in flavor and mild in property, pertaining to the liver, heart, and gallbladder meridians, and has the effects of nourishing the heart, tonifying the liver, calming the heart, and tranquilizing the mind. They are minister medicines. The combination of the king medicine and the minister medicines ensures the calm of heart and mind, coordinating yin and yang and enriching liver blood. Zhi Yuanzhi (processed Radix Polygalae) is pungent and bitter in flavor and warm in property, pertaining to the lung, heart, and kidney meridians, and has the effects of tranquilizing the mind, benefiting the intelligence, and communicating with the heart and kidney. In combination with Zhenzhumu (Concha Margaritiferae Usta), they can regulate both the heart and the kidney and achieve the balance between water and fire. Besides, this medicine enters the kidney meridian and has the effects of resolving phlegm and promoting resuscitation; Shouwuteng (Caulis Polygoni Multiflori), as the assistant medicine, is sweet in flavor and mild in property, pertaining to the liver and heart meridians, and has the effects of nourishing blood and calming the mind. In combination with Chao Suanzaoren (fried Semen Ziziphi Spinosae), it can nourish blood and tonify the liver and restrict the coldness of the king and minister medicines. Dengxincao (Medulla Junci), the guiding medicine, is slightly astringent in flavor, can enter the heart meridian, and has the effects of clearing heart fire, calming the mind, promoting urination, and guiding the fire to move downward. It can “induce pathogens to go out of the body”.¹⁰ The above-mentioned six medicines are complementary to each other with the combination of deficiency and excess and usage of cold and heat medicines for co-regulation of the heart, liver, and kidney, tranquilizing the mind with heavy medicines and nourishing blood so as to achieve the calming effects of the mind, suppressing yang and astringing yin.

Detailed Explanation of Zhenjing Anshen Granules (镇静安神颗粒)

This paper discusses and analyzes the theoretical basis, efficacy, and characteristics of the prescription from the perspectives of Chinese medical classics, ancient books of past dynasties, and modern pharmacology.

According to *The Complete Works of [Zhang] Jingyue* (*Jing Yue Quan Shu*), “Peaceful mind ensures sleep while uneasy mind leads to sleeplessness.” According to *Yellow Emperor's Inner Classic* (*Huang Di Nei Jing*): “If the monarch is wise, the subordinates will be peaceful. If the monarch is not wise, all

the twelve officials will be in danger and cannot function well." The heart is the master of the five Zang organs and six Fu organs and it is the monarch organ. It stores spirit, which dominates all spiritual activities and consciousness of the human body.¹¹ Failure of the storage of the spirit will cause uneasiness of the mind as well as soul and poor sleep quality.⁷ Therefore, storing and tranquilizing the mind should be the major therapy. The liver stores blood and the blood houses the soul.¹² The mind and soul will be separated due to liver blood deficiency and malnourishment or chronic illness and anxiety; depressed anger impairs the liver, resulting in the depression of liver qi, restlessness, and insomnia, so regulating the liver and nourishing blood is a common treatment. The kidney is the water organ, while the heart is the fire organ. The integration of the two achieves the balance between yin and yang, water and fire. If the mind is overflying or the kidney water is insufficient, water and fire fail to coordinate; it will lead to disharmony between yin and yang. Therefore, regulating the kidney is also a common treatment method which is helpful to suppress the mind. Zou et al¹³ collected sedative and tranquilizing prescriptions containing marine Chinese medicines, created a database through the Chinese medicine inheritance auxiliary platform, and conducted data mining on their medicine frequency, prescription rules, and new prescription analysis. The results showed that the core medicine pair of sedative prescriptions containing marine Chinese medicines includes Muli (Concha Ostreae), Zhenzhumu (Concha Margaritiferae Usta), and Suanzaoren (Semen Ziziphi Spinosae). The high-frequency medicines are in the following order: Suanzaoren (Semen Ziziphi Spinosae), Zhenzhumu (Concha Margaritiferae Usta), Muli (Concha Ostreae), and Yuanzhi (Radix Polygalae), which are highly compatible with the composition of the prescription. Thus, the scientific nature of the composition of the sedative and tranquilizing prescription is also verified.

Muli (Concha Ostreae)

In modern pharmacology, it has been proved that Muli (Concha Ostreae) has anti-tumor, anti-oxidation, anti-fatigue, and immune-enhancement pharmacological effects.¹⁴ Studies have confirmed that it contains a small amount of amino acids that have anticonvulsant and sedative effects.¹⁵ Since it has anti-tumor, sedative, softening, and dispelling effects and strong sedative power as well as stable, safe, and non-toxic medicine properties, it is the king medicine in this prescription.

Zhenzhumu (Concha Margaritiferae Usta)

According to *Compendium of Materia Medica* (Ben Cao Gang Mu), "it can calm the mind and soul." Disturbance of the soul will lead to difficulty in sleeping. Modern pharmacological studies have shown that Zhenzhumu (Concha Margaritiferae Usta) is rich in a variety of trace elements, which can inhibit nerve and skeletal muscle excitement, thereby exerting sedative and hypnotic effects. Liu et al¹⁶ and other studies have shown that its hypnotic effect is related to the promotion of central 5-HT secretion. In addition, Zhenzhumu

(Concha Margaritiferae Usta) also has an antidepressant effect,¹⁷ and the proteins in it inhibit tyrosine hydroxylase and interrupt the dopamine synthesis pathway, thereby down-regulating the level of norepinephrine.¹⁸ CRI is often associated with mental illnesses such as depression. Zhenzhumu (Concha Margaritiferae Usta) has multiple effects. By regulating these accompanying diseases, it has multiple effects on insomnia, so it is a minister medicine.

Suanzaoren (Semen Ziziphi Spinosae)

In *Explanation of Medicinals from Changsha* (Chang Sha Yao Jie), it says "It can calm the heart and remove restlessness, astringe mind and soul, ensure sleep sound." In *Miscellaneous Records of Famous Physicians* (Ming Yi Bie Lu), it was recorded that "it mainly treats insomnia due to restlessness. It can make people strong and healthy." The classics of the past dynasties all show that Suanzaoren (Semen Ziziphi Spinosae) has good effects of nourishing the heart and calming the mind. Modern pharmacological studies have also shown that Suanzaoren (Semen Ziziphi Spinosae) has various effects of tranquilization, myocardial protection, and anti-anxiety, anti-tumor, and anti-depression.¹⁹ Its main effective components are saponins and flavonoids; the main mechanism is to inhibit central excitement, regulate neurotransmitters, and cytokines.²⁰ Because of its strong power of nourishing the heart and calming the mind, it can increase the effect of the king medicine to soothe the mind as well as tonify liver deficiency and nourish liver blood, so it is the minister medicine.

Yuanzhi (Radix Polygalae)

In *Shen Nong's Materia Medica* (Shen Nong Ben Cao Jing), it records that "it can unblock the nine orifices...improves memory, will and physical strength." In *Treatise on Medicinal Properties* (Yao Xing Lun), it records that "it can relieve forgetfulness and calms the soul...remove dreaminess." In ancient classics, Yuanzhi (Radix Polygalae) has the functions of calming the mind and fright, resuscitating, and improving intelligence. Modern pharmacology proves that Yuanzhi (Radix Polygalae) has the brain-protective, sedative and hypnotic, anti-tumor, anti-anxiety, and anti-depression effects.²¹ Studies in recent years have also confirmed its anti-tumor activity. It is especially suitable for the treatment of "chemobrain," which can inhibit the release of neuro-inflammatory factors and improve nerve damage, memory, and cognition.²² Research by Li et al²³ showed that the antidepressant effects of Yuanzhi (Radix Polygalae) are related to the interference with the reuptake of monoamine neurotransmitters. Yuanzhi (Radix Polygalae) has anti-anxiety, anti-depression, anti-tumor, sedative, and hypnotic effects and is safe and non-toxic. Therefore, it is used as assistant medicine for the king and minister medicines.

Shouwuteng (Caulis Polygoni Multiflori)

Shouwuteng (Caulis Polygoni Multiflori) is also known as Yejiaoteng (Caulis Polygoni Multiflori). In *Orthodox Interpretation of the Materia Medica* (Ben Cao Zheng Yi), it records that "Yejiaoteng (Caulis Polygoni Multiflori) can be used to

improve poor sleep at night, so it can guide yang into yin. It reconciles yin and yang, which is beneficial and harmless.” Yejiaoteng (Caulis Polygoni Multiflori), as the name suggests, can induce yin and yang to intersect. Concordance between yin and yang ensures sound sleep. Modern pharmacology shows that it has various effects such as regulating the nervous system, improving sleep, anti-oxidation, immune regulation, etc., and confirms that its extracts may increase the contents of Ca^{2+} - Mg^{2+} -ATPase, Na^{+} - K^{+} -ATPase and improve the ultrastructure of mitochondria to treat insomnia.²⁴ Since it can communicate the upper and the lower parts and induce the concordance between yin and yang, it is the assistant medicine.

Dengxincao (Medulla Junci)

In *Explanation of the Material Medical Classic (Ben Cao Jing Jie)*, it records that “it is cold in nature which can clear heat, sweet in flavor which can transform qi, relieve the stagnation and purging fire.” In *Compendium of Materia Medica (Ben Cao Gang Mu)*, it says, “it can reduce heart fire and promote qi circulation.” It is light and clear in nature, going straight downward, guiding the heat of the heart and lung from top to the bottom. It has the effect of inducing heat downward, tranquilizing the mind, and eliminating restlessness for insomnia due to hyperactive heart fire. Modern pharmacology shows that Dengxincao (Medulla Junci) has sedative, antioxidant, and antibacterial pharmacological effects.²⁵ Wang et al²⁶ confirmed the sedative effect of its ethyl acetate extract through research. It can pave a way for the pathogens to go out, so it is the assistant and guiding medicine in the prescription.

Clinical Application Experience of Zhenjing Anshen Granules (镇静安神颗粒)

CRI is a concomitant disease with cancer. Its pathogenesis is the absence of mind and liver and kidney disorder. However, cancer is quite complicated. Due to factors such as different treatment stages and differences in constitutions of the patients, the selections of prescriptions and medicines should be differentiated. Since the composition of this prescription is simple and with special effects, it is often applied with other prescriptions to cure both the symptoms and the root causes.

Application Experience in Different Treatment Stages of Tumor

Tumor belongs to the category of “accumulation” in Chinese medicine. In *Required Readings from the Medical Ancestors (Yi Zong Bi Du)*, the accumulations were divided into three stages, the primary stage, the middle stage, and the final stage, and it formulated the therapeutic methods for each stage. As it says, “in the primary stage, healthy qi is not severely impaired and the pathogenic qi is not deep, then purgation can be applied; in the middle stage, the invasion is relatively longer and the pathogenic qi relatively deep and healthy qi rather deficient, then tonification and purgation should be applied simultaneously; in the final stage, long-

term pathogenic invasion leads to bullying of pathogenic qi to weak healthy qi, tonification should be applied.” Therefore, overall syndrome differentiation should be performed in addition to the treatment of insomnia for CRI patients. Based on the state of healthy qi in the patient and the depth of pathogenic factors, different therapeutic principles such as tonification, purgation or integrated tonification, and purgation should be applied.

Besides, with the intervention of modern medicine, the therapies for tumor is becoming increasingly diverse and different therapies produce different effects on the body. Therefore, flexible compatibility should be made according to different therapies in clinical practice.

Insomnia during Operation

After surgery, healthy qi declines, primordial qi is greatly impaired, and qi and blood become deficient. The treatment method should be reinforcing healthy qi on the basis of Zhenjing Anshen prescription (镇静安神方), Shiquan Dabu decoction (十全大补汤), Shuyu pill (薯蓣丸), and Dihuang Yinzi (地黄饮子) combination.

Insomnia during Chemotherapy

Sometimes it is accompanied by gastrointestinal reactions such as vomiting, nausea, poor appetite, etc., due to disharmony in the middle energizer, transport failure by the spleen, and upward flow of stomach qi.²⁷ It is recommended to apply the methods of strengthening the spleen, harmonizing the stomach, and changing the direction of the flow in a descending manner; Jianpi pill (健脾丸), Xuanfu Daizhe decoction (旋覆代赭汤), and Dingxiang Touge decoction (丁香透膈汤) can be combined for this. When accompanied by fatigue and low leukocyte, the disease is located in bone marrow, spleen and kidney, with the main syndromes of spleen deficiency, qi and blood deficiency and spleen and kidney deficiency.²⁸ At this time, the methods of strengthening the spleen and kidney combined with tonifying qi and blood should be applied with the combination of Shiquan Dabu decoction (十全大补汤), Liuwei Dihuang decoction (六味地黄汤), Bazhen decoction (八珍汤), and Shengyu decoction (圣愈汤).

Insomnia at the Stage of Radiotherapy

Radiotherapy belongs to the pathogen of “heat toxin” which consumes yin fluid and disturbs the mind. It should be treated by the combined methods of clearing heat, nourishing yin, and generating body fluid with the combination of Shashen Maidong decoction (沙参麦冬汤), Qingwei powder (清胃散), Zhuye Shigao decoction (竹叶石膏汤), Baihu decoction (白虎汤), and Shengmai drink (生脉饮).

Application Experience in Treating Cancer Patients with Different Constitutions

When the external pathogenic factor meets deficient healthy qi, the disease will occur. The occurrence of malignant tumor is closely related to the patient's constitution, and malignant tumor is a kind of wasting disease which depletes the body's healthy qi. The growth of tumor requires the nourishment of

yin blood, body fluid, and the promotion of yang qi, which will cause the deficiency of qi, blood, yin, and yang over time. According to the different clinical symptoms, constitutions and syndromes of the patients should be differentiated for further medicine administration. For example, for the treatment of qi-deficient patients with symptoms of general fatigue, overstraining, aggravated by movement, pale tongue with white tongue coating, thin pulse, etc., Sijunzi decoction (四君子汤), Buzhong Yiqi decoction (补中益气汤), and Yupingfeng powder (玉屏风散) can be combined. For patients with blood deficiency with symptoms of lusterless or sallow or pale complexion, lassitude, palpitation, lusterless nails, pale tongue, and thin and weak pulse, Siwu decoction (四物汤) and Danggui Buxue decoction (当归补血汤) can be combined. For patients of yin deficiency with symptoms such as afternoon tidal fever, dry mouth, irritability, low fever, dizziness, tinnitus, night sweating, feverish sensation of the five centers, red tongue with scanty coating, and thin and rapid pulse, Qinghao Biejia decoction (青蒿鳖甲汤), Liuwei Dihuang pill (六味地黄丸), and Danggui Liuhuang decoction (当归六黄汤) can be combined. For patients of yang deficiency with symptoms of pale complexion, tiredness with preference for lying, aversion to cold and cold limbs, hands and feet, poor appetite, loose stools, clear and profuse urination, white tongue, deep and thin pulse, etc., Shenqi pill (肾气丸), Shuyu pill (薯蓣丸), Fuzi Lizhong pill (附子理中丸), and Yougui pill (右归丸) can be combined. For patients of liver depression and spleen deficiency with symptoms of irritability, anxiety, nervousness, emotional depression, often accompanied by irritable temper or other bad habits, poor appetite, taut pulse, Danggui Shaoyao powder (当归芍药散), Yueju pill (越鞠丸), and Xiaoyao powder (逍遥散) can be combined.

Experience in Treating Cancer Patients with Accompanying Symptoms

CRI can be seen in a variety of cancers. Insomnia is the main symptom, but the accompanying symptoms are often different depending on the type of cancer. For instance, pleural effusion is often seen in lung cancer; poor appetite, abdominal distension, and bloody stool are common in gastric cancer; dry stools are common in pancreatic cancer; emotional depression, vexation, and irritability are common in breast cancer; and dizziness and headaches are often seen in brain cancer. In clinical practice, insomnia should be treated as the main symptom, along with the accompanying symptoms of cancer. For those with pleural effusion, add Zexie (Rhizoma Alismatis), Guizhi (Ramulus Cinnamomi), Zhuling (Polyporus), Tinglizi (Semen Lepidii), Fangji (Radix Stephaniae Tetrandrae), and Jiaomu (Semen Zanthoxyli) to warm yang and induce diuresis and clean up water retention; for those with poor appetite, add Sharen (Fructus Amomi), Baidoukou (Fructus Amomi Kravanh), Chao Jineijin (fried Endothelium Corneum Gigeriae Galli), Laifuzi (Semen Raphani), and Chao Shenqu (fried Massa Medicata Fermentata) to strengthen the spleen, promote digestion, and increase appetite; for those with dry stools, add Shudihuang (Radix Rehmanniae Praeparata), Xuanshen (Radix Scrophu-

lariae), Roucongrong (Herba Cistanches), Danggui (Radix Angelicae Sinensis), Baizhu (Rhizoma Atractylodis Macrocephalae), Baishao (Radix Paeoniae Alba), and Laifuzi (Semen Raphani), and in severe cases, add Dahuang (Radix et Rhizoma Rhei), Mangxiao (Natrii Sulfas), etc.; for those with loose stools, add Wumei (Fructus Mume), Dahuang (Radix et Rhizoma Rhei), Roudoukou (Semen Myristicae), Chao Shanzha (fried Fructus Crataegi), etc.; for those with dry mouth, bitter mouth, add Zhizi (Fructus Gardeniae), Chaihu (Radix Bupleuri), Huanglian (Rhizoma Coptidis), Huangqin (Radix Scutellariae), Zhimu (Rhizoma Anemarrhenae), Shengdihuang (Radix Rehmanniae), etc.; for those who are upset, irritable, and emotionally depressed, add Baishao (Radix Paeoniae Alba), Xiangfu (Rhizoma Cyperi), Bohe (Herba Menthae), Mudanpi (Cortex Moutan), etc.; for those with dizziness and severe phlegm and dampness, add Manjingzi (Fructus Viticis), Tianma (Rhizoma Gastrodiae), Tiannanxing (Rhizoma Arisaematis), and Shichangpu (Rhizoma Acori Tatarinowii) to clear the mind and open the heart orifice; for those with abdominal distension and fullness, add Houpo (Cortex Magnoliae Officinalis), Guangmuxiang (Radix Aucklandiae), Wuyao (Radix Linderae), Dafupi (Pericarpium Arecae), and Zhishi (Fructus Aurantii Immaturus) to promote qi flow and relieve distension; for those with excessive pathogens, add Danshen (Radix et Rhizoma Salviae Miltiorrhizae), Xiakucao (Spica Prunellae), Zhebeimu (Bulbus Fritillariae Thunbergii), Jineijin (Endothelium Corneum Gigeriae Galli), Yujin (Radix Curcumae), Biejia (Carapax Trionycis), and Lulutong (Fructus Liquidambaris) to soften the hardness and resolve the mass; and for those with strong constitution, add Sanleng (Rhizoma Sparganii), Shuizhi (Hirudo), Quanxie (Scorpio), Mangchong (Tabanus), Ezhu (Rhizoma Curcumae), Wugong (Scolopendra), Jiangcan (Bombyx Batryticatus), etc.

Typical Cases

Hong, 62 years old, female, from Zhengzhou City of Henan Province, went to see the doctor on November 1, 2020. The patient was diagnosed with clear cell carcinoma of the right ovary in February 2020 with the symptom of postmenopausal vaginal bleeding, and she then underwent radical surgery and adjuvant chemotherapy. Chief complaints included lower limb swelling and insomnia after post-operative chemotherapy of ovarian cancer. Current symptoms were mild swelling of both lower limbs, which worsened after walking; poor sleep quality, waking up easily at night and difficulty in falling asleep again; ordinary spirit, relatively normal appetite, and normal urination and defecation. The color of the tongue was pale and dark with thin, white, and greasy coating. Western medicine diagnosis reported (1) lower limb edema after post-operative chemotherapy of ovarian cancer and (2) insomnia. TCM diagnosis reported (1) edema, syndrome differentiation: deficiency of qi and blood, internal retention of water, and dampness; (2) mass; and (3) insomnia. The therapeutic principle included benefiting qi and harmonizing nutrient phase, warming yang and promoting diuresis. Following prescription was selected: Shuyu pill

(薯蓣丸) and modified Wuling powder (五苓散). The components of medicines were 30 g of Shanyao (*Rhizoma Dioscoreae*), 30 g of Shudihuang (*Radix Rehmanniae Praeparata*), 15 g of Baizhu (*Rhizoma Atractylodis Macrocephalae*), 12 g of Baishao (*Radix Paeoniae Alba*), 12 g of Baiji (*Radix Ampelopsis*), 30 g of Fuling (*Poria*), 6 g of Fangfeng (*Radix Saposhnikoviae*), 12 g of Chuanxiong (*Rhizoma Chuanxiong*), 30 g of Maidong (*Radix Ophiopogonis*), 12 g of Zhi Xingren (prepared Semen Armeniacae Amarum), 30 g of Danggui (*Radix Angelicae Sinensis*), 30 g of Dangshen (*Radix Codonopsis*), 12 g of Guizhi (*Ramulus Cinnamomi*), 15 g of Chao Shenqu (fried Massa Medicata Fermentata), 12 g of Zexie (*Rhizoma Alismatis*), 12 g of Jiegeng (*Radix Platycodonis*), 30 g of Zhuling (*Polyporus*), and 9 g of Zhigancao (*Radix et Rhizoma Glycyrrhizae Praeparata cum Melle*).

On the second visit (February 9, 2021), the effects of the prescription were found to be good: the strength increased and fatigue and edema were alleviated compared with the previous visit. Current symptoms were normal appetite, with weight gain by 10 kg in the past 3 months; the sleep quality was still poor, with the symptoms of difficulty in falling asleep, sleeping less than 5 hours at night, light sleep, dreaminess and awaking easily; unsmooth defecation, with slight leakage of urine; the color of the tongue was light red with thin and white coating, and the pulse was taut and slippery. Western medicine diagnosis reported insomnia after post-operative chemotherapy of ovarian cancer. TCM diagnosis reported insomnia. Syndrome differentiation indicated floating mind and liver and kidney disorder. The following prescription was selected: modified Zhenjing Anshen Granules (镇静安神颗粒). The components of medicines were 30 g of Muli (*Concha Ostreae*), 30 g of Longgu (*Os Draconis*), 30 g of Shenglongchi (*Dens Draconis*), 30 g of Suanzaoren (*Semen Ziziphi Spinosae*), 30 g of Shouwuteng (*Caulis Polygoni Multiflori*), 5 g of Zhenzhu (*Concha Margaritiferae Usta*), 15 g of Zishiying (*Fluoritum*), 5 g of Hupo (*Succinum*), and 2.5 g of Dengxincao (*Medulla Junci*).

On the third visit (February 28, 2021), after taking the upper prescription, sleep quality got improved slightly and defecation was smoother than before, with swollen hands and feet accompanied by hot sensation and sweating, and irascibility. The sleep quality was still poor and it was still difficult to fall asleep, with light sleep, waking up easily, and dreaminess, but it improved after taking the medicines. Appetite, urination, and defecation relatively normalized, and the tongue and pulse conditions were the same as reported earlier. Syndrome differentiation indicated restlessness due to liver depression and spleen deficiency. The therapeutic principle included soothing the liver and invigorating the spleen and tranquilizing the mind. The following prescription was selected: Danggui Shaoyao powder (当归芍药散) and modified Zhenjing Anshen Granules (镇静安神颗粒). The components of medicines were 30 g of Danggui (*Radix Angelicae Sinensis*), 15 g of Chuanxiong (*Rhizoma Chuanxiong*), 12 g of Baizhu (*Rhizoma Atractylodis Macrocephalae*), 30 g of Fuling (*Poria*), 12 g of Zexie (*Rhizoma Alismatis*), 12 g of Baishao (*Radix Paeoniae Alba*),

30 g of Muli (*Concha Ostreae*), 5 g of Zhenzhu (*Concha Margaritiferae Usta*), 30 g of Longgu (*Os Draconis*), 30 g of Shouwuteng (*Caulis Polygoni Multiflori*), 15 g of Zishiying (*Fluoritum*), 30 g of Shenglongchi (*Dens Draconis*), 5 g of Hupo (*Succinum*), 30 g of Suanzaoren (*Semen Ziziphi Spinosae*), 2.5 g of Dengxincao (*Medulla Junci*), 9 g of Chaihu (*Radix Bupleuri*), 30 g of Xianhecao (*Herba Agrimoniae*), 12 g of Douchi (*Semen Sojae Praeparatum*), 30 g of Fuxiao-mai (*Fructus Triticis Levis*), 6 g of Zhizi (*Fructus Gardeniae*), 15 g of Ezhu (*Rhizoma Curcumae*), and 30 g of Xiakucao (*Spica Prunellae*).

On the fourth visit (March 21, 2021), the effects of the upper prescription were found to be good: sleep quality improved considerably; defecation became smoother than before; the swelling of the hands and feet, hot sensation and sweating, and excessive breaking wind were all alleviated compared with the previous visit. Current symptoms were heavy right leg, edema, irritable temper, nausea, relatively normal appetite and sleep of 6 to 7 hours duration, and normal sleeping depth, sleep was more stable than before and symptoms of light sleep and easy waking up disappeared, with relatively normal urination and defecation and mild urine leakage. The tongue was light red with thin and white coating, and the pulse was slippery and moist. This was treated by adding 30 g of Yiyiren (*Semen Coicis*) to the former prescription.

On the fifth visit (April 18, 2021), the effects were good; sleep continued to improve and became basically normal; the swelling and discomfort of the hands and feet, the hot sensation and sweating, and excessive breaking wind improved compared with the previous visit. Current symptoms were heavy and swelling right leg, relatively normal appetite, basically normal sleep at night, and normal urination and defecation; the tongue and pulse conditions were the same as before. TCM diagnosis indicated edema. Syndrome differentiation indicated disharmony between liver and spleen, qi stagnation, and water retention. The therapeutic principles include harmonizing the liver and spleen, nourishing blood, and inducing diuresis. The following prescription was selected modified Danggui Shaoyao powder (当归芍药散). The components of medicines were 15 g of Baishao (*Radix Paeoniae Alba*), 15 g of Chuanxiong (*Rhizoma Chuanxiong*), 30 g of Danggui (*Radix Angelicae Sinensis*), 15 g of Fuling (*Poria*), 12 g of Zexie (*Rhizoma Alismatis*), 30 g of Xiakucao (*Spica Prunellae*), 12 g of Baizhu (*Rhizoma Atractylodis Macrocephalae*), 30 g of Yiyiren (*Semen Coicis*), and 15 g of Ezhu (*Rhizoma Curcumae*).

Conclusion

The symptom of insomnia in cancer patients not only negatively impacts their immune function, heart function, and blood sugar regulation but also aggravates the condition of the cancer patients, reduces their confidence in fighting against diseases, decreases the quality of life, and increases early mortality.²⁹ The treatment of insomnia is symptomatic

and can also improve the quality of life of cancer patients and enhance the tolerance of anti-tumor treatments through sleep adjustment.

Professor Zheng Yuling created Zhenjing Anshen Granules (镇静安神颗粒) by summing up her own clinical experience, combining it with modern pharmacological research, repeatedly exploring in the clinical practice, and adopting the method of suppressing yang and astringing yin, which can significantly improve CRI. This prescription has been used since September 10, 2017. So far, approximately 200 patients have taken this prescription. With regular follow-ups, it has shown good therapeutic effects on insomnia caused by anxiety, fear, and depression that occur during the course of cancer or cancer treatment. For moderate and severe insomnia caused by other diseases, it also has obvious curative effect, with an effectivity rate of 77%. At present, this prescription has been approved for national invention patent and the hospital preparations are also in process. In the future, Professor Zheng Yuling's team will use animal experiments, pharmacological and toxicological methods, clinical observations, and more other objective methods to study this prescription at multiple levels and aspects, and carry out in-depth explorations of its action mechanism and molecular pathways to benefit more patients.

Credit Authorship Contribution Statement

Ranpei Zhu: Conceptualization, visualization, and writing - original draft. **Xu Sun:** Methodology, writing review & editing. **Yuling Zheng:** Conceptualization, supervision, writing review & editing.

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Conflict of Interest

The authors declare no conflict of interest.

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