Treatment of post-coronary insomnia from the perspective of deficiency

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Abstract. The widespread epidemic of Coronavirus disease 2019 (COVID-19) worldwide has had a tremendous impact on both human life and health. The mechanism and treatment of the post-COVID symptoms after acute infection in patients with the COVID-19 has become an important research content at present. Insomnia is one of the most common sequelae after COVID-19. Modern medicine believes that the pathogenesis of insomnia after COVID-19 is related to psychological factors, persistent inflammatory reaction and immune system disorder, etc. According to the theory of traditional Chinese medicine (TCM), after the patient was infected with COVID-19, he had a deficiency after a serious illness, which led to the insomnia that the human body's Rong Wei was out of harmony and the yin and yang were out of harmony, and differentiate between different types of evidence found that the patient mostly manifested Deficiency of both qi and yin syndrome, Syndrome of non-interaction between the heart and kidney, Heart-spleen deficiency syndrome, Pattern of qi deficiency of both heart and gallbladder, etc., so the treatment should be based on the thesis of "deficiency" and should make full use of the theoretical features of Chinese medicine, such as "Theory of developing appropriate treatment according to three types of disease causes" and "Strengthening healthy qi to eliminate pathogenic factors", to adjust the physique of the patient after a serious illness, and at the same time take care of the spleen and stomach, so as to prevent the symptoms from recurring and to help the patient to restore his health as soon as possible.

Keywords: Coronavirus disease 2019; Long-COVID; Insomnia after COVID-19; Treat from the debilitated; treatment based on pattern differentiation.

1. Introduction

The novel coronavirus pneumonia (COVID-19) not only poses a serious threat to the life and health of individuals during its acute onset but also brings huge medical, social and economic burdens to the world. At the same time, infected people will also face severe sequelae and long-term health effects. According to the World Health Organization (WHO), about 10-20% of COVID-19 patients face sequelae. Since January 8, 2023, China has implemented "Class B and B tube" infectious disease prevention and control measures against novel coronavirus infection. The diagnosis and treatment of neocoronavirus sequelae have become the focus of clinical outbreak prevention and treatment.

Insomnia is one of the important sequelae after infection with COVID-19. Insomnia is a class of diseases characterized by difficulty in falling asleep or shallow sleep with easy awakening, or even inability to sleep throughout the night and affecting daytime function. A survey of 3,762 neocoronavirus-infected patients showed that about 78.58% of patients had sleep disorders, of which insomnia accounted for 60%, which could occur from 2 weeks to 4 months after discharge from the hospital and after a negative neocoronavirus test result. Currently, the pathogenesis of sleep disorders after COVID-19 is unclear and there is a lack of specific drugs. For insomnia, modern medicine mostly adopts sedative-hypnotic drugs as the preferred treatment program, but its side effects are obvious, long-term use will produce dependence and drug resistance, and some patients have psychological resistant to this kind of drugs. Traditional Chinese medicine (TCM) theory has a long history and rich therapeutic experience in treating epidemic diseases and insomnia, which can realize personalized treatment of one person, one policy and one party through clear diagnosis of the evidence and medication, effectively preventing recurrence and reducing drug dependence, so it is of great clinical significance and value to explore the treatment of insomnia after the new coronavirus.
based on the theory of TCM. This paper combines the etiology and pathogenesis of epidemic disease and insomnia in Chinese medicine theory, and comprehensively discusses the treatment of post-coronary insomnia from the theory of "deficiency", which provides a new way of thinking for the clinical prevention and treatment of insomnia after COVID-19.

2. Risk factors in the development of post-COVID-19 insomnia

Insomnia after COVID-19 is mainly triggered by psychosocial factors and physiological and pathological factors[5][6]. The COVID-19 pandemic has changed people's financial situation, education mode and social employment situation, and a series of isolation and containment measures taken by governments to control the development of the epidemic have disrupted people's life rules[7]. The publicity of disease information and its strong contagion cause a wide range of health anxiety in the population, while COVID-19 infection can produce adverse psychological states such as traumatic memory, stigma and social isolation, and the sympathetic nervous system thereby triggering sleep problems[8]. Meanwhile, after COVID-19 infection, persistent viral infection can suppress the immune system, invade organs such as the brain stem and the hypothalamus, disrupting the sleep-wake cycle. Both the intervention of the autoimmune system and mitochondrial dysfunction can activate the body's inflammatory response. Sustained inflammatory response releases a large amount of pro-inflammatory factors that damage the nerves in the sleep-regulating regions of the brain, increasing non-REM sleep and decreasing REM sleep and leading to insomnia[9].

3. TCM etiology and pathogenesis of post-COVID-19 insomnia

There is no clear conclusion on the etiology and pathogenesis of insomnia after COVID-19 in the theory of traditional Chinese medicine. Combined with the relevant TCM theories of epidemic disease and the etiology and pathogenesis of insomnia, the author believes that the occurrence and development of insomnia after COVID-19 is closely related to "deficiency". COVID-19 belongs to the category of "epidemic disease" and "plague" in traditional Chinese medicine[10]. In Ming and Qing dynasties, epidemics occurred frequently. The theory of plague was perfected day by day, and the plague of traditional Chinese medicine also attracted the attention of many medical practitioners. The so-called sequelae disease refers to the condition that the disease is repeated or accompanied by other diseases when the disease is cured or nearly healed, which is mostly caused by "residual evil that has not been exhausted, or by loss of conditioning, or by ignorance of taboos." Most of the epidemic is "wet turbid poison epidemic" and the pathogenic characteristics of the epidemic poison are easy to become latent pathogenic diseases. The common diseases are insomnia, cough, palpitations, diabetes after epidemic and so on. Among them, insomnia is one of the common plague diseases[11]. After COVID-19, patients mainly suffer from lung and spleen Qi deficiency syndrome and Qi Yin deficiency syndrome, and "After serious illness, the zang-fu organs are still deficient, Rongwei is not combined, so they are born in Cold and Hot Yin qi deficiency, and Wei Qi is in Yang, not in Yin, so they cannot sleep"[12]. It also discusses the relationship between the onset of insomnia and "deficiency". The core of pathogenesis of insomnia after epidemic disease is positive deficiency and evil stay duration. Positive deficiency is mainly caused by deficiency of lung, spleen and kidney three viscera and deficiency of Qi and Yin. At the same time, evil qi remains in the body, insufficient adjustment, positive qi is more weak, and residual Evil Qi is latent[13], resulting in Rongwei discord, deficiency of Yin essence qi and blood, and Yang not entering Yin, resulting in prolonged insomnia[14]. After infection with COVID-19, the continuous inflammation and immune disorders make the patients in a state of long-term deficiency. The patient has Yin deficiency, which leads to fire and excessive heat, burning body fluid resulting in Qi and Yin deficiency, and involves the heart and spleen, resulting in heart and spleen deficiency and deficiency of heart and qi. Patients are susceptible to shock, heart and gallbladder and qi deficiency, which affects the spleen and stomach, leading to a loss of appetite. Therefore, Yin deficiency, fire
flourishing, Qi and Yin deficiency, heart and spleen deficiency, heart deficiency cowardice, and even spleen and stomach disharmony are common deficiency syndromes. As a result, the occurrence and development of insomnia after COVID-19 is closely related to "deficiency". This article mainly treats the insomnia after COVID-19 from "deficiency".

4. TCM diagnosis and treatment of post-COVID-19 insomnia

4.1. Nourishing Yin to reduce pathogenic fire, benefiting Qi and tranquilizing the mind

Qi and Yin deficiency is the most common deficiency syndrome in patients with COVID-19, and it is also the pathological basis of insomnia. Due to the patient's long illness, qi deficiency leads to Yin blood deficiency can not transform Yang qi, Yang does not enter Yin. At the same time, the deficiency of ying qi, the poor operation of ying Wei's qi and blood, blood deficiency can not nourished the heart, heart deficiency makes people lose in mind and restless, so sleeplessness. In addition, long-term deficiency of yin and blood, deficiency and heat disturbing the mind, will lead to insomnia, and heart-kidney disconnection. Finally, it can develop into Yin deficiency and fire hyperactivity insomnia. Just like the following cloud in the Literature of traditional Chinese medicine, "Yin deficiency with fire will disturb you, so you can't lie down because you are upset."

For insomnia caused by this type of syndrome, nourishing Yin and lowering fire, improving qi and calming the mind are the key points of treatment, and Roasted Licorice Soup plus modified decoction can be selected for treatment.[15] Roasted Licorice Soup is originally designed for heart disease. It has the functions of tonifying qi and blood, nourishing Yin and qi, promoting Yang and reactivating meridians, involving the heart, liver, spleen, lung and kidney. In this prescription, roasted licorice is warm and beneficial to qi, nourishing blood and heart, and dredging meridians; Raw Rehmannia glutinosa can nourish yin and blood, nourish the heart and fill the pulse. The combination of the two drugs can benefit qi and promote blood circulation. Ginseng and jujube can supplement the heart and spleen, and jointly contribute to the source of qi and blood biochemistry with licorice. Radix ophiopogonis, ejiao, and fructus cannabis can help Rehmannia glutinosa nourish the yin blood of the heart and replenish the blood vessels. These five drugs are all ministers. Ramulus Cinnamomi and Rhizoma Zingiberis Recens can warm the heart-yang and clear the blood channels, as an adjuvant. Patients with severe qi deficiency and blood deficiency are added with Angelica sinensis and Ligusticum wallichii to reconcile qi and blood. Patients with severe insomnia symptoms are added with keel and oyster to calm the mind and soothe the nerves. The combination of these drugs can make yang qi benefit, yin blood be sufficient, meridians be unblocked, Yin and Yang Ying and Wei be harmonious, qi and blood be sufficient, peace of mind, and insomnia will heal itself. At the same time, drugs such as Radix Glycyrrhizae Preparata and Ginseng can moisten the lung and relieve cough, which can prevent the occurrence of myocarditis and pneumonia in the late stage of COVID-19.

4.2. Transporting the heart and kidneys, calming the heart and tranquilizing the mind

COVID-19's patients' retention of lung heat will damage the internal body fluid, which will lead to deficiency of kidney yin and hyperactivity of heart fire, and easily induce insomnia with deficiency of both heart and kidney. In the acute stage, the patient's symptoms are lung heat syndrome. After a long period of evil heat detention, Yin fluid in the body are consumed, which leads to yin and yang imbalance. After the illness, the qi and blood are deficient, the kidney yin can't go up to the heart to help the heart yin, and the kidney yang can't transpiration to support the heart yang. The yin and yang are not connected, and the heart and kidney don't cross. Kidney water can't help the heart, control the heart yang, the heart fire is excessive, the deficiency heat is endogenous, the heat disturbs the mind, and the heart is upset and sleepless. Such patients often appear Yin deficiency fire vigorous insomnia syndrome type, the main manifestations are: upset and insomnia, or waking up when sleeping, weak waist and knees, dizziness and tinnitus, palpitation, forgetfulness, or hot hands and feet, red
cheekbones, hot flashes, dry mouth and lack of body fluid. Red tongue, less fur, and thready and count pulse.

For patients with such clinical manifestations, we should choose the methods of communicating with the heart and kidney, nourishing yin and clearing heat, nourishing the heart and calming the mind. Tianwang Buxin Dan and Huanglian Ejiao Decoction are commonly used prescriptions to treat insomnia caused by heart-kidney disharmony. In Tianwang Buxin Dan prescription, Radix Rehmanniae and Radix Scrophulariae are both monarch drugs, which can nourish yin and blood and nourish liver and kidney. Radix Asparagi, Radix Ophiopogonis, Platycladus orientalis kernel, Spine Date Seed, and Radix Angelicae Sinensis are all ministerial drugs, which help monarch to nourish yin, moisten dryness, replenish blood, nourish heart and soothe the mind. With ginseng and Schisandra, it can nourish qi and yin, promote the production of body fluid and blood, nourish the heart and soothe the mind. Poria cocos and polygala tenuifolia can communicate with the heart and kidney, strengthen the spleen and calm the heart, improve intelligence and soothe the mind; Salvia miltiorrhiza and cinnabar can nourish yin and clear away heat, but also promote blood circulation, nourish the heart, soothe the mind, while Platycodon grandiflorum can induce drugs to clear the brain orifices. All the drugs are combined to play the roles of communicating the heart and kidney, regulating yin and yang, nourishing yin and nourishing blood, nourishing the heart and calming the mind. Modern pharmacological research shows that Tianwang Buxin Dan can shorten the sleep latency of rats, significantly prolong their sleep time, inhibit the over-expression of TLR4 signal pathway, inhibit the body's inflammatory response, adjust the body's immune function, and have a positive impact on the heart, blood vessels and hemorheology, thus improving the sleep problems after COVID-19[16].

Huanglian Ejiao Decoction has the effect of nourishing Yin and lowering fire, relieving restlessness and calming the mind. Coptis and Scutellaria baicalensis Georgi are bitter and cold, which can reduce heat by directly breaking the heart fire. Paeonia lactiflora, Colla Corii Asini and Egg Yolk nourish kidney Yin and kidney water, nourish heart and blood, nourish Yin and astringe Yang qi. The whole prescription is played together, which makes kidney water help the heart, water and fire are connected, yin and yang can be balanced, and insomnia can be relieved. At the same time, modern research shows that Huanglian Ejiao decoction can improve the content of neurotransmitter 5-HT in the brain[17], increase the concentration of GABA in the brain, and have the effect of anti-anxiety and improving sleep state[18]. In addition, Huanglian Ejiao Decoction can also promote the level of T1 cytokines in rats, reduce the expression of T2 cytokines, promote the balance of T1 and T2 ratio to shift to T1 direction, inhibit the inflammatory response of the body, and adjust the immune function of the body to improve insomnia[19]. To sum up, these drugs can improve the symptoms of insomnia after COVID-19 through anti-inflammatory and immune regulation mechanisms.

4.3. Tonifying the heart and spleen, nourishing blood and tranquilizing the mind

During the illness, the patient's diet and daily life are impermanent and his mind fluctuates, which leads to deficiency of both heart and spleen and is easy to induce insomnia of deficiency of both heart and spleen. COVID-19 patients can't get timely treatment and rest during the isolation period and illness period in COVID-19, they are too comfortable and lack of exercise too, which leads to disorder of diet and daily life, impaired spleen and stomach function and weak temper qi. In addition, patients lack of qi and blood, and emotional fluctuations disturb the mind, which will eventually cause deficiency of the heart and spleen. The mind of heart loses its nourishment, and his master, so it is uneasy. Spleen deficiency can't transport food essence, yin essence, qi and blood can't nourish the mind, and turbid qi can't drop, so it's distracting and insomnia. Patients often show insomnia, dreaminess, palpitation, forgetfulness, listlessness, mental exhaustion, Eat less and abdominal distension, loose stool, dizziness, fatigue of limbs, pale complexion, pale tongue with thin and white tongue coating, weak and thready pulse.

For patients with deficiency of both heart and spleen, the treatment is mainly to tonify the heart and spleen, nourish blood and calm the mind. Guipi decoction is the most commonly used prescription for both qi and blood in clinical practice. It can invigorate the spleen and nourish the heart, and is
often used to treat insomnia with deficiency of both heart and spleen. Astragalus membranaceus can replenish spleen and qi, longan can nourish heart and blood, and they are both monarch drugs. Ginseng, Atractylodes macrocephala, invigorating spleen and benefiting qi. Spine date seed calming the heart and the mind, Angelica sinensis nourishing the heart and enriching the blood. All the above are minister drugs. Sometimes poria cocos and polygala tenuifolia can be replaced by Poria cum Radix Pini to strengthen the spleen, soothe the mind, communicate with the heart and kidney, and to strengthen Roasted Licorice to tonify the qi of the heart and spleen. Jujube and ginger harmonize various medicines, tonify the middle energizer and stomach, so as to nourish the source of qi and blood biochemistry. While Radix Aucklandiae regulates qi and invigorating spleen, which can prevent the spleen and stomach from being injured by excessive nourishing. All of the above are assistant drugs. Experimental studies have found that Gupidecoction can significantly increase the levels of T3, T4, TRH and TSH, promote the homeostasis and balance of the hypothalamic-pituitary-adrenal axis, so as to control the content of neurotransmitters such as 5-hydroxytryptamine (5-HT), norepinephrine (NE) and dopamine (DA), and thus regulate inflammatory factors: The expression of IL-1, TNF-, IL-6, etc. regulates sleep-wake behavior, thereby increasing the sleep time of patients and improving the sleep state[20]. This prescription focuses on tonifying qi and nourishment of blood, tonifying the heart and spleen to calme the mind. It can not only treat the symptoms of insomnia in the recovery period of COVID-19, but also nourished the weak constitution of COVID-19 patients in the later stage, and treat both symptoms and root causes.

After being infected with COVID-19, people are usually "the spleen and stomach qi is still weak, so they can't eliminate the food". If patients don't pay attention to nursing, overeat, eat spicy, thick, greasy and cold things, and eat irregularly, which will lead to spleen and stomach damage, Phlegm, turbidity, damp-heat and food stagnation, and stomach qi disharmony. It will also induce insomnia. Most of the symptoms of such patients have deficiency and insufficiency, or deficiency and insufficiency are mixed. According to the specific manifestations of patients recovering from COVID-19, we can choose Baohe Pill, maiamenton decoction or Xiaojianzhong decoction for symptomatic treatment. Treatment should first take care of the spleen and stomach, restore the spleen and stomach transport function. Supporting the right qi without obstructing the transport, remove the evil without damaging the stomach qi, and then increase the formula and traditional Chinese medicine for regulating sleep, and pay attention to the use of drugs should not be too much. In this way, the drug effect can be more fully played, the treatment effect can be improved, and the disease can be prevented from recurring, becoming other diseases or causing residual diseases.

4.4. Replenish qi to relieve convulsion, soothe the nerves and settle down

In the face of large-scale and unknown infectious diseases, most people will feel anxious and depressed, and patients will suffer from sudden panic and lack of heart-qi, which will lead to insomnia syndrome of heart-gallbladder qi deficiency. The bravery governs the decision, and the heart governs the mind. Heart and gallbladder are closely related in mental activities and emotions. Patients suffering from a lack of heart and bravery will have difficulty falling asleep, light sleep, easy to wake up after sleep, palpitations and dreams, easy to be disturbed by nightmares, chest tightness and shortness of breath, fatigue and other symptoms[21].

In view of this type of syndrome, the therapeutic principles of Replenishing qi to relieve convulsion, soothing the nerves and settling down can be adopted. Anshen Dingzhi pills, Guigan Longmu Decoction and Wendan Decoction were selected for treatment[22]. Anshen Dingzhi Pill has reasonable combination, and is suitable for insomnia patients who are frightened or have great emotional influence during the recovery period in COVID-19. Among them, Codonopsis pilosula can benefit the Qi of heart and gallbladder, ginseng, poria cocos and poria cum radix pini can nourish the heart and qi, which are monarch drugs. Acorus gramineus and polygala can unblock the qi of the heart, communicate with the heart and kidney, soothe the mind, improve intelligence, resolve phlegm and resuscitating. Use Acorus gramineus and Dragon's Tooth as tranquilizer and sedative, and they also have the effect of calming the mind as well as calming the liver to suppress yang. The above are
Minister drugs. The combination of all kinds of drugs can tonify heart qi, improve intelligence, relieve convulsion, and calm the mind.

Modern research shows that Anshen Dingzhi Pill has obvious sedative and tranquilizing effects, which can effectively reduce the awakening times and prolong the sleep time of experimental mice\(^\text{[23]}\). Jiawei Guizhi Gancao Longgu Muli Decoction may improve sleep quality and duration by reducing the levels of TNF-α and IL-6\(^\text{[24]}\). Wendan decoction can reduce the content of NE in the brain of mice and restore the content of 5-HT in hypothalamus of insomnia mice, thus improving the insomnia state of mice\(^\text{[25]}\). At the same time, drugs for tonifying deficiency can be added according to the specific physical conditions of patients in recovery period, such as ginseng and white peony root, so as to help patients support healthy qi as soon as possible, harmonize yingwei, restore the function of viscera, improve sleep treatment and prolong sleep time.

5. Summary

Recently, the epidemic situation of COVID-19 in China has been basically controlled. However, with the passage of time, SARS-CoV-2 is constantly mutating, and it is still contagious, which will lead to low human immunity, and the level of SARS-CoV-2 protective antibody in the body will gradually decrease, so that some patients have been infected many times\(^\text{[26]}\). Post-covid-19 insomnia is mostly caused by physical weakness after a serious illness, deficiency of positive energy and Evil Qi retention, poor adjustment, Rongwei disharmony, zangfu function disorder, Yin essence Qi and blood insufficiency, Yang does not enter Yin. If not timely "care and protect Qi, benefit Qi to help Yang" to resist evil Qi, tranquilize the nerves and help sleep, it will develop into chronic insomnia, so its effective prevention and treatment cannot be ignored.

In clinical work, for insomnia after COVID-19, we can make full use of the theoretical characteristics of traditional Chinese medicine such as "three-factor regulation", "strengthen body resistance and eliminate disease", "treating both symptoms and root causes", and "preventing disease", pay attention to the protection of spleen and stomach qi, adjust the method with the changes of symptoms, adopt the treatment idea of planning ahead, from the perspective of disease, syndrome and person. The three stages of prevention, treatment and rehabilitation, as well as the three prevention and treatment principles of eliminating residual Evil Qi, combined with the bio-psycho-social-medical model of modern medicine, formulated a comprehensive rehabilitation treatment program of Chinese and western medicine, differentiated diseases and dialectics, treated from "deficiency", and realized the characteristic medication of one person, one TCM prescription medicine, and one treatment strategy\(^\text{[27]}\). The patients were given suggestions on regulating their emotions, moderate exercise, light diet, regular sleep schedule and other lifestyle. From the four dimensions of physiology, psychology, constitution and living habits, the patients were helped to get rid of the troubles of insomnia during the recovery period of COVID-19, reduce negative emotions such as anxiety and depression, restore the normal immune function and brain function of the body, and achieve the state of "Yin and Yang are constipated, and spirit problem will be cure". So that patients can actively face life, so as to achieve the cure of insomnia after COVID-19 in a real sense and improve the quality of life of them.

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