

The law of oral traditional Chinese medicine for insomnia based on Chinese medical code

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Abstract

Objective: This study aimed to collect, sort out and excavate the literature on the diagnosis and treatment of insomnia in Chinese Medical Code, and to explore the law of internal administration of traditional Chinese medicine in the treatment of insomnia. **Methods:** We used "Chinese Medical Code" as the source of data retrieval, "insomnia", "not sleepy", "no sleeping" and "eye not sleeping" as the key words, and excluded temporary insomnia, physiological insomnia, insomnia caused by other diseases, and excluded other methods such as acupuncture and massage, the medical cases. Prescriptions of insomnia treated with traditional Chinese medicine were screened out. The database was established by using Microsoft excel 2010. Descriptive statistics were used to analyze the frequency, menstruation of nature, taste and efficacy of traditional Chinese medicine. We analyzed the association rules between drugs and mined the rules of prescriptions by the Apriori algorithm in SPSS Modeler 14.1. **Results:** A total of 147 prescriptions, 138 traditional Chinese medicines, 20 pairs of core drugs, 57 common drug combinations and 3 core pharmaceuticals were included. The basic prescription is: Suan Zao Ren, Bai Zi Ren, Fu Shen, Fu Ling, Yuan Zhi, Dang Gui, Gan Cao (Zhi). **Conclusion:** In summary, according to the drug analysis above, the main disease of insomnia is in the heart, involving the liver, spleen and kidney. Because it involves different viscera and syndrome, the methods of treatment are also different. However, there is a basic pathogenesis, that's the loss of mental nourishment. By excavating the law of the use of traditional Chinese medicine in the treatment of insomnia on the Chinese Medical Code, we expect that it can guide the treatment of insomnia. **Keywords:** insomnia; literature mining; medicine law; Chinese Medical Code

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Introduction

Insomnia is described as “bu mei”, “bu de wo” and “mu bu ming” in traditional Chinese medicine. It is mainly manifested in the lack of sleep time and deep sleep, such as difficult to fall asleep, sleep without sound, wake up when they are asleep, difficult to sleep again after waking up, or stay up all night if it is serious [1]. There are many causes including physical, psychological, environmental factors, mental illness, physical disease, and drugs [2]. Chronic insomnia can lead to depression, endocrine disorders, decreased immunity, anxiety, suicide, and other adverse events [3-4]. The commonly used drugs include benzodiazepine receptor agonists or melatonin receptor agonists and antidepressants [5]. However, they may produce adverse reactions such as dizziness and drowsiness, which seriously affect normal work, life and interpersonal relationships, and long-term use can bring tolerance and dependence [6]. Traditional Chinese medicine has rich clinical experience in the treatment of insomnia, such as oral traditional Chinese medicine, acupuncture, moxibustion, cupping, scraping, massage, acupoint application, auricular point pressing pills and other therapies, which can adjust the function of viscera and dredge meridians [7]. In particular, oral traditional Chinese medicine has a significant effect on the treatment of insomnia based on Yin and Yang, and syndrome differentiation. This study summarized the medical literature and prescriptions related to insomnia by searching the Chinese Medical Code, and analyzed the rules of prescription by modern data mining technology in order to provide some references for the clinical treatment of insomnia

1 Methods

1.1 Prescription source

The prescriptions were used in Chinese Medical Code (National key Electronic Publishing Plan Project of the Ninth five-year Plan, 5th Edition of Hunan Electronic Audio and Video Publishing House) [8].

1.2 Search method

We manually searched Chinese Medical Code and literature reviews. The search words included “insomnia”, “not sleepy”, “no sleeping”, “eye not sleeping”, and so on.

1.3 Information extraction standard

2.3.1 Inclusion criteria

- (1) “XX as the main prescription” or “insomnia prescription” is appended to the explicit provisions in the ancient literature containing keywords;
- (2) prescription with same drugs regardless of dosage;
- (3) include only one of the prescriptions with same drugs and dosage;

- (4) soup, ointment, pill, powder and other forms;
- (5) include the first published one of articles with the same prescription.

2.3.2 Exclusion criteria

- (1) Short-term insomnia: such as temporary insomnia caused by changes of the living environment;
- (2) Insomnia caused by diseases, such as nasal congestion and pain;
- (3) Non-pharmaceutical treatments, such as acupuncture, moxibustion, etc.
- (4) Not oral traditional Chinese medicine, such as application, etc.
- (5) No specific drugs in the prescription.

2.3.3 Definition standard of drug names

The names of traditional Chinese medicines refer to the Chinese Pharmacopoeia (2015 Edition) and the textbook “traditional Chinese Medicine” of the 12th five-year Plan.

1.4 Database establishment

According to the search and inclusion criteria, we included 143 of 925 original texts including 147 prescriptions and 138 traditional Chinese medicines. The database was established using Microsoft excel 2010.

1.5 Data mining

The Apriori algorithm in SPSS Modeler 14.1 was used to analyze the association rules between drugs [9]. The parameters included a minimum support of 8% and a minimum confidence of 70%. The maximum number of antecedents was 5, in which the promotion ability was ≥ 1 , in order to explore the core medication rules for the treatment of insomnia.

2 Results

2.1 Frequency of drugs

The top 20 drugs with a frequency of more than 17 are listed in Table 1. According to the Table 1, the drugs with the highest frequency are Suan Zao Ren, Gan Cao(Zhi), Fu Shen, Ren Shen, Fu Ling, Yuan Zhi, Ban Xia, Dang Gui, Mai Dong, Sheng Jiang, Chen Pi, Bai Zi Ren, Di Huang (Shu), Zhu Ru, Di Huang (Sheng), Bai Shao, Wu Wei Zi, Huang Lian, Da Zao, Long Yan Rou and so on.

Five Tastes, Four Characters, Channel Distributions of the top 20 traditional Chinese medicines based on frequency rank are listed in Table 2. According to the Table 2, it is concluded that the Four Characters are mainly warm and flat, followed by slight cold. Five Tastes are mainly sweet, pungent, bitter, and sour. Channel Distribution is mainly heart.

The classification of drugs is listed in Table 3. According to the Table 3, in order from high to low, they are tonic medicine, soothing medicine, diuretic and dampness medicine, cough, phlegm and asthma medicine.

2.2 Prescription rule

The Apriori algorithm model was used with the support degree of 8%. Twenty core drug pairs are listed in Table 4.

According to the Table 4, Suan Zao Ren is closely related with Fu Shen, Yuan Zhi, Dang Gui, Mai Dong, Bai Zi Ren, Di Huang (Shu), Di Huang (Sheng), Wu Wei Zi, Huang Lian, Long Yan Rou, and Huang Qi. Fu Shen is closely related with Yuan Zhi, Bai Zi Ren. Gan Cao (Zhi) is closely related with Chen Pi and Da Zao. Ban Xia is closely related with Zhu Ru, Zhi Shi. Ren Shen is closely related with Wu Wei Zi. Huang Qi is closely related with Dang Gui.

Fifty-seven core drug combinations are listed in Table 5. According to the Table 5, there are the triple drugs with high support: Suan Zao Ren-Yuan Zhi-Fu Shen, Suan Zao Ren-Ren Shen-Fu Shen, Fu Ling-Ban Xia-Gan Cao(Zhi), Suan Zao Ren-Dang Gui-Fu Shen, Yuan Zhi-Dang Gui-Fu Shen, Ren Shen-Dang Gui-Fu Shen, Dang Gui-Mai Dong-Suan Zao Ren, Suan Zao Ren-Dang Gui-Yuan Zhi, Suan Zao Ren-Dang Gui-Gan Cao(Zhi), Suan Zao Ren-Bai Zi Ren-Fu Shen, Suan Zao Ren-Dang Gui-Ren Shen, and so on.

The core combinations with three drugs are presented in Table 6 and Figure 1. According to the Table 6 and Figure 1, by using the Apriori algorithm, three respective core pharmacies [Fu Shen, Suan Zao Ren, Gan Cao (Zhi)] were mined.

3 Discussion

3.1 High frequency drug analysis

In the top 20 flavors of drugs, there are Suan Zao Ren, Fu Shen, Yuan Zhi, Bai Zi Ren, Da Zao, Long Yan Rou and many other drugs, which are specific for insomnia. Some studies have shown that [10] Suan Zao Ren can improve slow wave sleep, induce physiological sleep, and increase the total sleep time. Studies have shown that licorice [11] and Fu Shen [12] have certain sedative effects. The regulatory effect of Ren Shen saponins in Ren Shen on the central nervous system mainly shows the bi-directional regulation of excitation and inhibition [13], and has the effect of reducing sleep disorders. Fu Ling has a sedative effect and can prolong sleep time. Yuan Zhi also has hypnotic effect. Ban Xia [17], Dang Gui [18], Mai Dong [19] and Bai Zi Ren [20] also have good sedative effects. Sheng Jiang [21] and Di Huang (Shu) [22] can inhibit central nervous system and prolong sleep time. Di Huang (Sheng) can also prolong sleep time [23]. Bai Shao [24], Wu Wei Zi [25] and Huang Lian [26] have sedative and hypnotic effects. Da Zao [27] and Long Yan Rou [28] can prolong sleep time. In these high-frequency drugs, Suan Zao Ren is used most frequently. Its benevolence is sweet and moist, while its shape is like the heart, as well as looking as dark red, and because the heart dominates the blood, Suan Zao Ren can nourish the heart and tonify the liver, especially suit for the treatment of heart-liver Yin as well as blood

deficiency, heart loss of deficiency and sleeplessness. And it is found that most of these high-frequency drugs have a common characteristic: they can enter the heart meridian to treat insomnia. For example, Suan Zao Ren can nourish the heart and calm the mind. Fu Ling can calm heart and tranquilize the mind. Gan Cao(Zhi) can eplenish Qi and nourish heart. Ren Shen can invigorate the spleen and calm the mind. Mai Dong can nourish Yin and clear the heart to get rid of annoyance. Fu Shen can calm heart and tranquilize the mind. Dang Gui can nourish blood and calm the mind. Da Zao and Long Yan Rou can nourish blood and calm the mind. Yuan Zhi can resolve phlegm and calm the mind. Di Huang (Sheng) can clear heart fire and nourish kidney water. Wu Wei Zi can Tonify the kidney and calm the heart as well as communicating the heart and kidney. Huang Lian can clear the heart and calm the mind. Zhu Ru can resolve phlegm and eliminate annoyance. Bai Zi Ren can nourish the heart, calm the mind, and so on.

According to the above high-frequency drugs, it is found that the one with high coincidence with the first 20 flavors of the drug frequency is Yangxin Decoction from “Renzhai Zhizhi”, which is composed of: Huang Qi(Zhi), Fu Ling, Fu Shen, Ban Xia(Qu), Dang Gui, Chuan Xiong, Yuan Zhi, Rou Gui, Bai Zi Ren, Suan Zao Ren, Wu Wei Zi, Ren Shen, Gan Cao(Zhi), Sheng Jiang, Da Zao. There are 12 medicines consisting of Fu Ling, Fu Shen, Ban Xia(Qu), Dang Gui, Yuan Zhiv, Bai Zi Ren, Suan Zao Ren, Wu Wei Zi, Ren Shen, Gan Cao(Zhi), Sheng Jiang, Da Zao in the top 20 medicines. It can be known that this prescription is important for the treatment of insomnia. The famous prescription nourishing the heart and calming the mind has the effect of replenishing Qi, nourishing blood as well as tonifying the heart, which is often used in the treatment of insomnia and palpitation. The compatibility of the prescription is characterized by: Ren Shen, Huang Qi(Zhi), Gan Cao(Zhi) tonifying heart Qi, Dang Gui, Chuan Xiong, Da Zao nourishing painstaking efforts, Fu Ling, Fu Shen, Bai Zi Ren, Suan Zao Ren, Wu Wei Zi calming heart and tranquilizing the mind;Yuan Zhi communicating between the heart and kidney, resolving phlegm and calming the mind;Rou Gui arousing the fire and returning to the origin;Ban Xia(Qu), Sheng Jiang harmonizing the stomach and resolving phlegm to help transport; Gan Cao (Zhi) reconciling drugs. Because weat is the liquid of the heart, Suan Zao Ren and Wu Wei Zi can not only calm the heart, but also converge the mind. The acidity can collect Yin fluid and prevent the heart from losing nourishment. The whole prescription has the function of tonifying Qi and tonifying blood, nourishing the heart and calming the mind.

3.2 Analysis of drug performance, taste and efficacy

Because the basic pathogenesis of insomnia is mental loss of nourishment, the use of warm tonic method is the most common. However, lung belongs to Gold, and hot injuries Yin as well as disturbing lung, so it

can not be war but gentle. In addition, clinically, liver depression often lead to fire, phlegm-heat disturbs the heart, heart fire and other syndrome, so there are mild cold, cold drugs to control heat. Sweet can nourish, mainly to tonify Qi, nourish blood and calm the heart, which is in line with the basic pathogenesis of insomnia. Pungent can disperse energy, Qi and blood circulation can make the head clear; Bitter can clear diarrhea to reduce the fire of the heart. Acidic can restrain body fluid to prevent injury of Yin in heart.

According to the classification chart analysis of the efficacy of high-frequency drugs, the deficiency medicine tonifies Qi, blood, and mind, which is divided into Qi-tonifying medicine, blood-tonifying medicine and Yin-tonifying medicine. Qi can be classified as Yang, while blood and water essence can be classified as Yin. The basic pathogenesis of insomnia is insufficiency of the mind. At the same time when recuperating the mind, it is necessary to pay attention to the root cause of the insomnia. For example, “the

Table 1: Top 20 drugs with a frequency of more than 17

No	Drugs	Frequency	No	Drugs	Frequency
1	Suan Zao Ren	89	11	Chen Pi	28
2	Gan Cao(Zhi)	66	12	Bai Zi Ren	25
3	Fu Shen	61	13	Di Huang (Shu)	24
4	Ren Shen	52	14	Zhu Ru	24
5	Fu Ling	48	15	Di Huang (Sheng)	23
6	Yuan Zhi	47	16	Bai Shao	23
7	Ban Xia	45	17	Wu Wei Zi	22
8	Dang Gui	43	18	Huang Lian	22
9	Mai Dong	35	19	Da Zao	20
10	Sheng Jiang	29	20	Long Yan Rou	17

Table 2 Five Tastes, Four Characters and Channel Distributions

Category	Drug frequency
Five Tastes	Sweet(14)Pungent(5)Bitter(4)Acidic(2)Slightly bitter(2)Light(2)
Four Characters	Warm(8)Flat(5)Slightly Cold(2)Cold(2)Slightly Warm(2)
Channel Distributions	Heart(14)Spleen(12)Lung(9)Kidney(7)Stomach(7)Liver(5)Large Intestine(2)Bile(2)

miraculous pivot” said that, “When Yang Qi ends while Yin Qi fulls, people can fall asleep with eyes closing, Yin Qi ends while Yang Qi fulls, people will wake up with eyes open.” Therefore, in the treatment of insomnia, it is necessary to use deficiency drugs to tonify Yin and blood, to nourish the mind and heart-Yang. At the same time, it is necessary to cooperate with heart-clearing drugs to prevent hyperactivity of heart-Yang from not entering Yin. The antipsychotic medicine is mainly used for nourishing the mind and the antipsychotic medicine, which is in line with the pathogenesis of insomnia. In high frequency drugs, there is no heavy material for tranquilizing, which can be seen that insomnia is mostly characterized by deficiency syndrome. In addition, it can be known that heart-soothing drugs can be used for various types of insomnia. The medicine of promoting diuresis and permeating dampness can invigorate the spleen and calm the heart, and the spleen dominates the transportation. If the spleen can be healthy, then there is a source of Qi and blood biochemistry, and the mind can be nourished. The drugs for relieving cough, resolving phlegm and relieving asthma are mainly drugs for clearing heat and resolving phlegm, which

disturbs the phlegm and fire, and makes the mind uneasy. The medicine for clearing heat and resolving phlegm can resolve phlegm and calm the mind, and its effect is consistent with the deficiency and reality of insomnia and the pathogenesis of loss of mind.

3.3 Analysis of core drug pairs

Based on the latter analysis of the core drug pair, it can be concluded that the most commonly used drugs for treating insomnia include Suan Zao Ren, Fu Shen, Gan Cao(Zhi), Ban Xia, Ren Shen, Zhu Ru, and Dang Gui. The pathogenesis of insomnia is a mixture of deficiency and solidness, which includes both insufficient blood and Phlegm-heat disturbs the heart. But overall there is a failure in nourishment of mentality. Among those drugs such as Suan Zao Ren, Fu Shen, Gan Cao (Zhi), Ren Shen and Dang Gui can replenish Qi, nourish the heart and calm the mind. Fu Shen, Ban Xia, and Zhu Ru can dispel dampness, resolve phlegm and calm the mind. “Benjing Fengyuan” said that Suan Zao Ren could converge the body liquid if ripen, which has an effort on insomnia due to insufficiency of the Gallbladder-Qi.” Bencao Beiyao” said that Fu Shen was more used into the heart channel, which can make

Table 3 Drug classification

No	Drug classification	Total frequency	Drug frequency	Proportion%
1	Deficiency-nourishing drugs	280	(Qi-invigorating Herbs): Ren Shen(52), Gan Cao(Zhi)(66), Da Zao(20) (Hematinic):Dang Gui(43), Di Huang (Shu)(24), Bai Shao(23), Long Yan Rou(17) (Yin-nourishing herbs):Mai Dong(35)	37.69
2	sedatives and tranquilizers	161	Suan Zao Ren(89), Bai Zi Ren(25), Yuan Zhi(47)	21.67
3	Diuresis and hygroscopic medicine	109	Fu Ling(48), Fu Shen(61)	14.67
4	antitussive and antiasthmatic drugs	69	Ban Xia(45), Zhu Ru(24)	9.30
5	Heat-clearing medicine	45	Huang Lian(22), Di Huang (Sheng)(23)	6.05
6	diaphoretics	29	Sheng Jiang(29)	3.90
7	Qi Regulating Drugs	28	Chen Pi(28)	3.76
8	astringent agent	22	Wu Wei Zi(22)	2.96

Table 4 20 pairs of core drugs

No	Consequent-Preceding paragraph	Support degree(%)	No	Consequent-Preceding paragraph	Support degree(%)
1	Suan Zao Ren-Fu Shen	42	11	Suan Zao Ren-Di Huang (Sheng)	16
2	Suan Zao Ren-Yuan Zhi	32	12	Ren Shen-Wu Wei Zi	15
3	Fu Shen-Yuan Zhi	32	13	Suan Zao Ren-Wu Wei Zi	15
4	Suan Zao Ren-Dang Gui	30	14	Suan Zao Ren-Huang Lian	15
5	Suan Zao Ren-Mai Dong	24	15	Gan Cao(Zhi)-Da Zao	14
6	Gan Cao(Zhi)-Chen Pi	19	16	Ban Xia-Zhi Shi	12
7	Fu Shen-Bai Zi Ren	17	17	Suan Zao Ren-Long Yan Rou	12
8	Suan Zao Ren-Bai Zi Ren	17	18	Suan Zao Ren-Huang Qi	12
9	Ban Xia-Zhu Ru	17	19	Zhu Ru-Zhi Shi	12
10	Suan Zao Ren-Di Huang (Shu)	17	20	Dang Gui-Huang Qi	12

the heart open, let the mind clear, tranquilize the soul and foster the spirit.” Elementary Medicine” said that Zhu Ru can treat insomnia caused by deficiency and restlessness.” Intergrating Chinese and Western Medicine” said that Ren Shen can not only nourish Qi, if used with hematinics, it can also enrich the blood, and the compatibility of Dang Gui here is even more complementary. ”Compendium of Materia Medica” said that Ban Xia could eliminate the flatulence of abdomen, can not close eyes. Therefore, there are many records of the medicines treating insomnia in ancient books.

There are many syndrome differentiation types of insomnia, and "Internal Medicine of traditional Chinese Medicine" [1] divides insomnia into liver-fire disturbing heart syndrome, phlegm-heat disturbing heart syndrome, heart-spleen deficiency syndrome, heart-kidney disharmony syndrome and heart-gallbladder-Qi deficiency syndrome. However, from this association

rule table, it can be found that the common syndrome types of insomnia are heart-spleen deficiency syndrome, heart-blood deficiency syndrome, heart-Yin deficiency syndrome and heart-kidney syndrome. Gan Cao (Zhi), Fu Shen, Ren Shen, Dang Gui, Da Zao, and Long Yan Rou belong to the structure of Guipi Decoction, and the syndrome of deficiency of both heart and spleen. Fu Ling, Ban Xia, Chen Pi, Zhu Ru, Huang Lian, and Sheng Jiang belong to the structure of Huang Lian Wendan Decoction, and phlegm-heat disturbing heart syndrome. Suan Zao Ren, Fu Ling, and Gan Cao(Zhi) belong to the structure of Suan Zao Ren Decoction, and the syndrome of lack of heart blood leading insomnia. Mai Dong, Di Huang (sheng), Suan Zao Ren, Bai Zi Ren, and Bai Shao belong to insomnia of heart Yin deficiency. Di Huang (Shu), Yuan Zhi, and Wu Wei Zi can communicate the heart and kidney, and treat heart-kidney syndrome of insomnia. Guipi Decoction from the "Zhengti Leiyao" is used for

Table 5 57 commonly used drug combinations

Item set	Support degree(%)	Item set	Support degree(%)	Item set	Support degree(%)
Suan Zao Ren-Yuan Zhi-Fu Shen	23	Ban Xia-Chen Pi-Gan Cao(Zhi)	14	Fu Ling-Zhu Ru-Gan Cao(Zhi)	10
Suan Zao Ren-Ren Shen-Fu Shen	19	Ren Shen-Sheng Jiang-Suan Zao Ren	14	Yuan Zhi-Di Huang (Sheng)-Fu Shen	10
Fu Ling-Ban Xia-Gan Cao(Zhi)	19	Fu Shen-Mai Dong-Dang Gui	14	Suan Zao Ren-Shi Chang Pu-Fu Shen	9
Suan Zao Ren-Dang Gui-Fu Shen	19	Zhu Ru-Chen Pi-Ban Xia	13	Dang Gui-Huang Qi-Gan Cao(Zhi)	9
Yuan Zhi-Dang Gui-Fu Shen	19	Dang Gui-Bai Zi Ren-Suan Zao Ren	12	Dang Gui-Shi Chang Pu-Fu Shen	9
Ren Shen-Dang Gui-Fu Shen	19	Suan Zao Ren-Wu Wei Zi-Ren Shen	12	Yuan Zhi-Shi Chang Pu-Fu Shen	9
Dang Gui-Mai Dong-Suan Zao Ren	18	Ban Xia-Chen Pi-Fu Ling	12	Yuan Zhi-Da Zao-Suan Zao Ren	9
Suan Zao Ren-Dang Gui-Yuan Zhi	17	Fu Shen-Di Huang (Sheng)-Suan Zao Ren	12	Ban Xia-Sheng Jiang-Fu Ling	9
Suan Zao Ren-Dang Gui-Gan Cao(Zhi)	17	Zhu Ru-Zhi Shi-Ban Xia	11	Gan Cao(Zhi)-Sheng Jiang-Yuan Zhi	9
Suan Zao Ren-Bai Zi Ren-Fu Shen	17	Ban Xia-Sheng Jiang-Gan Cao(Zhi)	11	Suan Zao Ren-Sheng Jiang-Yuan Zhi	9
Suan Zao Ren-Dang Gui-Ren Shen	16	Gan Cao(Zhi)-Sheng Jiang-Ban Xia	11	Ban Xia-Zhi Shi-Gan Cao(Zhi)	8
Suan Zao Ren-Gan Cao(Zhi)-Fu Shen	15	Fu Shen-Bai Zi Ren-Dang Gui	10	Suan Zao Ren-Huang Lian-Fu Shen	8
Suan Zao Ren-Yuan Zhi-Gan Cao(Zhi)	15	Yuan Zhi-Long Yan Rou-Suan Zao Ren	10	Yuan Zhi-Huang Qi-Dang Gui	8
Suan Zao Ren-Mai Dong-Fu Shen	14	Zhi Shi-Zhu Ru-Chen Pi	10	Zhu Ru-Zhi Shi-Gan Cao(Zhi)	8
Suan Zao Ren-Mai Dong-Ren Shen	14	Gan Cao(Zhi)-Zhu Ru-Chen Pi	10	Suan Zao Ren-Di Huang (Sheng)-Mai Dong	8
Fu Ling-Chen Pi-Gan Cao(Zhi)	14	Fu Shen-Bai Shao-Suan Zao Ren	10	Suan Zao Ren-Di Huang (Sheng)-Yuan Zhi	8
Suan Zao Ren-Sheng Jiang-Gan Cao(Zhi)	14	Gan Cao(Zhi)-Huang Qi-Suan Zao Ren	10	Yuan Zhi-Da Zao-Sheng Jiang	8
Gan Cao(Zhi)-Fu Ling-Ren Shen	14	Suan Zao Ren-Di Huang (Sheng)-Dang Gui	10	Gan Cao(Zhi)-Chen Pi-Ren Shen	8
Fu Shen-Yuan Zhi-Ren Shen	14	Dang Gui-Huang Qi-Suan Zao Ren	10	Gan Cao(Zhi)-Zhi Shi-Fu Ling	8

Table 6 three core drug combinations

No	Consequent	Preceding paragraph
1	Fu Shen	Bai Zi Ren-Dang Gui-Ren Shen-Suan Zao Ren-Yuan Zhi--Mai Dong-Gan Cao(Zhi)
2	Suan Zao Ren	Mai Dong-Dang Gui-Ren Shen-Fu Shen-Gan Cao(Zhi)-Yuan Zhi-Bai Zi Ren-Sheng Jiang
3	Gan Cao(Zhi)	Chen Pi-Ban Xia-Fu Ling-Huang Qi-Dang Gui-Zhi Shi-Sheng Jiang-Ren Shen-Suan Zao Ren-Zhu Ru

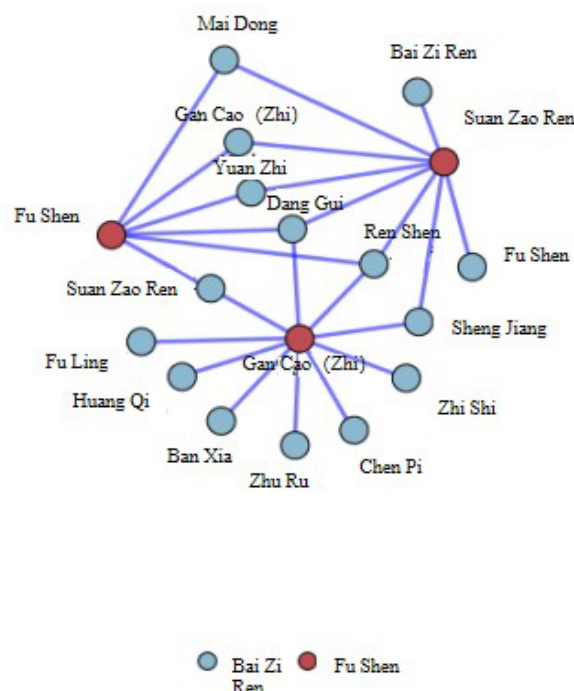


Figure 1 network display diagram (three core drug groups)

palpitation, forgetfulness, insomnia and dreaminess due to the lack of Qi and blood caused by the deficiency of heart and spleen. It has the function of tonifying Qi as well as blood, invigorating the spleen and nourishing the heart. Huang Lian Wendan Decoction comes from "LiuYin Tiaobian", which is based on the addition and subtraction of Wendan Decoction. It has the effect of resolving phlegm, reducing turbidity, clearing the heart and calming the nerves, so it is often used for insomnia caused by phlegm-heat which can disturb the heart. Suan Zao Ren Decoction is contained in synopsis of the "Golden Chamber". It is used to treat the lack of painstaking effort and insomnia.

3.4 Analysis of common drug combinations

The overall efficacy of the triple drug combination of commonly used drugs is similar to that of the core drug pair with tonifying deficiency, reducing excess, nourishing heart and tranquilizing mind. However, the combination of Fu Ling, Fu Shen, Ren Shen, Yuan Zhi, and Shi Chang Pu is very close to the composition of Anshen Dingzhi pill in "Medicine Comprehended". The composition of Anshen Dingzhi Pill is as follows: Fu Ling, Fu Shen, Ren Shen, Yuan Zhi, Shi Chang Pu, and Long Chi, which has the function of replenishing Qi, nourishing the heart and calming the mind. Insomnia is a disease which is most closely related to the heart, liver, spleen and kidney. Failure in nourishment of mentality is the direct cause of insomnia. If liver is lack of nourishment, Yin blood will be not enough to nourish the mind. If spleen deficiency lasts for a long time, the endogeny of turbid phlegm, the blocking of

blood as well as Qi, and the loss of mind and spirit can also lead to insomnia. Insufficient kidney water, can not help the fire, heart and kidney is not transmitted, and that can also lead to insomnia. These high-frequency triple drugs are mainly based on Suan Zao Ren, Yuan Zhi, Fu Shen, Dang Gui and Gan Cao (Zhi), reflecting the basic treatment of nourishing the heart and tranquilizing the mind. Suan Zao Ren nourishes heart Yin, tonifies liver and blood to calm mind; Yuan Zhi can stretch the Qi of heart, dredge kidney Qi, and communicate heart and kidney to calm mind; Fu Ling can benefit spleen and remove dampness to calm mind; Dang Gui can nourish blood heart to nourish heart spirit; Gan Cao (Zhi), invigorating Qi and the spleen, nourishing the heart, can harmonize various drugs. Therefore, the first way to treat insomnia is nourishing heart to calm the mind. Then on the base of that, we can use herbs to adjust liver, spleen, kidney and perform some clinical addition and subtraction.

3.5 Analysis of Core Pharmaceuticals

Yangxin Decoction, Anshen Dingzhi Pills and Wendan Decoction have the highest matching degree of prescriptions. Among them, Yangxin Decoction nourishes the heart and tranquilizes the mind, which mainly treats insomnia caused by deficiency of heart blood. Anshen Dingzhi Pills mainly treat panic, insomnia and restlessness at night. Wendan Decoction treats insomnia caused by timidity and phlegm-heat which can disturb the heart. Among the three core pharmaceuticals above, the one with Fu Shen as the core can replenish Qi, nourish the heart, and tranquilize

the mind. The one with Suan Zao Ren as the core can nourish the liver as well as blood, raise the heart and calm the mind. The last one with Gan Cao (Zhi) as the core can invigorate the spleen to remove dampness, and resolve phlegm to calm the mind. These three core pills respectively treat insomnia from the heart, liver and spleen, and all of them have good curative effects according to the literature. In addition, from the three core pharmacies, it can be seen that the pathogenesis of insomnia is mixed with deficiency and excess, which is not only a simple syndrome, especially phlegm-heat disturbance. The patients with the spleen deficiency for such a long time that may be have phlegm and dampness in the spleen. The movement of Qi is blocked by the phlegm, which hinder the decline of Qi in Lung, and disturb the heart and cause insomnia.

Conclusion

In summary, according to the drug analysis above, the main disease of insomnia is in the heart, involving the liver, spleen and kidney. Because it involves different viscera and syndrome, the methods of treatment are also different. However, there is a basic pathogenesis, that's the loss of mental nourishment. Therefore, no matter what type of syndrome in insomnia, in order to enhance the clinical effect, it is advisable to use some drugs to nourish the heart and calm the mind, on the basic of the dialectical treatment with tonifying deficiency, purging excess as well as adjusting Yin and Yang. Some scholars [29] think that the most common syndrome types of insomnia are like these: deficiency both in heart and spleen, heart disturbed by phlegm-fire, depression leading to fire in liver, incompatibility of heart and kidney, and so on. In the way of data mining combined with clinical experience, it is considered that the basic prescription for insomnia is: Suan Zao Ren, Bai Zi Ren, Fu Shen, Fu Ling, Yuan Zhi, Dang Gui, and Gan Cao(Zhi). Therefore, good effects can be obtained if we can add or reduce some drugs properly by dialectical addition and subtraction. For example, when patients suffer from the syndrome of deficiency of both heart and spleen, we can add Ren Shen, Long Yan Rou, Da Zao, and so on. When patients suffer from phlegm and fire disturb the heart, we can add Chen Pi, Ban Xia, Zhu Ru, Huang Lian, and so on. When patients suffer from liver depression turns into fire, we can add Zhi Zi, Chai Hu, He Huan Pi, Yu Jin and so on. When patients suffer from Heart-kidney incompatibility, we can add Huang Lian, Zhu Ye, Rou Gui, Wu Wei Zi, and so on. When patients suffer from Yin deficiency and exuberant fire, we can add Di Huang (Sheng), Di Huang (Shu), Shan Yu Rou,

Huang Bai, and so on. By excavating the law of the use of traditional Chinese medicine in the treatment of insomnia on the Chinese Medical Code, we expect that it can guide the treatment of insomnia.

References

- [1] Zhou ZY. Chinese internal medicine. Beijing: Chinese medicine publishing house, 2012, 146. (Chinese)
- [2] Jia JP, CHEN SD. Neurology. Beijing: People's Health Publishing House, 2016, 414. (Chinese)
- [3] Edward F P, Jared P Z, Ryan M B, et al. Resting state functional connectivity in primary insomnia, generalized anxiety disorder and controls. *Psychiatry Res Neuroimaging*, 2017, 265: 26-34.
- [4] Spira AP, Friedman L, Aulakh JS, et al. Subclinical anxiety symptoms, sleep, and daytime dysfunction in older adults with primary insomnia. *J Geriatr Psychiatry Neurol*, 2008, 6: 149-153.
- [5] Winkelman JW. CLINICAL PRACTICE. Insomnia disorder. *N Engl J Med*, 2015, 373: 1437-1444.
- [6] Peng L. Side effects of sedative and hypnotic drugs in the treatment of insomnia. *Capital Medicine*, 2010, 17: 34-35. (Chinese)
- [7] Zhao WW, Li GH, Li Y, et al. Application of traditional Chinese medicine nursing technique in hypertension with insomnia: A literature review. *TMR Integrative Nursing*, 2019, 3: 1-6.
- [8] Qiu PR. Classics of Traditional Chinese Medicine. Changsha: Hunan Electronic And Audio-visual Publishing House, 2014. (Chinese)
- [9] Su ZD, You FC, Yang BR. Comprehensive evaluation method of association rules and an practical example. *Computer Applications*, 2004, 24: 17-20. (Chinese)
- [10] Jia Y, Guo YF, Sun SJ, et al. Study on the sedative and hypnotic effects of volatile oil from Semen Ziziphi Spinosae by the supercritical CO₂ extraction. *Chin J Tradit Chin Med Pharm*, 2018, 33: 4181-4183. (Chinese)
- [11] Jin H. On the pharmacological action of Glycyrrhiza uralensis. *Lishizhen Medicine and Materia Medica Research*, 2000, 11: 78-79. (Chinese)
- [12] Zhang X, Xiang RP, Liu CH. Research progress in the chemical constituents and pharmacological action of poria. *Journal of Zhengzhou College of Animal Husbandry Engineering*, 2009, 29: 19-21. (Chinese)
- [13] Guo XL, Gao SL. A review on the ginseng chemical constituents and pharmacological. *Clinical Journal of Chinese Medicine*, 2012, 4: 26-27. (Chinese)
- [14] Kim H, Park C W, Cho S H. The Beneficial Effect of Korean Red Ginseng Extract on Atopic Dermatitis Patients: An 8 Weeks Open, Noncomparative Clinical Study. *Ann Dermatol*, 2018, 30: 304-308.
- [15] Shah VK, Choi JJ, Han JY, et al. Pachymic Acid Enhances Pentobarbital-Induced Sleeping Behaviors

- via GABA(A)-ergic Systems in Mice. *Biomol Ther*(Seoul), 2014, 22: 314.
- [16] Ma X, Wang J, Huang C, et al. Study on sedative and expectorant effects of processed products of Houpu zhiyuanzhi. *Pharmacology and Clinics of Chinese Materia Medica*, 2013, 29: 90-92. (Chinese)
- [17] Zhan AP, Wang P, Chen KL. Comparative study on sedative and hypnotic effects of *Pinellia ternata*, *pinellia palmata* and *Pinellia ternata* on mice. *Journal of Chinese Medicinal Materials*, 2006, 29: 964-965. (Chinese)
- [18] Huang HH, QIN RH, Liu XF. Analysis of chemical components and pharmacological action of *Angelica sinensis*. *World Latest Medicine Information*, 2019, 19: 127+153. (Chinese)
- [19] Zhao B, Wu CJ, Gao H. Sedative and Hypnotic Effect of *Ophiopogon Japonicus* on Mice. *Journal of Xianning College*, 2008, 22: 282-284. (Chinese)
- [20] Ma XY, Research on the component and preparation of *Platycladi* seed. *Liaoning University of Traditional Chinese Medicine*, 2017. (Chinese)
- [21] Jiang SZ, Zhou TT. Effect of Ginger (*Zingiber officinale* Roscoe) Oleoresin on Central Nervous System in Mice. *Chin J Exp Tradit Med Formulae*, 2010, 16: 180-182.
- [22] Cui H, Feng J, Cui Y, et al. Inhibition Effect of Shu Dihuang and the Polysaccharide on CNS. *Journal of Henan University of Chinese Medicine*, 2006, 21: 18-19. (Chinese)
- [23] Wang ZJ, Wei GD, Ma ST. Chemical and Pharmacological Effects of *Rehmanniae Radix* Polysaccharides. *Chinese Journal of Experimental Traditional Medical Formulae*, 2015, 21: 231-235. (Chinese)
- [24] Li NQ. A review on pharmacological effects and modern research of Baishao. *Clinical Journal of Chinese Medicine*, 2017, 9: 137-138. (Chinese)
- [25] Cao JH, Jia ZR, Yang RC, et al. Comparison on the Sedative-Hypnotic Effects of the Ethanol and the Water Extracts of *Schisandrae Chinensis*. *Acta Chinese Medicine*, 2017, 32: 1943-1946. (Chinese)
- [26] Qiu YP. A review on Huanlian. *Clinical Journal of Chinese Medicine*, 2018, 10: 141-143. (Chinese)
- [27] Qiu M, Xiong ZK, LV MY. Pharmacological research progress of jujube polysaccharides. *China Modern Doctor*, 2018, 56: 161-164. (Chinese)
- [28] Ma Y, Ma H, Eun JS, et al. Methanol extract of *Longanae Arillus* augments pentobarbital-induced sleep behaviors through the modification of GABA ergic systems. *J Ethnopharmacol*, 2009, 122: 245.
- [29] Chen DY, He SC, Zhou DY, et al. Traditional Chinese Medicine Treatment For Insomnia: A Systematic Review. *Chinese Archives of Traditional Chinese Medicine*, 2016, 34: 105-110. (Chinese)