## <u>Original Research</u>

# Combined Efficacy of Modified Yangxin Anshen Decoction and Western Medicine Treatment in Elderly Patients with Schizophrenia and Sleep Disorders

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#### ABSTRACT

**Objective** • To explore the combined efficacy of modified Yangxin Anshen decoction and Western medicine treatment in elderly patients with schizophrenia and sleep disorders.

**Methods** • A total of 144 elderly patients with schizophrenia and sleep disorders in Wuhan Wudong Hospital were enrolled as participants in this study from April 2021 to April 2022. The participants were randomly and equally divided into a control group (receiving conventional Western medicine treatment) and two study groups: study group 1 received modified Yangxin Anshen decoction, and study group 2 receive modified Yangxin Anshen decoction in addition to Western medicine treatment. TCM syndrome scores, sleep quality, polysomnography, serum levels of 5-HT, DA, and MT were compared between the two groups. Moreover, the efficacy and adverse reactions were recorded.

**Results** • After four weeks of treatment, the efficacy of study group 2 was significantly better than that of the control group and Study Group 1 (P < .05). There was no statistically significant difference between the three groups in secondary and main symptoms before treatment (P > .05), while the secondary and main symptoms of study group 2 were significantly lower than those of the control group and study group 1 after four weeks of treatment (P < .05). Before treatment, no statistically significant difference was found in sleep quality score between the three groups (P > .05), whereas the index of the study group 2 was evidently lower than that of the control group and study group 1 after four weeks of treatment (P < .05). Before treatment, there was no significant difference in terms of total recording time,

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#### INTRODUCTION

Schizophrenia is a serious mental disorder in clinical practice, which mainly affects patients' perception, thinking, emotions, and behavior.<sup>1</sup> Since the acceleration of the pace of total sleep time, sleep onset latency, sleep efficiency, and four stages (N1, N2, N3, and REM) between the three groups (P >.05). After four weeks of treatment, although no statistically significant difference was shown in total recording time between the three groups (P > .05), the total sleep time, sleep onset latency, sleep efficiency, and four stages (N1, N2, N3, and REM) of the study group 2 were significantly improved than those of the control group and the study group 1 (P < .05). Before treatment, there was no significant difference in serum levels of 5-HT, DA, and MT between the three groups (P > .05), while the three indexes were evidently lower than the control group and the study group 1 after four weeks of treatment (P < .05). During the treatment process, 1 case of mild dry mouth occurred in the study group who did not receive special treatment, and the incidence of adverse reactions was 1/48. In the control group, there were 3 cases of dry mouth, 1 case of constipation, 1 case of diarrhea, 1 case of decreased appetite, and 1 case of nausea, whose symptoms were not specially treated, with the incidence of adverse reactions of 7/48. Hence the incidence of adverse reactions in the study group was significantly lower than that in the control group (P < .05).

**Conclusion** • Combined treatment with modified Yangxin Anshen decoction and Western medicine improved sleep quality in elderly patients with schizophrenia and sleep disorders, which is available for wide clinical application. (*Altern Ther Health Med.* [E-pub ahead of print.])

life and the increased social burden in recent years, the incidence rate of mental diseases is climbing over time in China. Schizophrenic patients generally have clear awareness and normal intelligence, but they often experience cognitive dysfunction during the progression of the condition. The symptoms of schizophrenia can progressively worsen, with a high recurrence rate and disability rate. In more serious cases, patients harboring the condition may have mental disability, and develop functional incapability of daily activities, which is a huge burden for their family and society.<sup>2</sup>

Because of the population aging crisis in China, the physical and mental health problems of the elderly have been the focus of common concerns of the entire society.<sup>3</sup> Senile sleep disorder refers to primary insomnia commonly

occurring among the elderly, which is a painful problem for the patients.<sup>3</sup> The main manifestations of sleep in the elderly include long latency, decreased sleep continuity, early morning awakening, and nocturnal awakening.<sup>3</sup> Long-term sleep deprivation can affect the attention and memory of the elderly, resulting in psychological and emotional changes, cognitive dysfunction, and reduced quality of life of patients.<sup>4</sup> In clinical Western medicine, doctor currently uses sedative and hypnotic drugs to treat patients with schizophrenia and sleep disorders. Due to physical dysfunction and reduced drug metabolism in elderly patients, they are prone to multiple adverse reactions.<sup>5</sup> According to an earlier study, the combination of TCM (traditional Chinese medicine) and Western medicine can effectively improve the clinical symptoms of elderly patients with schizophrenia combined with sleep disorders, with significant therapeutic effects.<sup>5</sup> Based on the principle of syndrome differentiation and treatment, TCM has achieved satisfactory results in treating patients with schizophrenia and sleep disorders.<sup>6-7</sup> In TCM, middle-aged and elderly patients with schizophrenia and sleep disorders are characterized by a deficiency of both the heart and spleen, liver fire disturbing the heart, qi stagnation, and phlegm obstruction, among which liver fire disturbing the heart is the most common type in clinical practice.8 Yangxin Anshen decoction originates from the Jiyang *Compendium (Volume 54)*, the *Speculation Collection*, which has the efficacy of magnifying qi and blood, nourishing the heart and calming the nerves, and is mainly used to treat deficiency of qi and blood, and restlessness of mind syndrome.<sup>8</sup> A previous study proposed that Yangxin Anshen decoction can effectively treat insomnia.8 But very little information is available about the efficacy of modified Yangxin Anshen decoction combined with Western medicine treatment in elderly patients with schizophrenia and sleep disorders. This study aimed to explore the application value of modified Yangxin Anshen decoction in addition to Western medicine treatment for senile schizophrenia combined with sleep disorders.

#### METHODS AND MATERIALS

#### **General information**

A study was conducted on 144 elderly patients with schizophrenia and sleep disorders in Wuhan Wudong Hospital from April 2021 to April 2022. The participants were equally divided into a control group, a study group 1, and a study group 2 based on a random number table method. In the study group 1, there were 18 males and 30 females, aged 67 to 83 years, with a mean age of (73.19  $\pm$  8.76) years, and in the study group 2, there were 21 males and 27 females, aged 67 to 83 years, with a mean age of (73.07  $\pm$  8.84) years. The control group consisted of 20 males and 28 females, aged 66 to 82 years, with a mean age of (73.01  $\pm$  8.02) years. Comparison of general data between the two groups of patients did not differ (P > .05). This research protocol is performed according to the relevant requirements of the Helsinki Declaration of the World Medical Association.

#### Diagnostic criteria

**Diagnostic criteria for Western medicine.** Schizophrenia was confirmed based on the diagnostic criteria of the Chinese Classification of Mental Disorders Version 3 (CCMD-3)<sup>9</sup>; Patients with non-organic sleep disorders were diagnosed according to the International Classification of Diseases-10 (ICD-10).

**Diagnostic criteria of traditional Chinese medicine.** Syndrome of liver fire disturbing the heart was determined based on the Criteria for the Diagnosis and Efficacy of Diseases in Traditional Chinese Medicine.<sup>10</sup> Main symptoms: 1) difficulty falling asleep or easy to wake up from sleep, and difficulty sleeping after waking up; 2) dizziness; 3) impatience and irritability. Secondary symptoms: 1) dry mouth and bitter mouth; 2) constipation and short voiding of reddish urine; 3) feeling of fullness and discomfort in the chest and sides. Tongue and pulse: red tongue, yellow fur of the tongue, and stringy pulse. Patients can be diagnosed when meeting all the main symptoms, with one or two secondary symptoms, referring to the fur of the tongue and pulse condition. **Selection criteria** 

### Selection criteria

**Inclusion criteria** (1) Patients who met the above diagnostic criteria for traditional Chinese and Western medicine; (2) Patients without the use of sedative drugs one month before enrollment; (3)Age>60; (4) Patients signed an informed consent form.

**Exclusion criteria** (1)Other TCM syndromes; (2) Patients with organic dysfunction affecting the heart and lung, liver and kidney; or patients combined with endocrine and autoimmune diseases, hematopoietic system diseases, and tumors; (3) Patients with sleep disorders caused by drug abuse, pain, cardiovascular and cerebrovascular diseases. (4) Pregnancy and lactation. (5) Patients with other mental disorders. (6) Patients who were unable to continue treatment due to unexpected adverse events during the treatment process. (7) Patients who failed to complete the treatment course. (8) Patients who were lost to follow-up. (9) Patients who were allergic to this drug. (10) Patients who had experienced an infection or undergone surgical treatment in the past 1 week.

#### Methods

The control group was treated with conventional Western medicine, with oral administration of olanzapine tablets that were prescribed 10 mg/dose, twice a day (manufacturer: Zhejiang Longhua Pharmaceutical Co., Ltd.; batch number: OD00C1908001), oral administration of dezopiclone that was prescribed 30 minutes before bedtime, 3 mg/dose, once a day (manufacturer: Jingsen Beijia Biotechnology Co., Ltd.; batch number: SBJ2016032518), and oral administration of Alprazolam tablets that was prescribed 0.4 mg/day, once a day (manufacturer: Jiangsu Enhua Pharmaceutical Co., Ltd.; batch number: 20171106). The above drugs were taken continuously for 4 weeks.

The study group 1 was treated with modified Yangxin Anshen decoction. The modified Yangxin Anshen decoction,

consisting of Dragon Bone 30g, Sour Jujube Seed 15g, Bupleurum 15g, Fructus Aurantii 15g, Paeonia Alba 15g, Angelica Sinensis 15g, Baiziren 15g, Fushen 15g, Polygala tenuifolia 12g, Acorus tatarinowii 12g, Curcuma 12g, the flower of Albizia julibrissima 10g, and roasted licorice 10g, were soaked in 400mL for 2 hours, boiled under fire, and decocted under mild fire to about 100 mL. After extracting the juice, the residue was decocted with 400 mL of water in the same way. The combined liquid medicine was taken in 2 doses continuously for 3 months, which was decocted by the Department of Traditional Chinese Medicine in our hospital. The above drugs were taken continuously for 4 weeks.

The study group 2 was treated with modified Yangxin Anshen decoction in addition to Western medicine, the same as the control group.

**Observation indexes.** The TCM syndrome score, sleep quality, polysomnography, and serum levels of 5-HT, DA, and MT between the three groups were compared, and the efficacy and adverse reactions of the three groups were recorded before and after treatment.

TCM syndrome score. TCM syndrome score was determined according to the Criteria for the Diagnosis and Efficacy of Traditional Chinese Medicine Diseases. The score was calculated based on the severity of the main symptoms, including 1) difficulty falling asleep or waking up easily or difficulty falling asleep after waking up; 2) dizziness; 3) impatience and irritability, with 0-6 points of each item, and the severity of the secondary symptoms, including 1) dry mouth and bitter mouth; 2) constipation and hematuria; 3) feeling of fullness and discomfort in the chest and sides, with 0-3 points of each item. The higher the score, the more serious the clinical symptoms.

Efficacy evaluation. The efficacy was determined according to the Criteria for the Diagnosis and Efficacy of Traditional Chinese Medicine Diseases, including the following aspects: 1) cured: symptoms such as difficulty falling asleep or waking up easily or difficulty falling asleep after waking up, and dizziness disappeared, and the TCM syndrome score decreased by >95%; 2) significantly effective: symptoms such as difficulty of falling asleep or waking up easily or difficulty of falling asleep after waking up, and dizziness were significantly improved, and the TCM syndrome score decreased by >80% to 90%; 3) effective: symptoms such as difficulty of falling asleep or waking up easily or difficulty of falling asleep after waking up, and dizziness disappeared, and TCM syndrome scores decreased by>60% to 80%; 4) ineffective: none of the above symptoms improved or worsened. Total effective rate=cured rate + significantly effective rate + effective rate.

**Sleep quality.** Before and after four weeks of treatment, the Pittsburgh Sleep Quality Index (PSQI)<sup>11</sup> was used to assess the quality of sleep. This scale includes 7 items, including daytime function, sleeping drugs, sleep disorders, sleep efficiency, sleep duration, sleep latency, and subjective sleep quality. Each item has a score of 0-3 points. The higher the score, the poorer the sleep quality.

**Polysomnography.** Before and after four weeks of treatment, the polysomnography was measured using the E-type polysomnography detector of Kangdi Company, Australia. Sleep process parameters, including total recording time (total bedtime recorded by PSG), sleep onset latency (total bedtime from the beginning of PSG recording to the occurrence of sleep), sleep latency time (time from the beginning of PSG recording to the occurrence of any period of actual sleep lasting for 3 minutes), sleep efficiency (percentage of total sleep time in total recording time), were recorded. We also monitored sleep structural parameters, including non-rapid-eye movement (NREM) sleep which is further divided into three sleep stages: N1, N2, and N3, and rapid eye movement (REM) sleep. The sleep time of REM and NREM stages was recorded respectively.

**Serum levels of 5-HT, DA, and MT.** Before and after four weeks of treatment, 5 ml of venous blood from the patient was extracted, centrifuged, and submitted for testing. The serum 5-HT, DA, and MT levels were measured using an enzyme-linked immunosorbent assay (Shanghai Xitang Biotechnology Co., Ltd).

Adverse reactions. The occurrence of adverse reactions such as dry mouth, constipation, diarrhea, loss of appetite, nausea, vomiting, etc. was recorded during the treatment process.

#### Statistical analysis

SPSS version 21.0 software was applied to analyze data, and Excel was used to establish a database. The measurement data conforming to the normal distribution were expressed in  $\overline{x \pm s}$ , and the overall comparison of data in each group was performed using a one-way analysis of variance. Pairwise comparisons of data between groups and within groups were conducted with the use of the LSD method. The counting data was expressed in percentage (%) and compared using the chisquare  $\chi^2$  test. A P < .05 represents a significant difference.

#### RESULTS

#### Comparison of general data

There was no statistically significant difference in sex, age, BMI, course of disease, alcohol consumption, and comorbidities between the three groups (P > .05), as shown in Table 1.

#### **Comparison of therapeutic effects**

After four weeks of treatment, the efficacy of the study group 2 was significantly better than that of the control group and the study group 1 (P < .05), as laid out in Table 2.

	Study group 1	Study group 2	Control group		
Index	(n = 48)	(n = 48)	(n = 48)	X <sup>2</sup>	P value
Sex (male/female) (n)	18/30	21/27	20/28	0.174	.676
Age (year)	73.19±8.76	73.07±8.84	73.01±8.02	0.105	.917
BMI (kg/m <sup>2</sup> )	22.63±2.67	22.68±2.71	22.53±2.87	0.177	.861
The course of schizophrenia (year)	5.92±1.52	5.97±1.53	5.81±1.48	0.359	.719
Sleep disturbance course (mouth)	3.09±0.52	3.06±0.56	3.01±0.59	0.705	.483
Tobacco use (n)	11	10	9	0.253	.615
Comorbidity (n)				0.302	.584
Hypertension	7	9	9		

#### Table 2. Comparison of therapeutic effects

	Study group 1	Study group 2	Control group		
Index	(n = 48)	(n = 48)	(n = 48)	$\chi^2$	P value
Cured	19	23	16		
Significantly effective	13	16	9		
Effective	9	8	16		
Ineffective	7	1	7		
Total effective rate (%)	41 (85.42%)	47 (97.92) <sup>a,b</sup>	41(85.42%)	4.909	.027

Note: Compared with study group 1 (\* P < .05), compared with control group (\* P < .05)

#### Table 3. Comparison of TCM syndrome scores

Index	Time	Study group 1	Study group 2	Control group	$\chi^2$	P value
		(n = 48)	(n = 48)	(n = 48)		
Secondary	Before treatment	14.47±2.87	14.28±2.38	14.32±2.43	0.143	.887
symptom	After four weeks of treatment	6.09±1.36	3.87±1.01	6.37±1.08	-11.713	<.001
Main	Before treatment	7.65±2.36	7.32±2.06	7.29±0.71	0.199	.842
symptom	After four weeks of treatment	2.97±0.37	2.26±0.36	3.09±0.31	-12.104	<.001

#### Table 4. Comparison of sleep quality

	Study group 1	Study group 2	Control group		
Time	(n = 48)	(n = 48)	(n = 48)	t	P value
Before treatment	15.45±2.76	15.38±2.32	15.28±2.42	0.214	.831
After four weeks of treatment	7.18±1.86	4.09±1.32	7.37±1.79	-15.223	<.001

#### Table 5. Comparison of polysomnography

		Study group 1	Study group 2	Control group		
Index	Time	(n = 48)	(n = 48)	(n = 48)	t	P value
Total	Before treatment	701.73±90.11	695.53±82.42	675.65±80.98	0.532	.596
recording	After four weeks of	815.85±86.10	869.69±81.22	800.81±79.45	0.325	.746
time (min)	treatment					
Total sleep	Before treatment	294.92±27.98	290.38±23.24	292.09±23.35	-0.361	.722
time (min)	After four weeks of treatment	349.79±28.06	379.98±26.91	343.92±25.19	6.778	<.001
Sleep onset	Before treatment	60.76±6.54	62.39±5.91	62.27±6.01	0.099	.921
latency	After four weeks of	42.09±9.07	29.71±7.37	45.19±8.76	-13.619	<.001
(min)	treatment					
Sleep effi-	Before treatment	58.83±8.93	59.79±8.19	58.28±7.27	0.955	.342
ciency (%)	After four weeks of treatment	69.93±8.28	76.39±9.56	67.28±8.38	4.965	<.001
Stage N1	Before treatment	52.09±9.83	53.28±10.19	51.23±9.37	0.039	.969
	After four weeks of treatment	47.02±8.73	42.39±8.01	48.91±8.48	-7.385	<.001
Stage N2	Before treatment	156.39±21.92	152.19±22.29	154.38±20.48	-0.071	.944
Ū	After four weeks of treatment	202.19±21.02	217.26±18.27	197.93±16.36	5.461	<.001
Stage N3	Before treatment	29.03±6.98	27.27±6.31	28.21±7.18	0.131	.896
-	After four weeks of treatment	35.91±7.33	49.87±7.76	32.39±8.81	25.471	<.001
Stage REM	Before treatment	49.71±7.93	50.23±6.29	51.19±7.32		
-	After four weeks of treatment	68.92±3.61	74.09±3.34	65.19±3.47		

#### Table 6. Comparison of serum 5-HT, DA, and MT levels

		Study group 1	Study group 2	Control group		
Index	Time	(n = 48)	(n = 48)	(n = 48)	t	P value
5-HT(µg/L)	Before treatment	191.28±38.19	193.28±31.32	196.09±33.37	-0.123	.902
	After four weeks of treatment	252.29±33.28	328.87±31.26	247.87±31.39	12.668	<.001
DA(µg/L)	Before treatment	79.03±11.65	77.39±10.63	75.31±10.83	0.051	.959
	After four weeks of treatment	57.91±7.39	42.19±7.38	60.31±8.09	-14.233	<.001
MT(µg/L)	Before treatment	15.28±4.02	16.37±4.28	16.03±4.37	-0.185	.854
	After four weeks of treatment	28.91±3.29	33.29±3.32	25.29±4.43	28.481	<.001

#### Comparison of TCM syndrome scores

There was no statistically significant difference between the three groups in secondary and main symptoms before treatment (P > .05), while the secondary and main symptoms of the study group 2 were significantly lower than those of the control group and the study group 1 after four weeks of treatment (P < .05), as seen in Table 3.

#### Comparison of sleep quality

Before treatment, no statistically significant difference was found in sleep quality score between the three groups (P > .05), whereas the index of the study group was evidently lower than that of the control group after treatment (P < .05). (Table 4)

#### Comparison of polysomnography

Before treatment, there was no significant difference in terms of total recording time, total sleep time, sleep onset latency, sleep efficiency, and four stages (N1, N2, N3, and REM) between the three groups (P > .05). After four weeks of treatment, although no statistically significant difference was shown in total recording time between the three groups (P > .05), the total sleep time, sleep onset latency, sleep efficiency, and four stages (N1, N2, N3, and REM) of the study group 1 were significantly improved than those of the control group the study group 2 (P < .05), as shown in Table 5.

#### Comparison of serum 5-HT, DA, and MT levels

Before treatment, there was no significant difference in serum levels of 5-HT, DA, and MT between the three groups (P > .05), while the three indexes of the study group 2 were evidently lower than that of the study group 1 (P < .05), however, the three indexes of the study group 1 showed no difference compare to that of the control group after four weeks of treatment (P < .05), as seen in Table 6.

#### **Comparison of adverse reactions**

During the treatment process, 1 case of mild dry mouth occurred in the study group who did not receive special treatment, and the incidence of adverse reactions was 1/48. In the control group, there were 3 cases of dry mouth, 1 case of constipation, 1 case of diarrhea, 1 case of decreased appetite, and 1 case of nausea, whose symptoms were not specially treated, with the incidence of adverse reactions of 7/48. Hence the incidence of adverse reactions in the study group was lower than that in the control group, with a statistically significant difference ( $\chi^2 = 4.909$ , P = .027).

#### DISCUSSION

Schizophrenia is known as one of the common psychiatric diseases with slow onset. In addition to negative and positive symptoms, patients with this disorder often experience cognitive, emotional, and thinking difficulties that significantly impact their daily life and social activities.<sup>12</sup> According to the previous data released by the Chinese Center for Disease Control and Prevention, the number of psychiatric patients in China has reached more than 100 million, with a trend toward a gradual increase in the incidence rate of elderly schizophrenics due to the aging population in China.<sup>12</sup> An earlier study<sup>13</sup> showed that patients

with schizophrenia may have difficulties starting and maintaining sleep at various stages of the course of the disease (acute and stable stages) and under various medication states. The presence of sleep disorders can exacerbate the condition of patients, especially elderly patients, who have organ dysfunctions, and long-term sleep deprivation can lead to reduced memory. Therefore, elderly patients with schizophrenia and sleep disorders should seek early and appropriate intervention to improve their clinical symptoms and promote their recovery. Elderly patients with schizophrenia and sleep disorders are often treated with drugs such as dexzopiclone, olanzapine, and alprazolam.<sup>14</sup> Among the drugs, olanzapine is an atypical antipsychotic drug that has an affinity for multiple receptors and can not only antagonize serotonin, dopamine, and M-cholinergic receptors but also selectively inhibit dopaminergic nerve function in the diencephalic limbic system. Therefore, it plays a role in improving negative symptoms and cognitive function.<sup>15</sup> Dezopiclone is a Y-aminobutyric acid receptor agonist, and its parent zopiclone can bind to phenylenediamine receptors to produce pharmacological effects, thereby stimulating the Y-aminobutyric acid receptor and exerting sedative and hypnotic effects.<sup>16</sup> Alprazolam tablets belong to the benzodiazepine class of drugs, which have anti-anxiety, anti-depression, sedation, hypnosis, anticonvulsant, and muscle relaxation effects.<sup>5</sup> However, elderly schizophrenia with sleep disorders are prone to adverse reactions by receiving the abovementioned approaches. Focus has been laid on the combination of traditional Chinese and Western medicine treatment in clinical research.

According to the clinical symptoms of elderly patients with schizophrenia and sleep disorders, TCM classifies the condition as "insomnia" and "lack of sleep". In TCM, the liver governs catharsis and has the effect of regulating emotions and qi. Schizophrenia and sleep disorders are mostly caused by emotional abnormalities such as emotional compensation, depression, anger, or excessive thinking.<sup>17</sup> In Syndrome Differentiation of Insomnia, the sleep disorder caused by abnormal emotions is related to the loss of liver function due to emotional compensation, the stagnation of heat, and the disturbance of the mind and spirit, resulting in mental unease.<sup>18</sup> The "spirit" is the key to insomnia, and the "spirit" includes "the spirit controlled by the heart" and "the spirit controlled by the brain." As written in Medical Records of the West, "the spirit of human beings is related to physical functions, which is hidden in the brain, and derived from the heart," indicating that the "spirit" is jointly controlled by the heart and brain.<sup>18</sup> The nature of schizophrenic and sleep disorders is in the heart and brain, but their etiology is mainly related to abnormal liver cathartic function. Therefore, the treatment is to soothe the nerves and regulate liver qi.<sup>18</sup>

The Dragon Bone in the modified Yangxin Anshen decoction has the effects of calming the nerves, calming the liver, and suppressing the yang. Sour Jujube seed has sedative and hypnotic effects. Bupleurum can soothe the liver, relieving depression, and elevating yang qi. Fructus Aurantii can regulate gi and broaden the body. Paeonia Alba shows the effect of nourishing yin and softening the liver. Angelica Sinensis can nourish and activate blood. Baiziren has the effect of calming the nerves and nourishing the heart. Fushen shows the effects of calming the heart and the nerves and promoting diuresis. Polygala tenuifolia and Acorus tatarinowii can calm the mind and the nerves. Curcuma has the effects of promoting qi and resolving depression, clearing the heart, and cooling blood. Flower of Albizia julibrissima has the effect of relieving depression and calming the nerves. The effect of roasted licorice is to supplement qi and nourish yin. The combined use of various drugs has the effects of calming the mind and heart, relieving depression, soothing the liver, regulating qi and clearing the heart, and calming the liver and suppressing yang. Research by Yu et al.<sup>19</sup> asserted that olanzapine combined with risperidone can effectively improve the clinical symptoms and cognitive function of elderly patients with schizophrenia with a good overall treatment effect, without increasing adverse drug reactions. Xu et al.<sup>20</sup> also demonstrated that dezopiclone combined with olanzapine had a significant effect on the treatment of schizophrenia. It was suggested that it increased the total sleep time of patients, and improved sleep quality with a safety profile, which was worth further promotion in clinical practice. According to Peng et al.,<sup>21</sup> better treatment effects could be achieved by using TCM combined with alprazolam tablets among elderly patients with chronic insomnia, which improved their sleep status with a safety profile. Zheng et al. (22) showed that effective TCM treatment of diabetes patients with insomnia was able to significantly improve the clinical symptoms of patients, with significant effect. Consistent with earlier studies, our study showed that after treatment, the efficacy of the study group was significantly better than that of the control group, and the secondary and main symptoms of the study group were significantly lower than those of the control group (P < .05), indicating the combined use of modified Yangshen Anxin decoction and Western medicine could effectively improve the clinical symptoms of elderly patients with schizophrenia complicated with sleep disorders.

The PSQI was developed in 1989 by Dr. Buysse, a psychiatrist at the University of Pittsburgh in the United States.<sup>11</sup> This scale is suitable for evaluating sleep quality in patients with sleep disorders and mental disorders. Han et al.<sup>23</sup> depicted that Yangxin Anshen Qutan decoction combined with Dong-shi Qi-xue liaofa had a significant effect on the treatment of insomnia, which reduced TCM syndrome scores and improved sleep quality. According to Liu et al.,<sup>24</sup> the use of Dezopiclone combined with olanzapine in the treatment of schizophrenia with sleep disorders could obtain good efficacy, which improved the quality of sleep in patients and could be widely applied. Based on our results, after treatment, the sleep quality score of the study group 2 was significantly lower than that of the control group and the study group 1 (P < .05), suggesting the combined use of modified Yangshen Anxin decoction and Western medicine could effectively reduce the sleep quality score of elderly patients with schizophrenia complicated with sleep disorders.

Polysomnography is currently recognized as the gold standard for evaluating sleep, which particularly and objectively reflects the sleep status of patients. An earlier study showed that there was a conflicting phenomenon in the subjective and objective assessment of insomnia patients that most insomnia patients had a shorter perception of sleep time than polysomnography results.<sup>24</sup> Research by Shi et al.<sup>25</sup> proposed that polysomnography effectively assessed the sleep status of insomnia patients, and after treatment with effective traditional Chinese medicine decoction, it markedly improved their sleep status. According to Ren et al.,<sup>26</sup> the treatment of Alzheimer's disease and sleep disorders with Dezopiclone improved the overall treatment effectiveness, with good drug safety, which improved the sleep quality, mental state, and quality of life of patients, indicating dezopiclone was a valid drug for the disease. Our study demonstrated that after treatment, the total recording time of the two groups was comparable (P > .05), whereas the total sleep time, sleep onset latency, sleep efficiency, stage N1, N2, N3, and REM in the study group were improved when compared with the control group (P < .05), indicating that the treatment of modified Yangxin Anshen decoction combined with Western medicine was able to effectively prolong the total sleep time, stage N2, N3, and REM in elderly patients with schizophrenia and sleep disorders, improve sleep efficiency and conditions, shorten the sleep latency and stage N1.

5-HT is an inhibitory neurotransmitter that can regulate the sleep awakening cycle, promote slow-wave sleep, and thus play a sedative and hypnotic role. DA is an excitatory neurotransmitter that can promote the prolongation of arousal, stimulate DA neurons, increase arousal, and decrease sleep. MT is a physiological hypnotic agent, which is an amine hormone synthesized and secreted by the pineal gland. In the elderly, calcification of the pineal gland results in a disorder in the secretion of MT levels, resulting in an imbalance in the regularity of sleep and wakefulness.<sup>27-28</sup> A study supported by Hu et al.<sup>27</sup> showed that the serum levels of 5-HT, DA, and MT were abnormally low in the high-risk population of schizophrenia, and their levels increased after treatment with effective TCM decoction. Xu Jun<sup>28</sup> reported that traditional Chinese medicine decoction increased the serum 5-HT and DA levels in patients with insomnia after stroke, improving the sleep quality and the treatment effect. The results of this study showed that after treatment, the serum levels of 5-HT, DA, and MT in the study group were significantly lower than those in the control group (P < .05), indicating the three levels could be significantly improved using modified Yangshen Anxin decoction and Western medicine. This may due to the following aspects: according to modern pharmacology, Dragon Bone has sedative and anticonvulsant effects<sup>29</sup>; Sour Jujube seed shows pharmacological effects such as sedation, hypnosis, anticonvulsant, and enhancing immunity<sup>30</sup>; Bupleurum shows effects of anti-inflammatory, lipid lowering, enzymatic secretion, liver protection, immune regulation, and sedation<sup>31</sup>; Baiziren has sedative, hypnotic, and anoxic effects<sup>32</sup>; Polygala tenuifolia has central pharmacological activities for antidementia, anti-depression, and neuronal protection<sup>33</sup>; Acorus tatarinowii can improve cognitive impairment, which exerts anti-depression, anti-anxiety, and anti-epilepsy effects<sup>34</sup>; Curcuma is capable of regulating neurotransmitters and neuroendocrine, inhibiting neuroinflammation, protecting neurons, and has antithrombotic effect, which plays a preventive and therapeutic role in post stroke depression through multiple components, targets and and pathways<sup>35</sup>; Flower of Albizia julibrissima has various effects such as antianxiety, anti-depression, sedation, hypnosis, and oxidation resistance.36 It can be therefore concluded that modified Yangxin Anshen decoction can inhibit excitatory neurotransmitters and increase the level of inhibitory neurotransmitters.<sup>37</sup> Its combined treatment with Western medicine may change the level of neurotransmitters in patients via different mechanisms, promote the recovery of sleep structures, and thereby improve their sleep status.<sup>38</sup> However, the specific mechanism needs further research and confirmation.

This study further confirmed the effect of modified Yangxin Anshen decoction combined with Western medicine treatment on adverse reactions in elderly patients with schizophrenia and sleep disorders. The results showed that the incidence of adverse reactions in the study group was lower than that in the control group (P < .05), suggesting that modified Yangxin Anshen decoction combined with Western medicine treatment effectively reduced the incidence of adverse reactions in elderly patients with schizophrenia and sleep disorders, with safety profile.

In summary, the combined treatment of modified Yangxin Anshen decoction and Western medicine is safe and effective for elderly patients with schizophrenia and sleep disorders. It significantly alleviates the clinical symptoms, improves sleep quality and conditions, regulates polysomnography, and improves the levels of 5-HT, DA, and MT, with fewer adverse reactions, which is available for wide clinical promotion and application. However, considering the short duration of this study, more studies with longer follow-ups are warranted.

#### AUTHOR CONTRIBUTIONS

Nian Chen and Huichao Xia contributed equally to this paper.

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