

## Effects of Hyperbaric Oxygen-assisted Wuyintiaoshen Therapy on Post-stroke Depression Complicated with Insomnia and Neurotransmitter Levels

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### Keywords

Hyperbaric oxygen  
Wuyintiaoshen therapy  
Depression  
Stroke  
Neurotransmitters

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Received: 13 October 2023

Revised: 20 October 2023

Accepted: 27 October 2023

Published: 8 December 2023

*Pathogenesis and Treatment in Stroke* 2023;  
1(1): 29-38.

### Abstract

**Objective:** This study explores the effect of hyperbaric oxygen-assisted Wuyintiaoshen therapy on post-stroke depression complicated with insomnia and its effect on neurotransmitter levels. **Methods:** A total of 136 patients with post-stroke depression combined with insomnia admitted to our hospital from July 2020 to February 2023 were included and grouped according to treatment methods. 44 patients treated with hyperbaric oxygen were assigned to the hyperbaric oxygen group, 47 patients receiving Wuyintiaoshen therapy were allocated to the Wuyintiaoshen group, and 45 patients treated with hyperbaric oxygen combined with Wuyintiaoshen therapy were divided to the combined group. All three groups were treated for 5 weeks. After treatment, the clinical efficacy in the three groups was compared, and the effects of different treatment methods on the scores for Hamilton Depression Scale (HAMD) and Pittsburgh Sleep Quality Index (PSQI) were observed, and the changes of neurotransmitter levels were statistically analyzed. **Results:** After treatment, HAMD and PSQI scores in the three groups were decreased, the scores in the combined group were lower than those in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ), and the scores in Wuyintiaoshen group were lower than those in hyperbaric oxygen group ( $p < 0.05$ ). The serum levels of 5-hydroxytryptamine (5-HT) and norepinephrine (NE) in three groups were increased ( $p < 0.05$ ), the levels in the combined group were higher than those in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ), and the levels in the Wuyintiaoshen group were higher than those in hyperbaric oxygen group ( $p < 0.05$ ). The total effective rate in combined group was higher than that in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ). **Conclusion:** Hyperbaric oxygen-assisted Wuyintiaoshen therapy may have a better efficacy on patients with post-stroke depression complicated with insomnia, which can improve the degree of depression and sleep quality of patients, and promote the secretion of neurotransmitters.



## 1 Introduction

Stroke is a type of disease in which the blood vessels in the brain are blocked or suddenly ruptured, resulting in brain tissue damage caused by the obstruction of blood flow to the brain. Post-stroke depression combined with insomnia is a relatively common mood disorder in stroke patients after brain tissue damage [1,2]. Post-stroke depression combined with insomnia may be easily misdiagnosed or underdiagnosed due to the early onset of symptoms such as anxiety, depression, and sleep disorders, and may increase the risk of second stroke in patients with later severity [2].

Drugs and acupuncture are often used for clinical treatment of post-stroke depression combined with insomnia. However, there are still problems such as poor efficacy due to large individual differences between patients [3]. Acupuncture alone or in combination with other therapies has been reported to improve depression symptoms in stroke patients [4]. Hyperbaric oxygen is one of the main therapeutic methods in the rehabilitation period of stroke, previous studies have clarified the potential mechanism of hyperbaric oxygen therapy on stroke, which can promote brain oxygenation and improve the metabolism, protect the blood-brain barrier, anti-inflammation and brain edema, regulate intracranial pressure, reduce oxidative stress and cell apoptosis [5,6]. In addition, hyperbaric oxygen therapy can help stroke patients to regulate anxiety and depression, which used in the treatment of post-stroke depression combined with insomnia with better results [7,8]. For Wuyintiaoshen therapy, there is a tonal musical composition formed by fusing five scales with different emotional attributes, namely Gong, Yu, Jue, Zhi, and Shang, which can play a role in improving blood circulation, relieving depression, and improving sleep quality [9,10]. It has been reported that the Wuyintiaoshen therapy can effectively reduce

the degree of depression in patients with post-stroke depression [11]. At present, there are few researches on hyperbaric oxygen-assisted Wuyintiaoshen therapy in patients with post-stroke depression combined with insomnia in China.

Based on these data, the present study was conducted to investigate the efficacy of hyperbaric oxygen-assisted Wuyintiaoshen therapy on post-stroke depression combined with insomnia and its effect on neurotransmitter levels by comparing the changes in the scores for Hamilton Depression Scale (HAMD) and Pittsburgh Sleep Quality Index (PSQI), as well as neurotransmitter levels before and after the treatments, with the purpose of investigating the application value of hyperbaric oxygen-assisted Wuyintiaoshen therapy in the treatment of patients with post-stroke depression combined with insomnia, and providing reference and guidance for the treatment of this disease in the clinic.

## 2 Materials and methods

### 2.1 General data

#### 2.2.1 Inclusion criteria

A total of 136 patients with post-stroke depression combined with insomnia admitted to our hospital from July 2020 to February 2023 were included and grouped according to treatment methods. 44 patients treated with hyperbaric oxygen were assigned to the hyperbaric oxygen group, 47 patients receiving Wuyintiaoshen therapy were allocated to the Wuyintiaoshen group, and 45 patients treated with hyperbaric oxygen combined with Wuyintiaoshen therapy were divided to the combined group. There was no statistically significant difference in the comparison of gender, age, duration of disease, and type of stroke among the three groups ( $p > 0.05$ ), as shown in Table 1.

**Table 1** Comparison of general data between the three groups.

Groups	Hyperbaric	Wuyintiaoshen	Combined group	$\chi^2/F$	<i>p</i>	
	oxygen group (n = 44)	group (n = 47)	(n = 45)			
Gender (case)	Male	28	22	26	2.708	0.258
	Female	16	25	19		
Age (years old)	46.38 ± 3.10	45.87 ± 3.25	46.12 ± 2.96	0.306	0.737	
Duration of disease (h)	47.21 ± 5.36	48.14 ± 5.78	46.88 ± 5.29	0.654	0.521	
Type of stroke (cases)	Cerebral infarction	24	21	23	0.918	0.632
	Cerebral hemorrhage	20	26	22		

## 2.2 Inclusion and exclusion criteria

### 2.2.1 Inclusion criteria

(1) Patients met the criteria for the diagnosis of stroke, depression, and insomnia in Chinese Guidelines for the Diagnosis and Treatment of Cerebral Hemorrhage (2019) [12], Chinese Classification of Mental Disorders-Third Edition [13], and Sleep-related Breathing Disorders in the International Classification of Sleep Disorders-3 [14]. (2) Patients aged 20-65 years. (3) Patients with stable vital signs. (4) Patients without symptoms such as teeth grinding, somniloquy, and snoring when they were living alone, living apart, or sleeping with their partners

### 2.2.2 Exclusion criteria

(1) Patients receiving psychotropic drugs or related treatment within the last 3 months. (2) Patients with insensitivity or non-acceptance of music therapy. (3) Patients with sleep disorders prior to the onset of the

disease. (4) Patients with cardiac, hepatic, and renal insufficiencies. (5) Patients with malignant tumors. (6) Patients with psychiatric disorders and poor treatment adherence. (7) Patients with incomplete clinical data. (8) Pregnant and lactating women.

## 2.3 Methods

Patients in all three groups were given antidepressant medication, and 0.99 g of Wuling capsule (Zhejiang Jolly Pharmaceutical Co., Ltd., National Medical Products Administration (NMPA) Approval No.: Z19990048, 0.33 g/capsule) was taken orally after meals 3 times a day.

On the basis of antidepressant medication, a large medical air-pressurized oxygen chamber (Yantai Moon Hyperbaric Oxygen Chamber Co., Ltd., model: YG3600J-X) was applied in hyperbaric oxygen group. Patients were asked to take the supine position, with the pressure set to 2.0 ATA. The pressure was

stabilized for 60 min after 20 min of pressurization, followed by inhalation of pure oxygen for 1 h after disconnecting masks and change to breathe the air in the chamber. After 20 min, patients could get out of the chamber. Above hyperbaric oxygen therapy was performed once a day, with 10 times as a course of treatment and 3-5 days of intervals between each course.

On the basis of antidepressant medication, patients in Wuyintiaoshen group underwent treatment from Traditional Five Elements Music of China (Orthodox Form)-Jue Tune (People's Electronic Audiovisual Publishing House). Patients emptied their bladder before the treatment, lay flat in the treatment room with a quiet environment and soft light, and relaxed for 2-3 min. Then the music of Jue tone was played with the decibel of 40-60 dB, and needling was carried out on Baihui, Shenting, and Yindang acupoints for 1 min at the interval of 15 min, a total of 30 min every day and 5 times per week.

Additionally, patients in combined group received hyperbaric oxygen-assisted Wuyintiaoshen therapy. The treatment in the three groups was performed for 5 weeks.

## 2.4 Observational indicators

### 2.4.1 HAMD score

HAMD score in the three groups of patients before and after treatment was evaluated and compared. There were 17 items in HAMD scale [15] (7-17 points: mild depression, 17-24 points: moderate depression, above 24 points: severe depression). The higher score of HAMD suggested the more severe depression.

### 2.4.2 PSQI

PSQI score was assessed and compared among the three groups of patients before and after treatment. PSQI score [16] included seven dimensions, including sleep duration, sleep latency, subjective sleep quality,

etc., with a total of 21 points. The higher PSQI score hinted the poorer sleep quality.

### 2.4.3 Clinical efficacy

Clinical efficacy in the three groups of patients after treatment was quantified and compared. Assessment criteria were listed below. Significantly effective: disappearance of patients' clinical symptoms; no depression, and sleep disorder. Effective: alleviation of patients' clinical symptoms and improvement of depression and sleep disorder. Invalid: no obvious change or even deterioration of patients' clinical symptoms. Total effective rate = the number of (significantly effective + effective) cases/total number of cases  $\times$  100%.

### 2.4.4 5-hydroxytryptamine (5-HT) and norepinephrine (NE) levels

Levels of 5-HT and NE before and after treatment in the three groups of patients were tested and compared. 5 mL of fasting peripheral venous blood was drawn from all patients in the early morning, left to stand at room temperature for 30-60 min and centrifuged at 3,000 r/min for 10 min. Afterwards, serum was separated and stored at  $-20\text{ }^{\circ}\text{C}$  for measurement. Levels of 5-HT (ml057425) and NE (ml024646) were detected by enzyme-linked immunosorbent assay (ELISA), with the kits from Shanghai Enzyme-linked Biotechnology Co., Ltd (Shanghai, China).

## 2.5 Statistical methods

Statistical analysis was performed using SPSS 20.0. Count data were expressed as cases (%), comparisons between the three groups were carried out using  $\chi^2$  test, and measurement data were described as mean  $\pm$  standard deviation. One-way ANOVA was used for comparisons between groups, LSD test was employed for two-by-two comparisons between groups, and

paired samples *t*-test was applied for the comparison in the same group at different time points. Differences were considered to be statistically significant at  $p < 0.05$ .

### 3 Results

#### 3.1 Comparison of HAMD score before and after treatment in three groups

Before treatment, there was no statistically significant difference in the comparison of HAMD score among the three groups ( $p > 0.05$ ). After treatment, HAMD score in the three groups was decreased ( $p < 0.05$ ). HAMD score in combined group was lower than that in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ), and the score in Wuyintiaoshen group was lower than that in hyperbaric oxygen group ( $p < 0.05$ ). The results were displayed in [Table 2](#).

**Table 2** Comparison of HAMD score before and after treatment in three groups (mean  $\pm$  standard deviation, point).

Groups	Cases	HAMD score	
		Before treatment	After treatment
Hyperbaric oxygen group	44	17.65 $\pm$ 3.47	11.38 $\pm$ 2.05*
Wuyintiaoshen group	47	17.43 $\pm$ 3.62	9.93 $\pm$ 1.78** <sup>a</sup>
Combined group	45	17.96 $\pm$ 2.86	6.54 $\pm$ 1.32* <sup>ab</sup>
<i>F</i>		0.292	91.020
<i>p</i>		0.747	0.000

Note: \* $p < 0.05$  vs before treatment; <sup>a</sup> $p < 0.05$  vs hyperbaric oxygen group; <sup>b</sup> $p < 0.05$  vs Wuyintiaoshen group.

#### 3.2 Comparison of PSQI score before and after treatment in three groups

Before treatment, the difference of PSQI score in the three groups was of no statistical significance ( $p > 0.05$ ). After treatment, PSQI score in the three groups was decreased ( $p < 0.05$ ). PSQI score in the combined group was lower than that in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ), and the score in

Wuyintiaoshen group was also lower than that in hyperbaric oxygen group ( $p < 0.05$ ). The results were seen in [Table 3](#).

#### 3.3 Comparison of clinical efficacy in three groups

The total effective rate in combined group was higher than that in hyperbaric oxygen group and Wuyintiaoshen group ( $p < 0.05$ ). The results were shown in [Table 4](#).

**Table 3** Comparison of PSQI score before and after treatment in three groups (mean ± standard deviation, point).

Groups	Cases	PSQI score	
		Before treatment	After treatment
Hyperbaric oxygen group	44	11.98 ± 4.26	10.13 ± 2.41*
Wuyintiaoshen group	47	12.15 ± 4.30	8.56 ± 2.17* <sup>a</sup>
Combined group	45	11.76 ± 3.45	6.34 ± 2.11* <sup>ab</sup>
<i>F</i>		0.108	32.460
<i>p</i>		0.897	0.000

Note: \**p* < 0.05 vs before treatment; <sup>a</sup>*p* < 0.05 vs hyperbaric oxygen group; <sup>b</sup>*p* < 0.05 vs Wuyintiaoshen group.

**Table 4** Comparison of clinical efficacy in three groups [case (%)].

Groups	Cases	Significantly effective	Effective	Invalid	Total effective rate
Hyperbaric oxygen group	44	9 (20.45)	14 (31.82)	21 (47.73)	23 (52.27)
Wuyintiaoshen group	47	18 (38.30)	16 (34.04)	13 (27.66)	34 (72.34)
Combined group	45	24 (53.33)	17 (37.78)	4 (8.89)	41 (91.11)
$\chi^2$					16.670
<i>p</i>					0.000

### 3.4 Comparison of serum 5-HT and NE levels before and after treatment in three groups

Before treatment, there was no statistically significant difference in the comparison of serum 5-HT and NE levels among the three groups (*p* > 0.05). After treatment, the serum levels of 5-HT and NE in three

groups were increased (*p* < 0.05). Specifically, 5-HT and NE levels in the combined group were higher than those in hyperbaric oxygen group and Wuyintiaoshen group (*p* < 0.05). Likewise, these levels in Wuyintiaoshen group were higher than those in hyperbaric oxygen group (*p* < 0.05). The results were shown in [Table 5](#).

**Table 5** Comparison of serum 5-HT and NE levels before and after treatment in three groups (mean  $\pm$  standard deviation,  $\mu\text{g/L}$ ).

Groups	Cases	5-HT		NE	
		Before treatment	After treatment	Before treatment	After treatment
Hyperbaric oxygen group	44	74.58 $\pm$ 11.42	96.52 $\pm$ 12.65*	4.21 $\pm$ 0.36	4.96 $\pm$ 0.34*
Wuyintiaoshen group	47	72.84 $\pm$ 10.39	99.34 $\pm$ 11.40* <sup>a</sup>	4.18 $\pm$ 0.30	5.28 $\pm$ 0.54* <sup>a</sup>
Combined group	45	73.65 $\pm$ 9.46	153.27 $\pm$ 13.72* <sup>ab</sup>	4.23 $\pm$ 0.28	6.17 $\pm$ 0.43* <sup>ab</sup>
<i>F</i>		0.315	290.100	0.295	88.240
<i>p</i>		0.730	0.000	0.745	0.000

#### 4 Discussion

With the purpose of finding a more effective way to treat patients with post-stroke depression combined with insomnia, this study explored the application value of hyperbaric oxygen-assisted Wuyintiaoshen therapy for them. Results in our study revealed that hyperbaric oxygen-assisted Wuyintiaoshen therapy had a better efficacy for patients with post-stroke depression combined with insomnia.

HAMD scale is clinically used to assess the degree of depression, with higher score indicating more severe depression. This study uncovered that the degree of depression improved in all patients after treatment, and the efficacy of patients treated with hyperbaric oxygen-assisted Wuyintiaoshen therapy was better, with greater improvement in the degree of depression. Neurological deficits in post-stroke patients lead to impaired physical functioning and trigger emotional and behavioral changes [17]. Hyperbaric oxygen therapy can improve tissue oxygen supply and brain tissue metabolism, and prevent the damage of oxygen free radicals to the neural structure, thus promoting the repair of brain damage, increasing the levels of 5-HT and NE in the body, and achieving the purpose of

treating post-stroke depression [18]. By the way of adjusting the music and sound waves based on the patient's own condition, Wuyintiaoshen method, which includes psychological, physiological, and physical therapies, can regulate the abnormal vibration frequency caused by the patient's organs, and strengthen the effect of acupuncture while treating the specific vibration frequency to soothe the patient's emotion, and then effectively reduce the depression [19]. Therefore, hyperbaric oxygen-assisted Wuyintiaoshen therapy may be able to better improve the degree of depression in patients with post-stroke depression combined with insomnia.

PSQI scale is clinically used to estimate patients' sleep, with a higher score indicating poorer sleep quality. In our current study, the sleep quality of all patients was improved after treatment, and better improvement of the sleep quality was witnessed in patients treated with hyperbaric oxygen-assisted Wuyintiaoshen therapy. Post-stroke patients with impaired cerebral aerobic metabolism will trigger changes in brain cell function and morphology, blocking neural pathways and inhibiting nervous system excitability, thereby leading to sleep disorders such as difficulty in falling asleep and inability to sleep deeply. Some medications

used in the treatment of stroke and its comorbidities will also trigger sleep disorders [20,21]. Hyperbaric oxygen therapy can help patients accelerate the establishment of collateral circulation and cerebral vascular repair process, elevate the tissue oxygen content, maintain the normal level of intra- and extracellular ions, enhance cerebral microcirculation, activate the aerobic metabolic activity of cerebral nerve cells, restore the function of cerebral cortex, potentiate the ability of self-regulation, and improve the quality of sleep [22,23]. Wuyintiaoshen therapy stimulates the parietal and frontal lobes of the brain by needling Shenting, Yindang, and Baihui acupoints to build up the damaged neural reflex arcs, and simultaneously regulates 5-HT neurons in the medulla oblongata and pons to promote the secretion and synthesis of 5-HT and help them convert into melatonin to regulate patients' sleep [19]. Hence, hyperbaric oxygen-assisted Wuyintiaoshen therapy may be able to better improve the sleep quality of patients with post-stroke depression combined with insomnia.

5-HT, as an inhibitory neurotransmitter, is mainly secreted and regulated by the hypothalamus, which can regulate physiological activities such as mood, sleep, behavior, etc. NE mainly acts in the hypothalamus, thalamus, and basal forebrain, which can stimulate and regulate cortical activity and arousal, and is involved in the maintenance of electroencephalographic arousal. A decrease in its level indicates depression and poor quality of sleep [24,25]. Our study demonstrated that the sleep quality of patients treated with hyperbaric oxygen-assisted Wuyintiaoshen therapy was better, further illustrating the better efficacy of hyperbaric oxygen-assisted Wuyintiaoshen therapy. Hyperbaric oxygen-assisted Wuyintiaoshen can strengthen the nerve repair function, reduce the severity of neuroinflammatory response to stroke, regulate the abnormal release of neurotransmitters, inhibit 5-HT

uptake, promote the synthesis and secretion of NE in large quantities, and effectively prevent the occurrence of depression and sleep disorders [26,27]. Thus, hyperbaric oxygen-assisted Wuyintiaoshen may have better efficacy on the patients with post-stroke depression complicated with insomnia, which can increase the 5-HT and NE levels.

In conclusion, hyperbaric oxygen-assisted Wuyintiaoshen therapy may have a better efficacy on patients with post-stroke depression complicated with insomnia, which can improve the degree of depression and sleep quality of patients, and promote the secretion of neurotransmitters.

#### **Acknowledgements**

Not applicable.

#### **Conflict-of-Interest**

The authors declare no conflicts of interest.

#### **Authors' contributions**

Conceptualization: Xiaoyang Chen; Data curation: Chenfei Huang; Formal analysis: Xiaoyang Chen; Methodology: Chenfei Huang; Writing – original draft: Xiaoyang Chen; Writing – review and editing: Chenfei Huang; All authors have read and agreed to the published version of manuscript.

#### **Ethics approval and consent to participate**

This study was approved by Medical Ethics Committee, and patients were informed and agreed.

#### **Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### **Availability of Data and Materials**

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

#### **Supplementary Material**



Not applicable

## References

- [1] Xu Y GY, Liu Z, et al. Prevalence and recurrence of different types of stroke combined with chronic diseases in Bao'an District, Shenzhen, China, 2010-2019. *Chinese Journal of Prevention and Control of Chronic Diseases* 2022; 30(10): 784-787.
- [2] J K. Post-stroke Mood and Emotional Disturbances: Pharmacological Therapy Based on Mechanisms. *Journal of Stroke* 2016; 18(3): 244-255.
- [3] Tramacere I BG, Banzi R, et al. Comparison of statins for secondary prevention in patients with ischemic stroke or transient ischemic attack: a systematic review and network meta-analysis. *BMC Medicine* 2019; 17(1): 67.
- [4] Ching WL LH, Guo JW, et al. Acupuncture for post-stroke depression: a systematic review and network meta-analysis. *BMC Psychiatry* 2023; 23(1): 314.
- [5] Zhai WW SL, Yu ZQ, et al. Hyperbaric oxygen therapy in experimental and clinical stroke. *Medical Gas Research* 2016; 6(2): 111-118.
- [6] Yan Y ZX, An X, et al. The application and perspective of hyperbaric oxygen therapy in acute ischemic stroke: From the bench to a starter? *Frontiers in Neurology* 2022; 13: 928802.
- [7] Hadanny A GH, Fishlev G, et al. Hyperbaric oxygen can induce neuroplasticity and improve cognitive functions of patients suffering from anoxic brain damage. *Restorative Neurology and Neuroscience* 2015; 33(4): 471-486.
- [8] Hadanny A AS, Suzin G, et al. Effect of hyperbaric oxygen therapy on chronic neurocognitive deficits of post-traumatic brain injury patients: retrospective analysis. *BMJ Open* 2018; 8(9): e023387.
- [9] Wang J ZH, Zhu W, et al. Application of five-tone divine method in patients with secondary insomnia and post-stroke depression. *Nursing Research* 2022; 36(1): 114-117.
- [10] Tian J ZC, Wang XH. Application effect of five-tone god method in patients with post-stroke depression and sleep disorders. *Chinese Journal of Convalescent Medicine* 2023; 32(3): 290-293.
- [11] Liu L DY, Wang J, et al. Clinical, gut flora, and serum serotonin responses to Wuyintiaoshen therapy in patients with mild-to-moderate post-stroke depression and liver qi stagnation and spleen deficiency syndrome. *Chinese General Practice Journal* 2021; 24(30): 3882-3887.
- [12] Branch CMAN. Chinese Medical Association Neurology Branch Cerebrovascular Disease Group. Chinese Guidelines for the Diagnosis and Treatment of Cerebral Hemorrhage (2019). *Chinese Journal of Neurology* 2019; 52(12): 994-1005.
- [13] Chinese Classification of Mental Disorders-Third Edition (Classification of Mental Disorders). *Chinese Journal of Psychiatry* 2001; 3): 59-63.
- [14] Li Q WQ. Sleep related breathing disorders in international classification of sleep disorders-3. *Chinese Journal of Tuberculosis and Respiratory Diseases* 2014; 37(12): 883-884.
- [15] M H. A rating scale for depression. *Journal of Neurology, Neurosurgery, and Psychiatry* 1960; 23(1): 56-62.
- [16] Buysse D RC, Monk T, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 1989; 28(2): 193-213.
- [17] Wang L FX, Wang H, et al. Association of post-stroke depression with demographic factors, vascular risk factors and stroke features in Chinese elderly population. *Chinese Journal of General Practitioners* 2017; 15(2): 286-288.
- [18] Liu S QX, Wei Q, et al. A controlled view of venlafaxine alone and in combination with mirtazapine in the treatment of first-episode depression. *Journal of Guangxi Medical University* 2014; 31(6): 1001-1002.
- [19] Wang Y WT. Theoretical Basis and Clinical Application of Five Tone Therapy in the Treatment of Emotional Diseases. *Chinese Medical Journal* 2022; 37(1): 50-53.
- [20] Hermann D BC. Role of sleep-disordered breathing and sleep-wake disturbances for stroke and stroke recovery. *Neurology* 2016; 87(13): 1407-1416.
- [21] Cai H WX, Yang G. Sleep Disorders in Stroke: An Update on Management. *Aging and disease* 2021; 12(2): 570-585.
- [22] Mei S WM. Efficacy of hyperbaric oxygen treating insomnia after cerebral infarction. *Chinese Journal of Rehabilitation* 2018; 33(3): 195-198.
- [23] Peng Z YA, Yang Q. The effect of hyperbaric oxygen on intracerebral angiogenesis in rats with intracerebral hemorrhage. *Journal of the Neurological Sciences* 2014; 342(1-2): 114-123.
- [24] Guo C LH, Zhuang H, et al. Efficacy and Mechanism of Action of Wuyintiaoshen Therapy in Patients with Post-stroke Insomnia. *Chinese General Practice Journal* 2022; 25(12): 1475-1481.
- [25] Chen N LM. Efficacy of Jieyu Pills Combined with

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Citalopram on Refractory Depression and Its Effects on Serum Norepinephrine, 5-HT, and Brain-derived Neurotrophic Factor. *Chinese General Practice Journal* 2017; 20(S2): 338-340.

[26] Bhatt S DT, Manjula S, et al. 5-HT<sub>3</sub> receptor antagonism a potential therapeutic approach for the treatment of

depression and other disorders. *Current Neuropharmacology* 2021; 19(9): 1545-1559.

[27] Boku S NS, Toda H, et al. Neural basis of major depressive disorder: Beyond monoamine hypothesis. *Psychiatry and Clinical Neurosciences* 2018; 72(1): 3-12.