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CLINICAL RESEAPCH

Effect of Auricular Acupuncture Combined with Electroacupuncture on Sleep Quality, Neurotransmitter and Hormone Levels in Menopausal Insomniacs

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Keywords

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Abstract

Objective To explore the effects of auricular acupuncture combined with electroacupuncture on sleep quality, neurotransmitter and hormone levels in menopausal insomniacs, in order to provide a potential clinical treatment method. **Methods** A total of 138 patients with menopausal insomnia who treated in our hospital from February 2018 to February 2020 were selected and divided into a control group (received electroacupuncture treatment) and an observation group(received combined treatment of auricular acupuncture and electroacupuncture) , with 69 cases in each group. The Traditional Chinese Medicine syndrome scores, sleep quality, sex hormone levels, and neurotransmitter levels before and after treatment were compared between the two groups of patients, and the occurrence of adverse reactions during the treatment of the two groups was compared. **Results** After treatment, in the observation group,no serious adverse reactions and higher levels of estradiol, 5-hydroxytryptamine were observed ,while the rest indices were found to be lower compared to those before treatment and those in the control group. **Conclusion** The combined therapy of auricular acupuncture with electroacupuncture has potential in treating menopausal insomniacs.

Introduction

Climacterium refers to a period of time before and after menopause. Women in this period often suffer from a series of menopausal syndrome symptoms such as irritability, anxiety, hot flashes, sweating and insomnia due to the influence of factors such as ovarian function decline, endocrine disorder, social role change and so on [1]. Therein, insomnia is one of the most common symptoms of menopausal women, with insomnia-affected patients mainly manifested as difficulty in falling asleep, frequently dreaming, easy to wake after sleep and early wakening. Long-term insomnia will affect the physical recovery of menopausal women, leading to decreased immunity, waning attention and declined memory, which seriously harms women's physical and mental health [2]. Currently, most patients with menopausal insomnia are treated clinically with western medicine, such as sedative or hypnotic pills and hormone replacement therapy. Although this kind of therapy can solve the problem of falling asleep for patients, long-term use of sedative sleeping drugs has great side effects, and patients are prone to drug dependence and can appear with other adverse reactions such as drug resistance and addiction [3]. Therefore, seeking a safer and more effective treatment method is an urgent problem to be solved in clinical practice. With the continuous deepening on the theoretical research of Chinese medicine, Chinese medicine has achieved better curative effects in the treatment of insomnia. Acupuncture and moxibustion, as a simple and inexpensive external treatment of traditional Chinese medicine (TCM) with small adverse reactions, has its unique advantages in the clinical treatment of insomniacs [4]. Auricular acupuncture is an important part of acupuncture and moxibustion, and it is a method of treating diseases through acupuncture and moxibustion on the auricle [5]. At present, research reports on the treatment of menopausal insomniacs by auricular acupuncture combined with electroacupuncture are rare. This study explored the effects of auricular acupuncture combined with electroacupuncture on the sleep quality and the levels of neurotransmitter and hormone of menopausal insomniacs, in order to provide a reference for the selection of clinical treatment methods.

Materials and Methods

General information

A total of 138 patientss of menopausal insomniacs treated in our hospital from February 2018 to February 2020 were selected and divided into a control group and an observation group according to the random number table method, with 69 cases in each group. Control group: aged 42-58 years, with an average age of (49.34±5.64) years old and a disease course of 3 months to 4 years, with an average disease course of (2.28±0.70) years; Observation group: aged 44-56 years, with an average age of (50.40±4.92) years old and a disease course of 5 months to 4 years, with an average disease course of (2.40±0.65) years; There was no significant difference between the two groups in general information (P>0.05), which however indicates comparability. This study was approved by the Medical Ethics Committee of our hospital, and all patients voluntarily participated in the study and had signed the informed consent. Inclusion criteria: ①40 years old ≤ age ≤ 60 years old; ②Patients were diagnosed with menopausal insomnia according to the clinical symptoms and physical examinations[6]; ③Patients who have not taken sedative hypnotics in the most recent month; ④Patients with complete clinical medical records. Exclusion criteria: ①Patients with secondary insomnia caused by other reasons; ②Patients with a history of mental illness; ③Patients with organic ovarian disease, bilateral ovariectomy, and premature ovarian failure; ④Patients with severe cardiac, hepatic and renal dysfunction.

Methods

Control group

The control group was treated with electroacupuncture**.** The acupoints selected were listed: the Shenmen, Sanyinjiao, Sishencong, Zhaohai, Anmin, Shenmai, Xinyu and Shenyu. Operation method: after the local skin at the acupoints of the patients was disinfected with medical alcohol, the 0.25×40mm (Wujiang

Jiachen Acupuncture Equipment Co., Ltd.) disposable sterile acupuncture needles of Jiachen brand were used to pierce directly. Then, the needle was connected to Han's WQ1002F therapeutic device, whose positive and negative electrodes were connected on the both sides of the Anmian, Shenmen, Xinyu, Sanyinjiao, and Shenyu respectively, with current intensity at 0.5-1 mA, density wave and frequency at 2Hz/2Hz, and the tolerance of patients and their muscle fibrillation taken as the degree. The needle was retained for 30 minutes, and used for piercing once every other day, 3 times a week, with 6 times counted as a course of treatment, and 3 consecutive courses of the treatment were performed.

Observation group

The observation group was treated with auricular acupuncture combined with electroacupuncture. The electroacupuncture treatment was the same as it performed in the control group. Auricular acupuncture: the auricular acupoints are the sensitive points of the distribution area of the auricular vagus nerve between the cymba and cavity of the auricular conchae (such as the Sympathy, Heart, Kidney, Subcortex and Shenmen). After the local skin at the acupoints of the patients was disinfected with medical alcohol, the 0.25 40mm (Wujiang Jiachen Acupuncture Equipment Co., Ltd.) disposable sterile acupuncture needles of Jiachen brand were inserted in the skin with a depth of 0.3 inches in the direction of 15°, and the gain of gas was considered as the end of needle piercing. The needle was retained for 30 minutes, and used for piercing once every other day, 3 times a week, with 6 times counted as a course of treatment, and 3 consecutive courses of the treatment were performed.

Observation index

TCM symptoms scores

According to the "Guiding Principles for Clinical Research of New Chinese Medicines" [7], the scores of TCM syndromes of the two groups of patients were evaluated, including seven dimensions, including dizziness and tinnitus, insomnia and dreaminess, dysphoria in chestpalms-soles, heat flashing and night sweating, waist and knee weakness, fatigue and forgetfulness, and heart palpitations and restlessness. Each dimension is scored as 0, 2, 4, and 6 points according to degrees, namely no, being light, being moderate, and being heavy. The higher the score was, the more severe the patient's symptoms were.

Sleep quality

The Pittsburgh Sleep Quality Index (PSQI) Rating Scale [8] was used to evaluate the patient's sleep quality. The scale contains 7 dimensions including sleep quality, time to fall asleep, sleep duration, sleep efficiency, sleep disorders, and daytime dysfunction. The score for each dimension was 0-3 points, and the score range for each dimension was 0-21 points. The higher the score was, the worse the patient's sleep quality was.

Serum indexes

Three mL of fasting peripheral venous blood was extracted from the patients before and after treatment. After the separation of serum from the blood, the levels of serum estradiol (E2), follicle stimulating hormone (FSH), and luteinizing hormone (LH) was detected by an automatic chemiluminescence immune-analyzer. The levels of 5-hydroxyserotonin (5-HT) and norepinephrine (NE) in 2 groups were detected by high performance liquid phase fluorescence assay, which was strictly followed the instructions of the kits provided by Abbott Laboratories (China) .

Adverse reactions

The incidence of adverse reactions, including needle sickness and broken needles, was observed and recorded in the two groups.

Statistical analysis

Statistical analysis was performed using SPSS 22.0. Measurement data were presented by mean ± standard deviation ($\bar{x}\pm s$), and compared by the *t* test. $P<0.05$ was considered statistically significant.

Results

Comparison of TCM syndrome scores between the two groups before and after treatment

Before treatment, there was no significant difference in TCM syndrome score between the two groups of patients (P>0.05); the scores of TCM syndromes including dizziness and tinnitus, insomnia and dreaminess, dysphoria in chestpalms-soles, heat flashing and night sweating, waist and knee weakness, fatigue and forgetfulness, and heart palpitations and restlessness after treatment were significantly lower than those before treatment, and those in the observation group was significantly lower than those in the control group (P>0.05), as shown in Table 1.

Table 1 Comparison of TCM syndrome scores between the two groups before and after treatment

Groups	Number of cases	Insomnia and dreaminess		Dysphoria in chestpalms-soles		Waist and knee weakness		Dizziness and tinnitus	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	69	4.12±1.10	1.46±0.53*	4.32±1.25	1.95±0.65*	3.72±0.84	2.16±0.65*	4.18±0.95	1.74±0.50*
Control group	69	4.03±1.16	2.15±0.64*	4.38±1.30	2.67±0.82*	3.67±0.72	2.65±0.58*	4.08±1.06	2.64±0.76*
t		0.464	-6.847	-0.274	-5.674	0.373	-4.672	0.584	-8.218
P		0.643	0.000	0.784	0.000	0.710	0.000	0.560	0.000

Groups	Number of cases	Heart palpitations and restlessness		Heat flashing and night sweating		Fatigue and forgetfulness	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	69	4.56±0.84	2.10±0.62*	4.22±0.87	2.20±0.64*	3.76±0.91	1.92±0.60*
Control group	69	4.44±0.90	2.84±0.78*	4.12±0.93	2.95±0.79*	3.85±0.99	2.48±0.66*
t		0.810	-6.169	0.652	-6.128	-0.556	-4.963
P		0.420	0.000	0.515	0.000	0.579	0.000

Note: Compared with those before treatment: *P<0.05

Comparison of PSQI scores between the two groups before and after treatment

Before treatment, there was no significant difference in PSQI scores between the two groups of patients (P>0.05); the PSQI scores including sleep quality, time to fall asleep, sleep duration, sleep efficiency, sleep disorders, and daytime dysfunction after treatment were significantly lower than those before treatment, and those in the observation group was significantly lower than those in the control group (P>0.05), as shown in Table 2.

Comparison of sex hormone levels between the two groups before and after treatment

Before treatment, there was no significant difference in sex hormone levels between the two groups of patients (P>0.05); the levels of LH and FSH in the two groups after treatment were significantly lower than those before treatment, and those in the observation group was significantly lower than those in the control group (P<0.05); The level of E2 in the two groups after treatment was significantly higher than that before treatment, and that in the observation group was significantly higher than that in the control

group (P<0.05), as shown in Table 3.

Table 2 Comparison of PSQI scores between the two groups before and after treatment

Groups	Number of cases	Sleep quality		Time to fall asleep		Sleep duration		Sleep efficiency	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	69	2.18±0.52	1.12±0.37*	2.34±0.60	1.40±0.32*	2.28±0.54	1.38±0.41*	2.34±0.54	1.42±0.45*
Control group	69	2.12±0.48	1.45±0.45*	2.25±0.57	1.62±0.48*	2.34±0.62	1.64±0.50*	2.30±0.57	1.80±0.57*
t		0.704	-4.705	0.903	-3.168	-0.606	-3.340	0.423	-4.346
P		0.482	0.000	0.368	0.002	0.545	0.001	0.673	0.000

Groups	Number of cases	Sleep disorders		Daytime dysfunction		Total points	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	69	2.40±0.55	1.16±0.37*	2.02±0.44	1.03±0.33*	13.56±3.44	7.51±2.12*
Control group	69	2.32±0.59	1.58±0.43*	2.10±0.53	1.45±0.56*	13.43±3.56	9.54±2.87*
t		0.824	-6.150	-0.965	-5.367	0.218	-4.726
P		0.411	0.000	0.336	0.000	0.828	0.000

Note: Compared with those before treatment: *P<0.05

Table 3 Comparison of sex hormone levels between the two groups before and after treatment

Groups	Number of cases	E_2（pmol/L）		LH（IU/L）		FSH（IU/L）	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	69	36.42±9.56	60.58±7.48*	42.34±6.85	30.46±5.58*	58.62±9.45	32.40±5.68*
Control group	69	37.58±8.37	52.62±8.50*	43.68±7.15	35.58±6.70*	60.35±8.74	40.62±7.22*
t		-0.758	5.840	-1.124	-4.878	-1.116	-7.433
P		0.450	0.000	0.263	0.000	0.266	0.000

Note: Compared with those before treatment: *P<0.05

Comparison of neurotransmitter levels between the two groups before and after treatment

Before treatment, there was no significant difference in the levels of neurotransmitter between the two groups (P>0.05); the level of NE in the two groups after treatment were significantly lower than that before treatment, and that in the observation group was significantly lower than that in the control group (P<0.05). The 5-HT level in the two groups after treatment were significantly higher than that before

treatment, and that in the observation group was significantly higher than that in the control group (P<0.05), as shown in Table 4.

Table 4 Comparison of neurotransmitter levels between the two groups before and after treatment

Groups	Number of cases	NE（ng/mL）		5-HT（ng/mL）	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	69	0.62±0.20	0.34±0.11*	0.42±0.12	0.59±0.18*
Control group	69	0.59±0.16	0.45±0.14*	0.44±0.14	0.51±0.15*
t		0.973	-5.132	-0.901	2.836
P		0.332	0.000	0.369	0.005

Note: Compared with those before treatment: *P<0.05

Comparison of adverse reactions between the two group

During the treatment, there were no serious adverse reactions in patients of the two groups, and no phenomena such as needle sickness and needle breaking occurred.

Discussion

At present, the exact pathogenesis of menopausal insomnia has not yet been fully elucidated. Clinical studies believe that the occurrence of menopausal insomnia is related to a variety of factors, such as reduced melatonin secretion, social psychological factors, changes in the level of sex hormones in the body, and emotional changes caused by menopause [9]. Menopausal insomnia belongs to the categories of "insomnia at night", "unrested eyes" and "pre- and post-menopausal symptoms" in TCM. "Suwen•Ancient innocence" has documented that when women live at the age of 49 which is 7 years multiplied by 7 years, they become weak in the conception vessel, deficient in the Taichong vessel, and lacking in the Tiangui, which leads to menopause, thus inducing body aging and infertility, and it has also said that the Qi in the kidney flourishes will result in the beginning of the menstruation, while the pause of the menstruation is related to the weakened Qi in the kidney

, indicating that the strength of female reproductive function is the result of the ups and downs of kidney Qi. Women at the age of 7 multiplied by 7, namely menopausal women, would appear with kidney Qi gradually declining, exhaustion of the thoroughfare and conception vessels, the Tiangui gradually exhausted, and Kidney Yin deficiency, which results in imbalance of yin and yang. In addition, since the liver and kidney are homologous, a lack of blood in the liver will pose emptiness of the heart arteries and veins to deprive nutrition offered by the blood to the heart and cause restlessness, resulting in insomnia [10-11]. Therefore, exhaustion of the thoroughfare and conception vessels, deficiency of kidney Yin, overactive heart fire, and incompatibility of Yin and Yang are the basic pathogenesis of menopausal insomnia, and the treatment should focus on tonifying kidney, regulating qi, and modulating Yin and Yang.

At present, acupuncture-moxibustion therapy is the most widely used “green therapy” in non-drug treatment with TCM, and it is safe and easy to perform with fewer adverse reactions. Electroacupuncture and auricular acupuncture are the more common treatment methods in acupuncture-moxibustion therapy [11]. This study selected the acupoint for electroacupuncture in the treatment of menopausal insomnia mainly based on the theories of yin-yang-dominated sleep, nutrition-immunity-dominated sleep and God-dominated sleep in TCM. These theories have held that acupuncture on the Shenmen acupoints can effectively distribute the "original energy", nourish the mind, regulate the heart function, so as to command the spirit and emotions. when acupuncture is performed on the Shenmen combined with the Sishencong and Anmian, mind-tranquilizing and

excitement-allaying effects can be achieved, and the function of invigorating the spleen, nourishing the heart, nourishing the blood and calming the mind can be exerted through acupuncture on the Sanyinjiao. Shenmai and Zhaohai, the intersection points of the eight meridians, are connected to the Yang and Yin Qiao meridian that dominate sleep respectively. Acupuncture on the Xinshu and Shenshu can play the role to tonify the kidney, comfort the heart, awaken the brain and calm the mind [12]. According to TCM, the ear is closely connected with the viscera, and among the twelve meridians, there are six yang meridians directly ascending to the ears, and these meridians can communicate with the various viscera of the human body through acupuncture on the auricular acupoints via the meridians that enter the ear or pass through the ear, thus coordinating the whole body [13]. Acupuncture on the acupoints in the sympathy of ear has a strong role in calming the mind and tranquilizing the mind. Acupuncture under the ear cortex can reinforce yang and nourish essence, regulate essence and blood, nourish the brain and calm the mind. Acupuncture at the related reaction points of the ear, heart, and kidney exerts effects such as clearing the heart fire and tranquilize the mind. Kidneys has the function of nourishing Yin, clearing heat and calming the mind. Therefore, acupuncture on the ear sympathy, heart, kidney, subcortex, and Shenmen acupoints can collaborate with the functions of the heart, kidney, liver, spleen and other sleep regulation-related viscera to achieve the balance of Yin and Yang, improve clinical symptoms, and prolong the sleeping time. In addition, modern pharmacological studies have found that the five acupoints, namely the ear sympathy, heart, kidney, subcortex, and Shenmen acupoints selected in this experiment are all distributed in the vicinity of the concha cavity, triangle fossa, and helix foot, and all located at the sensitive points in the distribution area of the ear vagus nerve. Stimulation by acupuncture increases the blood flow velocity of the left and right vertebral artery and basilar artery, improves cerebral blood supply, and relieves symptoms such as dizziness and headache [15]. The results of this study found that the dimensions and total score of TCM symptoms and PSQI in the observation group after treatment were significantly lower than those before treatment and significantly lower than those in the control group, which indicates that compared with electroacupuncture alone, auricular acupuncture combined with electroacupuncture in the treatment of menopausal insomnia is more beneficial to improving the patient's clinical symptoms and quality of sleep.

Studies have shown that the pathogenesis of menopausal insomnia is closely associated with factors such as imbalance in the body's estrogen secretion and disordered neurotransmitter levels [16]. The most obvious change in perimenopausal women is the decline of ovarian function and the decreased sensitivity of follicles to FSH and LH, which leads to a decrease in the body's estrogen level but increases in the levels of FSH and LH. In menopausal women, lowered estrogen levels cause vasomotor symptoms such as hot flashes and night sweats, which often result in wakening at night and thus trigger insomnia in the patients. In addition, estrogen can affect the concentration of neurotransmitters in the central nervous system such as dopamine, 5-HT and NE to induce autonomic nervous dysfunction, thereby affecting the sleep and wake cycles of menopausal women [17]. 5-HT is an inhibitory neurotransmitter that can make the human body produce pleasant emotions. Menopausal women affected by the decline of estrogen levels can easily experience the inhibited synthesis and secretion of 5-HT in the body, which can cause depression, irritability and other symptoms, thus triggering insomnia. NE is an excitatory neurotransmitter synthesized and secreted by sympathetic postganglionic neurons, and its excessive secretion can easily cause the cerebral cortex to become highly excited and create difficulty falling asleep [18]. The results of this study found that the levels of LH, FSH, and NE in the observation group were significantly lower than those before treatment and those in the control group, and the levels of E_2 and 5-HT were significantly higher than those before treatment and those in the control group, indicating that compared with treatment with electroacupuncture

alone, treatment with auricular acupuncture combined with electroacupuncture is more conducive to improving the level of sex hormones in insomniacs and maintaining the stability of their body's neurotransmitter levels. The adjustment mediated by auricular acupuncture on the body's sleep mechanism mainly plays a role in neuroendocrine homeostasis through the vagus nerve [19]. Stimulating the sensitive points in the distribution area of the auricular vagus nerve in the cymba and cavity of the auricular conchae can activate the visceral sensory afferent fibers that project to the nucleus of the solitary tract from the auricular branch of the vagus nerve, thereby regulating the function of inner organs, such as endocrine. Acupuncture at acupoints in the ear sympathy can adjust vasomotion and improve the blood supply to the brain, thus reducing symptoms such as dizziness and headache. The subauricular cortex has functions including regulating the excitation and inhibition of the cerebral cortex, and improving the levels of the body's neurotransmitters such as NE and 5-HT. Acupuncture on the Erxin and kidney acupoints can increase estrogen levels in the serum of patients with menopausal insomniacs, reduce the levels of LH and FSH, promote the body's absorption of calcium, and improve the clinical symptoms caused by endocrine disorders [20]. Adjustment of the relationship between the vagus nerve and the sympathetic nerve by stimulating the acupoints regulates the neuroendocrine system and thus redress the symptoms of insomnia. The results of this study also suggested that during the treatment period, there were no serious adverse reactions occurring in the two groups of patients, indicating that the application of auricular acupuncture combined with electroacupuncture in the treatment of menopausal insomniacs exerts effects that are safer and more effective.

In conclusion, the application of auricular acupuncture combined with electroacupuncture in the treatment of menopausal insomniacs is more beneficial to enhancing the patients' sleep quality, improving the body's levels of sex hormones and neurotransmitters, and alleviating the patients' clinical symptoms, and exerts safe and reliable effects.

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Declaration of conflict-of-interest

The authors declare no conflict-of –interest.

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