

Clinical Observation on the Treatment of Pre and Postmenopausal Syndromes by Modified Wumei Decoction

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Abstract: *Objective:* To compare the efficacy of Wumei Decoction in pre and postmenopausal patients and its effect on follicle-stimulating hormone (FSH) and estradiol (E2). *Methods:* Sixty-four patients who attended the Department of Traditional Chinese Medicine I in Cangzhou City Central Hospital from January 2020 to January 2022 were selected and randomly divided into treatment group and control group, 32 cases in each group. The treatment group took modified Wumei Decoction orally, 1 dose of water boiled 2 times a day, divided into 2 warm doses; the control group took Livial orally, 2.5 mg/times, 1 time/day, and the observation cycles were all for 3 months. Kupperman score, FSH, E2, clinical symptoms and clinical efficacy were compared between the two groups before and after treatment. *Results:* The Kupperman score of the two groups decreased after treatment, and the difference was statistically significant; the total effective rate of the treatment group was higher than that of the control group, and the difference was statistically significant; there was no statistical significance in the comparison of FSH before and after the treatment of the two groups, but the FSH values of the two groups were significantly lower than those before, and the difference was statistically significant; there was no statistically significant difference in the comparison of E2 of the two groups before treatment, and the E2 values of the two groups were higher than those of the control group after the treatment. After the treatment, E2 of the two groups of patients was significantly higher than before, and the difference was statistically significant. After treatment, E2 of the treatment group was higher than that of the control group, and the comparison between the groups was statistically significant. *Conclusion:* There was no significant difference between modified Wumei Decoction and Livial in lowering follicle-stimulating hormone levels; modified Wumei Decoction was superior in raising oestradiol; and modified Wumei Decoction was relatively effective in improving clinical symptoms.

Keywords: Pre and postmenopausal symptoms; Estradiol; Follicle-stimulating hormone; Wumei Decoction

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1. Introduction

Due to the gradual decrease of ovarian function before and after menopause, with the fluctuation or decrease of sex hormones, women clinically manifest irregular menstruation or menopause, feeling hot and sweating, fear

of cold, dizziness and tinnitus, irritability and anxiety, depression, palpitation and insomnia, fatigue and even organic pathologies, such as high blood pressure in menopause ^[1] and osteoarthritis in menopause ^[2], which are called the evidence of pre and post-menopausal period in traditional Chinese medicine. Before and after menopause, the kidney Qi gradually declines, the decadal will be exhausted, the Yin essence is insufficient, and the heart and liver are not nourished, which is a physiological phenomenon of female reproduction ^[3], but due to the degree of decline of the kidney Qi of some women is too early or too fast, or due to external interference, which causes an imbalance of Yin and Yang (mainly in the kidneys), and then upwardly reverses to the heart, liver, and spleen, and then a series of symptoms occur, which is issued as the evidence of pre and post-menopausal period, The study investigates the usage of modified Wumei Decoction for treatment and the observations are reported below.

2. Information and methods

2.1. General information

The 64 study subjects were all patients, aged 40–55 years old, who attended the Department of Traditional Chinese Medicine I in Cangzhou City Central Hospital from January 2020 to January 2022. There were 32 cases in the treatment group, with an average age of 46.5 ± 4.4 years old; an average disease duration of 0.5 ± 5.0 years; 32 cases in the control group, with an average age of 47.1 ± 3.6 years old; an average disease duration of 0.3 ± 5.0 years; the difference between the general data of the 2 groups was not statistically significant ($P > 0.05$) and was comparable.

2.2. Case selection

Inclusion criteria:

- (1) Patients with pre and post-menopausal diagnosis:
 - (a) Menstrual disorders, mostly irregular cycles;
 - (b) Vasodilatory symptoms: Hot flashes or bouts of redness of the skin on the face or even the neck, accompanied by hot feeling, chills and sweating, lasting as short as a few seconds or as long as a few minutes, and can occur several times a day;
 - (c) Psychoneurological symptoms: Common ones include irritability, anxiety, depression, depressed mood, shortness of breath, insomnia and dreaminess;
 - (d) Auxiliary examination: FSH $> 10\text{IU/L}$, ultrasound to know the thickness of endometrium to exclude uterine and ovarian tumors.
- (2) No other medication is used during the application of modified Wumei Decoction protocol.
- (3) Those who voluntarily accept the internal treatment of traditional Chinese medicinal herbs soup and are able to adhere to it.
- (4) Those who voluntarily accept and are able to cooperate with the relevant examination.

Exclusion criteria:

- (1) Those who have used medication within 3 months;
- (2) Those who have combined gynecological tumors, cardiovascular, cerebrovascular, hepatic, renal and hematopoietic systems and other serious diseases, and patients with mental illness;
- (3) Those who have not used medication according to the regulations and who are unable to judge the efficacy of the medication, or whose information is incomplete and so on, which affects the judgment of the efficacy and safety;
- (4) Those who have an allergy to the medication in the treatment plan.

2.3. Treatment methods

2.3.1. The treatment group received modified Wumei Decoction for internal administration

- (1) Composition: black plum 30 g, *Coptidis Rhizoma* 6 g, *Phellodendron amurense* 6 g, *Pao Fuzi* 15 g (boiled), *Polygonum multiflori* 20 g, *Cistanches deserticola* 20 g, *Ramulus cinnamomi* 15 g, Stir fried white peony 15g, *Angelicae sinensis* 15 g, *Codonopsis pilosula* 15 g, *Polygni multiflori caulis* 15 g, *Triticum aestivum* 30 g, *Morus alba* leaves 30 g, *Glycyrrhiza uralensis* 10 g. One dose daily, boil in water, and take it warmly in 2 portions.
- (2) Supplement: For those individual with heavy dryness and heat, add *Lycii chinense* and *Rehmanniae glutinosa*; For excessive sweating, add calcined dragon bone and calcined oyster; For heavy menstrual flow, add *Artemisiae argyi* and *Rubia cordifolia*; For those with low menstrual flow due to deficiency of blood, add *Spatholobus suberectus* and *Rehmannia* root; For cough with phlegm, add *Acorus gramineus*; For excessive leucorrhoea, add *Kochiae scoparia* and *Cnidium monnier* fruit; For insomnia, add Jujube seed; For weak stomach, add *Poncirus trifoliata*, malt; For individual with liquified stools, reduce *Cistanches deserticola* and *Polygonum multiflori* while adding *Psoralea corylifolia* and yam. The quantities of the above medicines should not exceed 3 doses.

2.3.2. The control group received hormone replacement therapy

Oral Livial (Nanjing Ougannon Pharmaceutical Co., Ltd., National Drug Code: H20051085), 2.5 mg/d, during the period of uninterrupted and fixed time of the daily dose. 2 groups of patients should not be stopped from taking Livial and during the period of treatment of the main symptoms of other drugs have a therapeutic effect.

2.4. Monitoring indicators

Compare the efficacy of the two groups of patients and the relief of symptoms such as feeling of hotness, sweating, insomnia, dreaminess, etc. before and after treatment, as well as the changes of sex hormones FSH and E2.

2.4.1. Measurement of serum reproductive endocrine hormones

Five mL of fasting venous blood was drawn from patients before and after treatment, and the electrochemiluminescence method was used to measure FSH and E2 in serum.

2.4.2. Kupperman score

- (1) Hot rashes and sweating: Basic score: 4 points; degree score: 3 points for not less than 10 times/day, 2 points for 3–9 times/day, 1 point for less than 3 times/day.
- (2) Irritability: Basic score: 2 points; degree score: 3 points for not being able to control oneself and frequently occurring, 2 points for being able to control oneself and frequently occurring.
- (3) Insomnia: Basic score: 2 points; degree score: 3 points for frequent and serious need for medication while 2 points for frequent occurrence.
- (4) Anxiety and depression: Basic score: 1 point; degree score: 3 points for frequent occurrence and loss of confidence in life, 2 points for frequent occurrence but self-control.
- (5) Shortness of breath and fatigue: Basic score: 2 points; degree score: 3 points for serious illness requiring treatment, 2 points for frequent occurrence but not affecting work.

The total score is calculated by the sum of multiple symptom scores, and the symptom score is equal to the degree score \times basic score^[4]. Efficacy index = (pre-treatment score - post-treatment score) / pre-treatment tie score \times 100%.

2.4.3. TCM symptom score

Referring to the “*Diagnostic and therapeutic efficacy standards of Chinese medicine*” [5], there are 7 symptom items, including vaginal dryness, dreamy insomnia, irritability, tinnitus, dizziness, fatigue, lumbar and knee soreness as well as coldness and feeling of hotness and sweating. The absence of the above symptoms is counted as 0; occasional episodes but do not affect daily life is 1; frequent occurrences but can not affect daily life is counted as 2; frequent occurrences, not being able to sleep, affecting life and work, and seriously need to take medication to relieve, is counted as 3. The total score is the sum of the scores of each symptom.

2.5. Criteria for determining efficacy

Refer to the efficacy index in Kupperman’s score [6], as follows: When the efficacy index is less than 30%, it is ineffective; When the efficacy index is between 30% and 75%, it is effective; When the efficacy index is between 75% and 90%, it is very effective; When the efficacy index is more than 90%, it is considered cured. Effective rate = (number of effective cases + number of apparent effect cases + number of cured cases)/total number of cases × 100%.

2.6. Statistical methods

SPSS 16.0 statistical software was used for analysis, the comparison of the rate of count data was tested by χ^2 test, and the measurement data was expressed by mean ± standard deviation (SD), and *t* test was used. The difference was considered statistically significant at $P < 0.05$.

3. Results

3.1. Kupperman score

After treatment, the Kupperman score of the treatment group was significantly lower than that of the control group, and the difference was statistically significant. Refer **Table 1**.

Table 1 Comparison of Kupperman score between the two groups before and after treatment (Mean ± SD)

Group	Before treatment	After treatment
Treatment group (<i>n</i> = 32)	26.34 ± 4.26	9.03 ± 2.12
Control group (<i>n</i> = 32)	26.06 ± 4.23	11.57 ± 2.7
<i>t</i>	0.264	4.186
<i>p</i>	0.793	< 0.001

3.2. Clinical efficacy

The total clinical effective rate of the treatment group was significantly higher than that of the control group, and the difference was statistically significant. Refer **Table 2**.

Table 2 Comparison of clinical efficacy between the two groups (*n*, %)

Group	Very effective	Effective	Overall effective rate
Treatment group (<i>n</i> = 32)	16	13	90.63%
Control group (<i>n</i> = 32)	14	12	81.25%

3.3. FSH score

After treatment, there was no significant difference in FSH level scores in the treatment group compared to the control group ($P > 0.05$). Refer **Table 3**.

Table 3 Comparison of FSH between the two groups before and after treatment (Mean \pm SD, IU/L)

Group	Before treatment	After treatment	<i>p</i>
Treatment group ($n = 32$)	60.21 \pm 4.32	51.43 \pm 3.19	< 0.001
Control group ($n = 32$)	60.19 \pm 4.29	52.15 \pm 3.24	< 0.001
<i>t</i>	0.019	0.896	
<i>p</i>	0.985	0.374	

3.4. E2 score

After treatment, E2 level scores were elevated in the treatment group compared to the control group, and the difference was statistically significant. Refer **Table 4**.

Table 4 Comparison of E2 scores between the two groups before and after treatment (Mean \pm SD, pg/mL)

Group	Before treatment	After treatment	<i>p</i>
Treatment group ($n = 32$)	11.52 \pm 0.66	18.92 \pm 1.17	< 0.001
Control group ($n = 32$)	11.51 \pm 0.65	16.89 \pm 1.18	< 0.001
<i>t</i>	0.061	6.911	
<i>p</i>	0.952	< 0.001	

4. Typical case

Zhao XX, female, 49 years old (20 June 2021). Consultation with dryness and heat, excessive sweating, and fear of cold for 3 years, about 3–5 times a day, feeling dryness and heat, red face, she then removes her clothes, followed by sweating profusely, fear of cold after the sweating subsided, then covers the clothes and blankets back, recurrent episodes, deeply suffered from it. At the same time, the symptoms are accompanied by heartburn and impatience, insomnia and sleeplessness. There is discontinuous traditional Chinese medicine treatment, due to lack of effect. The menstrual cycle of 26 days, the menstruation period of 3 days, the last menstruation on 6–13 days, with small amount of blood, reddish colour, a small amount of blood clots, leucorrhoea is abundant and yellowish.

Sex hormones: estradiol (E2) < 5.0 pg/mL, progesterone (PROG) 0.434 ng/mL, testosterone (TESTO) 0.137 ng/mL, prolactin (PROL) 70.90 ng/mL, luteinizing hormone 47.66 mIU/mL, follicle stimulating hormone 120.8 mIU/mL, liver and kidney function, blood lipids, blood glucose are normal. Liver and kidney function, blood lipid, blood sugar are normal, with no obvious cough and phlegm, abdominal distension and dysmenorrhea. In addition, the patient has acceptable appetite, no constipation, tongue is light red with thin white greasy coating, pulse is slightly “stringy.”

Diagnosis: Imbalance of Yin and Yang, uneven heat and cold. Treatment: Calmly regulating heat and cold, adjusting Yin and Yang. Prescription: black plum 30 g, *Coptidis Rhizoma* 6 g, *Phellodendron amurense* 6 g, *Pao Fuzi* 15 g (boiled), *Ramulus cinnamomi* 15 g, fried white peony 15g, *Angelicae sinensis* 15 g, *Codonopsis pilosula* 15 g, calcined dragon bone 30 g, calcined oyster 30 g, *Polygna multiflora caulis* 15 g, *Triticum aestivum*

30 g, *Morus alba* leaves 30 g and *Glycyrrhiza uralensis* 10 g. One dose daily, boil in water, and take it warmly in 2 portions, in addition to drinking water with jujube seeds 30g every night before going to bed, and drinking water brewed with 5 slices of ginger and 5 jujubes every day.

Second diagnosis (30 June 2021): Dryness, feeling of hotness and sweating were reduced, the remaining symptoms, tongue and pulse were the same as before. Calcined dragon bone and calcined oyster were removed from the upper part of the dosage and changed to *Pao Fuzi* 15 g with an addition of *Polygonum multiflori* 20g.

Third diagnosis (12 July 2021): Normal leucorrhoea, further reduction of dryness, heat and sweating, fear of cold and better sleep. The volume of menstruation was more frequent than before, on the third day of menstruation, and is red in colour, with occasional blood clots. The patient is seen with a pale red tongue with slightly white and a slow pulse. The prescription was adjusted: black plum 300 g (kernels removed), *Rehmanniae glutinosa* 200 g, *Phellodendron amurense* 60 g, *Ramulus cinnamomic* 150 g, fried white peony 150 g, *Angelicae sinensis* 150 g, *Codonopsis pilosula* 150 g, Dansheng 200 g, *Polygmi multiflori caulis* 150 g, *Triticum aestivum* 300 g, *Polygonum multiflori* 200 g, *Cistanches deserticola* 150 g and *Glycyrrhiza uralensis* 90 g grinded into powder and added with *Pao Fuzi* 150 g and *Spatholobus suberectus* 300 g before boiling in the water for 40 minutes twice. The products are made into concentrated pills with each serving of 15 g, 2 times a day, to consolidate the treatment.

Fourth diagnosis (15 September 2021): Dryness, coldness and sweating basically disappeared, only occurring occasionally after excitement or exhaustion. Emotion became stable, diet, physical strength, excretion, menstruation is normal, tongue light red with thin white and slow pulse. The review of sex hormone six: Estradiol (E2) 15.26 pg/mL, progesterone (PROG) 0.322 ng/mL, testosterone (TESTO) 0.074 ng/mL, prolactin (PROL) 11.05 ng/mL, luteinizing hormone (LH) 28.76 mIU/mL, follicle-stimulating hormone (FSH) 81.24 mIU/mL. The medication was stopped for observation, and the patient was followed up for six months without recurrence.

5. Discussion

Women's symptoms before and after menopause are mainly due to the decline or disappearance of ovarian function. The kidney weakened early among the "five organs." The liver and kidney are the same source and the lack of kidney essence makes it difficult to run the source of blood, liver blood deficiency, there is no way to regulate^[7]. Therefore, a series of uncomfortable symptoms, such as hot, cold, excessive sweating, palpitations, irritability, insomnia, dreamy, shortness of breath, fatigue, etc. occurs, and the clinical symptoms can last for 2–5 years^[8]. Ji S *et al.* believe that women's menstruation is based on the materiality of Yin and blood, Yin and Yang are compatible, Qi and blood rushing then only menstruation starts^[9], but the Yin itself is difficult to become easy to lose, mannerisms, words and deeds are all consuming Yin, women's life and blood for use, through the birth of the foetus, childbirth and breastfeeding number of injuries to the blood, so that the body is often in the Yin and blood deficient state^[10].

Wumei pills from the "*Treatise of Fibrile Diseases*" are the main treatment of ascariasis, but the clinical application is by no means limited to this, for the cold and hot mishmash of the disease can be used. The physiological and pathological characteristics of menopause are the deficiency of Yin and Yang, the exhaustion of Tiangu, and the bias of "water and fire." Zhang Jingyue: "Yin can not be without Yang, no Qi can not be born to form, and Yang can not be without Yin, no form can carry the qi." Li Shicai in "*Water and Fire, Yin and Yang*" mentioned that "water and fire" should not be biased and should not be divided." The method of treatment when the Yin and Yang take into account, as "*Spiritual Centre: The End*" stated that Yin and Yang are

insufficient, complementary Yang is Yin exhaustion, Yin is gone when Yang off. Wumei pills traffic Yin and Yang, leveling cold and heat, reducing sweating effect is accurate, and nourish the insufficient of the Tiangui, so the original formula for the appropriate changes, more suitable for the evidence before and after the menopause. Yang deficiency is cold outside, and the loss of guards outside the Yin can not be focussed. There is a saying that “People of forty years old will have their Yin becoming half”, “water” element does not contain “wood” element, syncopated Yin are the phases of the fire delusion. Yin deficiency is the internal heat steaming compulsion of the “Jin” leakage, and therefore sweating occurs, with an astringent effect.

“Internal heat will cause disturbance” and “Hot people should be treated with cold.” Thus, *Coptidis rhizoma* and *Phellodendron amurense* can clear the heat of the upper, middle and lower triple heat and clear the annoyance in addition to its bitter cold and firm Yin properties. “Less fire will stimulate the birth of Qi” and “When the form is insufficient, it is warmed with Qi.” *Pao Fuzi* is pungent and warm, white peony is acidic and astringent. Both of them collect sweat, calm the liver and subdue Yang, which is the same as *Ramulus cinnamom* and *Glycyrrhiza uralensis*, pungent and sweet to transform Yang, sour and sweet to transform Yin. “If the essence is insufficient, replenish it with flavour.” *Polygonum multiflori* nourishes kidney Yin and replenishes kidney essence. “Strengthens the main body of water to gain more Yang” *Cistanches deserticola* warms the kidney Yang and benefits the kidney essence, to make sure it is calm and not dry. “Benefits the source of fire to eliminate Yin.” Yin and Yang are rooted in each other, Yin and Yang complement each other, Yang gets Yin” to help it become biochemically infinite, “if Yin gets help from Yin, then biochemistry will be endless,” “If Yin gets help from Yang, then everything will be inexhaustible”, total adjustment of the bias of cold and heat, balancing the misbehaviour of Yin and Yang. “Those who are good at replenishing the essence must make the Qi produce essence”, *Ginseng rhizoma* and *Angelicae sinensis* benefit Qi and blood, essence and blood of the same origin, and “accumulation of years will be more congestion”, “Yang deficiency blood will be coagulated”, “Yin deficiency blood will be stagnant.” With the increase in age, the incidence of cardiovascular disease increases, and women to blood-based, *Angelicae sinensis* nourish blood in addition to the blood, but also can activate the blood through the menstruation. *Polygoni multiflori caulis* communicate Yin and Yang, and have the effect of tranquillity. Sweat symbolizes the heart, sweat and fluid injury will damage the heart Qi, coupled with “false fire” disrupting the mind, thus the dream of restlessness, palpitations difficult to stop. “The heart disease should be treated with ingestion of wheat”, *Triticum aestivum* stabilizing the heart and mind, providing astringent effect. *Morus alba* leaves are sweet, can cool liver system and produce the element “wood.” *Glycyrrhiza uralensis* then reconcile the nature of the medicine, mediating between cold and heat, not contrary to each other and each build its own merit, Yin and Yang are balanced, cold and heat equilibrium, the days of the Tiangui to be full, sweat can be collected, mind can be peaceful, and thus menopause with no worries.

The results of this study showed that there was no significant difference between modified Wumei Decoction and Livial in lowering follicle-stimulating hormone levels; modified Wumei Decoction was superior in raising oestradiol; and modified Wumei Decoction was relatively effective in improving clinical symptoms. In terms of improving clinical symptoms, the effects of modified Wumei Decoction were relatively significant. In conclusion, modified Wumei Decoction can effectively improve clinical symptoms and sex hormone levels in pre and post-menopausal patients.

Disclosure statement

The authors declare no conflict of interest.

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