

Effects of Pressing Needles at Four Umbilical Points and Bushen Huoxue Tiaozhou Recipe Combined with Western Medicine on Follicle Stimulating Hormone, Estradiol, Anti-Mullerian Hormone, Antral Follicle Count and Ovarian Artery Blood Flow Parameters in Patients with Decreased Ovarian Reserve

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Sang *et al.*: Bushen Huoxue Tiaozhou Recipe Combined with Western Medicine

To observe the effects of pressing acupuncture at four points of the umbilical point and Bushen Huoxue Tiaozhou prescription combined with western medicine. A total of 80 patients with hypoovarian function who were admitted to our hospital from December 2018 to December 2020 were selected and divided into groups according to their treatment plan. The control group was given four-point naval acupuncture combined with western medicine treatment and the observation group was based on the control group and was treated with Bushen Huoxue Tiaozhou recipe. The number of clinically cured cases in the observation group reached 15 cases and 18 cases and 5 cases were markedly effective and effective. The total effective rate was 95.00 %, which was higher than that of the control group and was statistically significant ($p < 0.05$). After treatment, estradiol, anti-Mullerian hormone and antral follicle count of the observation group were higher than those of the control group ($p < 0.05$) and follicle stimulating hormone was lower than the control group ($p < 0.05$). After treatment, peak systolic velocity and end-diastolic velocity of the ovarian artery in the observation group were higher than those in the control group ($p < 0.05$) and resistance index and pulsatility index were low in the control group ($p < 0.05$). Pressing acupuncture at the four points of the umbilical cord and Bushen Huoxue Tiaozhou decoction combined with western medicine can promote the blood supply of the ovaries, improve the ovarian function and improve the curative effect.

Key words: Bushen Huoxue Tiaozhou recipe, ovarian artery blood flow parameters, estradiol, follicle stimulating hormone

Ovarian dysfunction refers to the decline in the ability of follicles to grow, develop and form mature follicles in the ovarian cortex and the egg quality and fertility also decline. The clinical manifestations include menstrual cycle disorders, abnormal uterine bleeding, decreased menstrual flow and even amenorrhea. It can also be accompanied by similar perimenopausal symptoms of varying degrees. If effective intervention is not carried out in time, it can progress to premature ovarian failure within a few years, which seriously affects women's reproductive health^[1].

The theory of traditional Chinese medicine (TCM) summarizes ovarian dysfunction in the categories of "little menstruation", "menstrual periods without

regular periods", "premature menstrual break" and other categories, which are related to the weakness of visceral qi and blood, stagnation of liver qi and imbalance of impaired disorders. The treatment is to promote blood circulation to remove blood stasis^[2,3]. Snap needle is a kind of thumbtack type intradermal needle, which combines the treatment advantages of burr and needle retention. Snap needle embedding has a continuous therapeutic effect, which can promote the circulation of meridian qi and blood and stimulate the body's righteousness^[4]. In this study, we observed the effects of pressing acupuncture at four points on the umbilical point and invigorating kidney and activating blood circulation combined with western medicine

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treatment on follicle stimulating hormone (FSH), estradiol (E2), anti-Mullerian hormone (AMH) and antral follicle count (AFC) in patients with ovarian dysfunction and the influence of ovarian artery blood flow parameters.

MATERIALS AND METHODS

General data:

80 patients with diminished ovarian function admitted to our hospital from December 2018 to December 2020 were selected and divided into two groups according to their treatment regimens, with 40 cases in each group.

The control group was given umbilical, 4 point press acupuncture combined with western medicine treatment. The youngest was 20 y old, the elder was 40 y old and the average was (33.25±4.15) y old. The shortest course of disease was 4 mo, the longest was 2 y, the average was (1.22±0.37) y. The minimum body mass index is 18.91 kg/m², the maximum is 25.45 kg/m² and the average is (22.28±1.41) kg/m². The observation group was treated with Bushen Huoxue Tiaozhou prescription on the basis of the control group. The youngest was 19 y old, the elder was 40 y old, the average was (32.98±4.27) y; the shortest course of disease was 4 mo, the longest was 2 y and the average was (1.20±0.39) y; the minimum body mass index is 18.86 kg/m², the maximum is 25.23 kg/m² and the average is (22.15±1.43) kg/m².

Inclusion criteria: Ovarian dysfunction meets the criteria of the “2015 Expert consensus on low ovarian response”^[5]; the onset is before the age of 40; menstrual disorders or amenorrhea, with or without infertility and laboratory indicators confirmed; age ≥18 y old, ≤40 y old; TCM dialectical classification conforms to the standard of kidney deficiency and blood stasis type in “Chinese Medicine Gynecology”^[6]; late menstruation or low volume, inability to stop menstruation, infertility is the main symptom, lumbosacral soreness, dizziness, tinnitus, hot flashes and sweating are secondary symptoms. Tongue and pulse are manifested as ecchymosis on the side of the tongue and a thin or astringent pulse; the clinical data is complete.

Exclusion criteria: Menstrual arrest during puberty, pregnancy and menopause; sensitive physique; there is a history of related systemic treatment in the past 3 mo; decreased ovarian function caused by ovarian surgery; accompanied by other serious physical diseases. The comparison of general information between the two groups of patients was not statistically significant ($p > 0.05$).

Methods:

The control group was given umbilical four-point press needles combined with western medicine treatment. On the 5th d of menstruation, the E2 tablets/estradiol dydrogesterone tablets composite package 1/10 (trade name: fenmetone, Abbott Healthcare Products BV, Netherlands, Registration Certificate No. H20110159) 1 tablet/d, taken 3 mo continuously. Pressing acupuncture points-moisture, vaginal intercourse, bilateral Yushu, disinfecting the local skin, using Japanese Qingling needles with a needle length of 1.2 mm (Japan Soriya Co., Ltd., National Instruments Injection 20162271259) were applied to the above acupoints. Patients were asked to press each point vertically for 1 min and press each point 5 times a day. Continuously pressing for 3 d, rest after 1 d and continuous use for 3 mo results in menstrual cease.

The observation group was treated with Bushen Huoxue Tiaozhou prescription on the basis of the control group. Basic prescription of Bushen Huoxue Tiaozhou prescription: Dodder 15-30 g, *Eucommia* 15 g, wolfberry 15 g, *Angelica* 12 g, *Rehmannia* 15 g, Huangjing 12 g, Dangshen 15 g, *Atractylodes* 12 g, Poria 12 g, Yam 20 g, *Ligusticum wallichii* 9 g, the root of red-rooted salvia 12-15 g, *Rhizoma Cyperi* 6 g, excrementum pteropi 10 g (wrap-decoct), pollen typhae 10 g (wrap-decoct). Add vinegar tortoise shell 12-24 g during follicular phase. Add *Cimicifuga* 3-6 g, seville orange flower 6 g, herba lycopi 10 g to promote ovulation, sliced Cornus Cervi 9 g (first decoction), Epimedium 10-12 g, raspberry 10-12 g were added in luteal phase. Liver qi stagnation, take in *Akebiae trifoliata* fruit 9 g, toosendan fruit 3-6 g. The patients of asthenic cold dysmenorrhea take cassia bark tree 3-6 g, fennel 6-9 g, 1 dose daily, decoction juice 300 ml, two times in the morning and evening. Since the 5th d of menstruation began take medicine which results in menstrual withdrawal and take continuous treatment for 3 mo.

Observation indicators and detection methods:

The efficacy standards refer to the “Guiding Principles of Clinical Research on New Chinese Medicines”^[7]: Clinical recovery: Menstrual cycle, menstrual volume returned to normal, ≥95 %, or pregnancy with infertility. Effectiveness: Menstrual cycle and menstrual volume were significantly improved, $n \geq 70$ %, < 95 %. Effective: Menstrual cycle or volume improved, $n \geq 30$ %, < 70 %. Invalid: Does not meet the above standards. Efficacy index calculation formula: $n = (\text{integral before treatment} - \text{integral after treatment}) / \text{integral before treatment} \times 100$ %.

Detection method: Before treatment and 3 mo after treatment, 5 ml fasting venous blood samples were collected and centrifuged after 1 h at room temperature and Centrifugal parameters are 3500 r/min, 10 min. The upper serum was taken to detect FSH and E2 by chemiluminescence method and AMH, leukemia inhibitory factor (LIF) and pregnancy-related proteins were detected by enzyme-linked immunosorbent assay. FSH, E2, AMH kit from Roche products, LIF, pregnancy-related protein kit from Shanghai enzyme-linked biotechnology Co., Ltd was used. The detection instrument is of RT-96A enzyme labelling instrument of Shenzhen Mairui Bio Medical Electronics Co., Ltd.

The parameters of peak systolic velocity (PSV), resistance index (RI) and pulsatility index (PI) of ovarian artery blood flow were detected by transvaginal ultrasound before treatment and 3 mo after treatment and AFC was observed. On the 3rd-5th d of menstruation, the patient took the lithotomy position and placed the probe in the posterior vaginal dome. Detection instrument used is Toshiba SAL-77A vaginal ultrasound diagnostic instrument, Japan, with probe frequency of 5.0 MHz.

Statistical methods:

Data were processed with statistical package for the social sciences (SPSS) 19.0, ($\bar{x}\pm s$) was used to describe measurement indicators, t-test was used for comparison, count data was used for the number of cases (percentage) and χ^2 test was used for comparison, with a test level of 0.05.

RESULTS AND DISCUSSION

Comparison of curative effect between two groups was carried out. In the observation group, 15 cases were cured, 18 cases were markedly effective and 5 cases were effective and the total effective rate was 95.00 %, which was higher than that of the control group, with statistical significance ($p<0.05$) (Table 1).

Comparison of FSH, E2, AMH and AFC between the two groups was observed. Before treatment, there was no significant difference in FSH, E2, AMH and AFC between the two groups ($p>0.05$). Compared with before treatment, E2, AMH and AFC in the two groups increased ($p<0.05$) and FSH decreased ($p<0.05$). After treatment, E2, AMH and AFC in the observation group were higher than those in the control group ($p<0.05$) and FSH was lower than that in the control group ($p<0.05$) (Table 2).

Comparison of endometrial receptivity indexes between the two groups was observed. Before treatment, there was no significant difference in ovarian artery blood flow parameters between the two groups ($p>0.05$). Compared with before treatment, PSV and end-diastolic velocity (EDV) of ovarian artery in the two groups increased ($p<0.05$), RI and PI decreased ($p<0.05$). After treatment, PSV and EDV of ovarian artery in the observation group were higher than those in the control group ($p<0.05$), RI and PI were lower than those in the control group ($p<0.05$) (Table 3).

TABLE 1: COMPARISON OF CURATIVE EFFECT BETWEEN THE TWO GROUPS [n (%)]

Group	Number of cases	Clinical recovery	Remarkable effect	Effective	Invalid	Total effective rate
Control group	40	9 (22.50)	15 (37.50)	8 (20.00)	8 (20.00)	32 (80.00)
Observation group	40	15 (37.50)	18 (45.00)	5 (12.50)	2 (5.00)	38 (95.00)
χ^2						4.114
p						0.043

TABLE 2: COMPARISON OF FSH, E2, AMH AND AFC BETWEEN THE TWO GROUPS ($\bar{x}\pm s$)

Group	Number of cases	FSH (IU/l)		E2 (pg/ml)		AMH (ng/ml)		AFC (↑)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	40	16.58±2.74	10.12±1.56*	27.56±3.63	38.98±4.12*	0.23±0.05	0.26±0.04*	2.61±0.59	3.85±0.65*
Observation group	40	15.98±2.82	6.38±1.02*	28.01±3.52	46.33±4.56*	0.22±0.06	0.29±0.05*	2.65±0.63	4.25±0.54*
t		0.965	12.691	0.563	7.564	0.810	2.963	0.293	2.994
p		0.337	0.000	0.575	0.000	0.421	0.004	0.770	0.004

Note: Comparison with pre-treatment * $p<0.05$

TABLE 3: COMPARISON OF OVARIAN ARTERY BLOOD FLOW PARAMETERS BETWEEN THE TWO GROUPS ($\bar{x}\pm s$)

Group	Number of cases	PSV (cm/s)		EDV (cm/s)		RI		PI	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	40	10.52±1.21	12.02±1.32*	5.12±1.01	6.56±0.98	0.75±0.08	0.70±0.06*	1.45±0.46	1.31±0.36*
Observation group	40	10.45±1.26	12.85±1.21*	5.09±1.11	7.53±1.14	0.74±0.12	0.63±0.08*	1.47±0.42	1.22±0.31*
t		0.253	2.932	0.126	4.081	0.439	4.427	0.203	1.198
p		0.801	0.004	0.900	0.000	0.662	0.000	0.840	0.234

Note: Compared to this group before treatment, *p<0.05

Comparison of safety was also observed. No adverse reactions such as gastrointestinal discomfort, rash and dizziness occurred in 80 patients during medication.

Pressing acupuncture belongs to the category of intradermal acupuncture. Pressing the needle body into the skin can play a role in acupoints massage. It can be used during shoulder-hand syndrome, migraine, primary dysmenorrhea, insomnia, cardiovascular disease, postoperative analgesia and chemotherapy. It is widely used in many fields such as anti-spitting^[8-10]. The water point selected in this study is the main point of the Ren channel, which can regulate water channels, regulate qi and relieve pain; Yinjiao is the intersection of Chongmai, Renmai and foot shaoyin, which can adjust the meridian solid band, promote water and reduce swelling. The meeting of pulse and foot shaoyin can regulate qi and relieve pain, moisten the intestines and relax bowel movements. The above mentioned four-point pressing acupuncture treatment at the umbilical can regulate Chong Ren, activate blood and regulate menstruation^[11,12].

The level of E2 in patients with hypoovarian function decreases and FSH and luteinizing hormone jointly promote the secretion of E2^[13,14]. When E2 is at a low level, negative feedback regulates the large amount of FSH secreted by the pituitary gland, which causes the level of FSH to increase^[15]. AMH is derived from female primordial germ cells, which is a stable indicator of ovarian function and is not affected by menstrual cycle, hormones, drugs, etc.,^[16]. AFC refers to the larger follicles between ovarian granulosa cells and is an important indicator of ovarian reserve function^[17]. This study found that pressing acupuncture at four umbilical points and Bushen Huoxue Tiaozhou prescription combined with western medicine can improve the curative effect, improve menstrual cycle and clinical symptoms, promote pregnancy and through laboratory index tests, it was found that four umbilical

points press acupuncture and Bushen Huoxue Tiaozhou recipe combined with western medicine to treat ovarian dysfunction can regulate the level of reproductive hormones and improve ovarian function. This study also detected two groups of ovarian artery blood flow parameters before and after treatment, found that umbilical four point press needle and Bushen Huoxue Tiaozhou prescription combined with western medicine treatment of ovarian dysfunction can improve ovarian artery PSV, EDV, reduce RI, PI, suggesting that umbilical four point press needle and Bushen Huoxue Tiaozhou prescription combined with western medicine treatment of ovarian dysfunction can improve ovarian blood supply, reduce ovarian injury caused by ischemia and hypoxia, is conducive to the protection of ovarian function. This is because the umbilical four-point press needle can promote local blood circulation and improve the blood supply of the uterus and ovaries. Kidney-tonifying drugs such as *Cuscuta*, *Eucommia ulmoides*, *Lycium barbarum* and *Rehmannia glutinosa* in Bushen Huoxue Tiaozhou prescription have similar sex hormone like effects. They can regulate the function of the hypothalamus pituitary ovarian axis and have a two way regulatory effect on reproductive function and can increase the body's immunity, function, improve ovarian responsiveness and other ways to improve ovarian reserve function^[18]. *Ligusticum wallichii*, the root of red-rooted salvia, *Rhizoma Cyperi*, excrementum pteropi, cattail pollen and other TCM for promoting blood circulation and removing blood stasis can improve pelvic blood rheology and improve uterine and ovarian microcirculation^[19].

In summary, the combination of four-point umbilical acupuncture and Bushen Huoxue Tiaozhou prescription combined with western medicine to treat ovarian dysfunction can promote blood supply to the ovaries, improve ovarian function and improve curative effect.

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Conflicts of interest:

The authors declared no conflict of interest.

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