**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 64261

**Manuscript Type:** ORIGINAL ARTICLE

***Retrospective Study***

**Clinical observation of Kuntai capsule combined with Fenmotong in treatment of decline of ovarian reserve function**

Lin XM *et al.* Kuntai capsule in reduced ovarian reserve function

Xin-Miao Lin, Miao Chen, Qiao-Ling Wang, Xiao-Min Ye, Hao-Fan Chen

**Xin-Miao Lin, Miao Chen, Qiao-Ling Wang, Xiao-Min Ye, Hao-Fan Chen,** Department of Reproductive Health and Infertility, Zhanjiang Central People’s Hospital, Zhanjiang 524037, Guangdong Province, China

**Author contributions:** Lin XM designed the experiment; Chen M drafted the work, Chen HF, Wang QL and Ye XM collected the data; Lin XM analysed and interpreted data; Chen M wrote the article. Lin XM and Chen M contributed equally.

**Corresponding author: Hao-Fan Chen, PhD, Chief Doctor,** Department of Reproductive Health and Infertility, Zhanjiang Central People’s Hospital, No. 236 Yuanzhu Road, Chikan District, Zhanjiang 524037, Guangdong Province, China. tony\_chen8928@163.com

**Received:** May 27, 2021

**Revised:** July 4, 2021

**Accepted:** August 5, 2021

**Published online:** October 6, 2021

**Abstract**

BACKGROUND

Decreased ovarian reserve function is an ovarian hypofunction disease that occurs in women before 40 years of age, leading to a decline in fertility and perimenopausal symptoms, such as irregular menstruation, amenorrhea, infertility, decreased libido, and autonomic nervous dysfunction. Fenmatong (FMT) is a compound mixture of estradiol tablets and estradiol didroxyprogesterone tablets, which can improve ovarian reserve function by supplementation of exogenous estrogen. However, this treatment has also been shown to cause breast pain, gastrointestinal discomfort, irregular vaginal bleeding, and changes in sexual desire. In severe cases, FMT can promote the development of breast cancer, endometrial cancer, and venous embolic disease.

AIM

To observe the effects of kuntai capsules and FMT on endocrine indexes and uterine artery blood circulation in patients with decreased ovarian reserve function.

METHODS

Patients (130) with decreased ovarian reserve function, who were treated in our hospital from May 2018 to May 2020, were divided into two groups: The FMT group, in which patients were treated with FMT, and the observation group, in which patients were treated with kuntai capsules. Chinese medicine symptom scores, uterine artery blood flow parameters, ovarian ultrasound test indexes, pictorial blood loss assessment chart (PBAC) scores, and hormone levels were recorded, and total effective rates were calculated for both groups.

RESULTS

The total effective rate in the observation group was higher than that in the FMT group (*P* < 0.05).After treatment, primary symptoms, including low menstrual volume, delayed menstruation, red color and thick consistency of menses, dizziness, palpitation, weakness at the waist and knee, insomnia and excessive dreaming, irritability, and dryness and astringency of the pudendal canal in the observation group decreased, and scores for primary and secondary symptoms in the observation group were significantly lower than those in the FMT group (*P* < 0.05).The systolic peak flow rate (PSV), end-diastolic flow rate (EDV), ovarian diameter, sinus follicle count, and resistance index (RI) of the uterine arteries in the observation group and FMT group increased after treatment. Notably, the PSV, EDV, ovarian diameter, and antral follicle count in the observation group were higher than those in the FMT group, whereas the RI in the observation group was lower than that in the FMT group (*P* < 0.05).The PBAC scores in the observation and FMT groups increased after treatment, with that in the observation group becoming significantly higher than that in the FMT group (*P* < 0.05). After treatment, estradiol (E2) and anti-Mullerian hormone (AMH) levels increased, whereas follicle-stimulating hormone (FSH) levels decreased in the observation group and FMT group; E2 and AMH levels became significantly higher and FSH levels became significantly lower in the observation group than in the FMT group (*P* < 0.05).

CONCLUSION

Compared with FMT, kuntai capsules promoted uterine artery blood circulation, improved menstruation, relieved symptoms, regulated endocrine function, and improved curative effects.

**Key Words:** Kuntai capsule; Fenmatong; Ovarian reserve function decline; Endocrine index; Blood circulation

**©The** **Author(s) 2021.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Lin XM, Chen M, Wang QL, Ye XM, Chen HF. Clinical observation of Kuntai capsule combined with Fenmotong in treatment of decline of ovarian reserve function. *World J Clin Cases* 2021; 9(28): 8349-8357

URL: https://www.wjgnet.com/2307-8960/full/v9/i28/8349.htm

DOI: https://dx.doi.org/10.12998/wjcc.v9.i28.8349

**Core Tip:** This paper verified that Kuntai capsule combined with Fenmatong in the treatment of decreased ovarian reserve function can promote uterine artery blood circulation, improve menstruation, alleviate symptoms, regulate endocrine and improve the curative effect.

**INTRODUCTION**

According to the theory of traditional Chinese medicine (TCM), decreased ovarian reserve function belongs to the categories of “blood exhaustion”, “early break of menopause,” and “syndrome before and after menopause”. The kidneys dominate reproduction, kidney qi filling and kidney essence deficiency lead to Tiangui failure, and blood stasis blocks collaterals. The syndrome of deficiency and excess is caused by a lack of liver qi. The principle of treatment is to nourish the liver and kidney, calm the mind, and eliminate stress. Kuntai capsules are a commonly used proprietary Chinese medicine in the clinical treatment of menopause and postmenopausal syndromes[1-3]. Although this treatment has been shown to alleviate symptoms[4], few studies have evaluated the mechanisms of action of this treatment[5-10].

In this study, we evaluated the effects of kuntai capsules compared with FMT on endocrine indexes and uterine artery blood circulation in patients with decreased ovarian reserve function.

**MATERIALS AND METHODS**

***General information***

In total, 130 patients with decreased ovarian reserve function treated in our hospital from May 2018 to May 2020 (28–40 years old; mean ± standard deviation: 33.88 ± 4.18 years) were divided into two groups according to the treatment plan after admission. There were no significant differences in general demographic characteristics between the two groups (*P* > 0.05; Table 1).

***Diagnostic criteria***

Decreased ovarian reserve function was defined according to the criteria defined by the Chinese Obstetrics and Gynecology committee[11-15], as follows: Less than 40 years of age; follicle-stimulating hormone (FSH) levels 15–25 IU and basic luteinizing hormone FSH greater than or equal to 2–3.6; menstruation disorders and rare menstruation occurring for more than 4 mo; and ultrasound showing fewer than five follicles in the ovary.

Syndrome differentiation for TCM was consistent with the standard of yin deficiency of the liver and kidney in the Diagnostic Efficacy Standard of TCM Diseases; the primary symptoms were reduced menstruation, delayed menstruation or amenorrhea, and discharge of a thick red substance, whereas secondary symptoms were dizziness and palpitations, sore waist and knees, insomnia and excessive dreaming, dryness of the vulva, irritability, and weak pulse.

***Inclusion and exclusion criteria***

The inclusion criteria were as follows: Diagnosed with decreased ovarian reserve function according to the above-listed criteria; TCM syndrome differentiation of liver and kidney yin deficiency syndrome; age greater than or equal to 18 years old and less than or equal to 40 years old; not taking other drugs; and complete clinical data available.

The exclusion criteria were as follows: History of endocrine drug use within the 3 mo prior to enrollment in the study; presence of pelvic infection, uterine fibroids, endometrial lesions, or other gynecological diseases; history of hyperandrogenemia, hyperthyroidism, hypothyroidism, or other endocrine diseases; presence of important organ diseases or hematopoietic, respiratory, and immune system diseases; and allergies to the study medications or components.

***Methods***

Patients in the FMT group were treated with a compound mixture of estradiol tablets and estradiol didroxyprogesterone tablets (trade name: fenmatong; Dutch Abbott BiologicalsB.V.; 2/10 mg; registration number H20150345),oral white tablets (containing estradiol 1 mg) once per day for 14 d before the menstrual cycle, and gray tablets (containing estradiol 1 or 10 mg) once a day during the last 14 d of the menstrual cycle; the course of treatment was 28 d, and three consecutive courses of treatment were administered. Patients in the observation group were treated with kuntai capsules (Guiyang Xintian Pharmaceutical Co., Ltd.; 0.5 g; Chinese medicine no. Z20000083) at a dose of four tablets per treatment, three times per day; the course of treatment was 28 days, and three consecutive courses of treatment were administered.

***Detection method***

Uterine artery blood flow parameters, including the systolic peak flow rate (PSV), end-diastolic flow rate (EDV), resistance index (RI), ovarian diameter, and antral follicle count were measured by ultrasound before and after three courses of treatment. The patients were instructed to avoid urination until collection, and the above indexes were evaluated in urine samples using a Philips IE33 color Doppler ultrasound with a probe frequency of 3.5 MHz.

The levels of serum sex hormone estradiol (E2), anti-Mullerian hormone (AMH), and FSH were detected *via* radioimmunoassay before treatment and on days 2–3 of the menstrual cycle. In the morning, 3 mL venous blood was collected from patients after fasting overnight and centrifuged at 3000 rpm for 10 min. The above indexes were detected using Roche E601 chemiluminescence immunoassays and a kit from Nanjing Jiancheng Bioengineering Institute.

***Analysis of curative effects***

After the treatment course, the treatments were assessed as being highly effective, wherein symptoms such as menstrual disorder, rare menstruation, vaginal dryness, and decreased libido disappeared, E2 Levels returned to normal, and FSH levels decreased by at least 50%; effective, wherein the above symptoms improved, E2 Levels improved but did not reach normal, and FSH levels decreased by 20% to 50%; or ineffective, wherein the above criteria were not met.

***Scoring standard***

TCM symptom scores were evaluated before treatment and 4 wk after treatment based on the Therapeutic Effect Criteria for Disease and Syndrome Diagnosis of TCM, including primary and secondary symptoms. The severity of symptoms was classified as none, mild, moderate, or severe, with scores of 0 to 6 for primary symptoms and 0 to 3 for secondary symptoms.

Pictorial blood loss assessment chart (PBAC) scores for menstrual bleeding were evaluated before treatment and 4 wk after treatment, according to the common score of blood staining degree and lost blood clotting for a single sanitary napkin. The blood staining degree was calculated as follows: 1, blood staining area less than or equal to 1/3; 5, blood staining area between 1/3 and 3/5; and 20, blood staining of the entire sanitary napkin. Lost blood clot:

***Statistical methods***

The data were processed using SPSS19.0, and quantitative indexes were described as means and standard deviations. Student’s *t*-tests and *χ*2 tests were used to compare quantitative data.

**RESULTS**

***Comparison of curative effects between the two groups***

In the observation group, highly effective treatment was observed for 47 cases (72.31%), whereas effective treatment was observed for 14 cases (21.54%). The total effective rate was 93.85%, which was higher than that in the FMT group (32 cases of highly effective treatment, 21 cases of effective treatment; total effective rate of 81.54%); this difference was statistically significant (*P* < 0.05; Table 2).

***Comparison of TCM symptom scores between the two groups***

Before treatment, TCM syndrome scores did not differ significantly between the observation group and FMT group (*P* > 0.05). After treatment, scores for primary symptoms, such as low menstrual flow, delayed menstruation, thick red discharge, dizziness, heart palpitations, weakness of the waist and knees, insomnia, excessive dreaming, and irritability, and scores for secondary symptoms, such as genital dryness, were significantly lower in the observation group than in the FMT group (*P* < 0.05; Table 3).

***Comparison of uterine artery blood flow parameters and ovarian ultrasound detection indicators in the two groups***

Before treatment, there were no significant differences in uterine artery blood flow parameters and ovarian ultrasound detection indexes between the observation and FMT groups (*P* > 0.05). After treatment, the PSV and EDV of the uterine artery increased in the observation group, whereas the ovarian diameter and antral follicle count increased and the RI decreased in the FMT group. Additionally, in the observation group, the PSV (38.96 ± 3.11 cm/s), EDV (15.89 ± 1.57 cm/s), ovarian diameter (2.64 ± 0.14 cm), and antral follicle count (4.91 ± 0.43) were higher, whereas the RI (0.73 ± 0.10) was lower than those in the FMT group (*P* < 0.05; Table 4).

***Comparison of PBAC scores between the two groups***

The PBAC scores increased in both groups after treatment, and the PBAC score in the observation group was higher than that in the FMT group (*P* < 0.05; Table 5).

***Comparison of hormone levels between the two groups***

After treatment, E2 and AMH levels increased, whereas FSH levels decreased in both groups. In the observation group, E2 (57.96 ± 5.17 pg/mL) and AMH (0.29 ± 0.09 ng/mL) levels were higher than those in the FMT group, whereas FSH levels (10.14 ± 1.57 IU/L) were lower than those in the FMT group (*P* < 0.05). Additionally, the total effective rate in the observation group was higher than that in the FMT group (*P* < 0.05; Tables 6 and 7).

***Safety analysis***

None of the 130 patients had adverse reactions, such as abnormal echocardiograms, abnormal liver and kidney functions, or allergic reactions.

**DISCUSSION**

The mechanism of decline in ovarian reserve function is complex and related to heredity, immunity, environment, diet, psychological factors, repeated abortion, improper contraceptive methods, and chronic ovarian diseases, among other factors[16-18]. The incidence of decline in ovarian reserve function caused by increases in life and work pressures placed on modern women is increasing every year, with a tendency to occur at younger ages. Abrahami *et al*[19] believe that unexplained infertility in young women may be a risk signal for decreased ovarian reserve function and can be used as a quantitative rather than qualitative risk factor[19]. In a cohort study, Yücel *et al*[20] found that the decline in ovarian reserve function may be an undiagnosed cause of unexplained infertility. In Western medicine, estrogen and progesterone replacement therapy is the first-line treatment for ovarian function decline, and FMT is a representative drug used for such treatment. Supplementation with exogenous estrogen and progesterone can inhibit the release of FSH and restore follicular development and ovulation through a negative feedback mechanism. The Leeangkoonsathian *et al*[21]’ study suggested that estrogen and progesterone supplementation could improve the sleep quality of postmenopausal women.

In this study, we found that treatment with kuntai capsules combined with FMT was associated with improved menstruation, reduced menstruation, delayed menstruation, thick red discharge, dizziness and palpitations, sore waist and knees, insomnia and excessive dreaming, irritability, pudendal dryness, and other symptoms. The mechanisms may be related to the effects of FMT on regulating the hypothalamus-pituitary-ovary axis through negative feedback by supplementation with estrogen and progesterone to promote follicular development and ovulation[21]. Water extracts of cooked *Rehmannia glutinosa* in kuntai capsules can regulate the response of the human body to gonadotropin and modulate endometrial receptivity. Moreover, donkey-hide gelatin can promote the function of the hematopoietic system, regulate calcium balance, improve autonomic nervous function, and alleviate symptoms of the perimenopausal period. Berberine in *Coptis chinensis* and baicalin in *Scutellaria baicalensis* Georgi not only have antipathogenic effects but also have anti-inflammatory, antipyretic, sedative, and hypnotic effects. β-Sitosterol contained in Radix Paeoniae Alba has pharmacological effects, such as hypolipidemic, anti-inflammatory, and antitumor effects. *Poria cocos* can increase the level of sex hormone secretion and protect the secretory function of the ovary.

The decrease in blood supply to the uterus and ovary is an important cause of decreased ovarian reserve function. Some researcher studied the effects of ovarian blood supply on ovarian function in healthy hybrid adult female dogs. Ligation of ovarian vessels caused a continuous decrease in 17β-estradiol and progesterone in experimental animals as well as follicular necrosis and fibrosis of ovarian tissue. These findings suggest that ligation of ovarian vessels should be used as an alternative to ovariectomy. In the current study, we found that kuntai capsules combined with FMT promoted uterine artery blood circulation, improved ovarian blood supply, prevented ovarian atrophy, and facilitated follicle formation, as demonstrated by detection of uterine artery PSV and EDV, RI, ovarian diameter, and antral follicle counts before and after treatment. This is because TCMs in kuntai capsules that promote blood circulation and tonify blood, such as *Rehmannia glutinosa* and Ejiao, can dilate the uterine artery, reduce vascular resistance, increase local blood perfusion, and reduce ischemic injury to the uterus and ovary, which is beneficial to the recovery of ovarian function.

E2 is produced by granulosa cells of growing follicles and is a common index used to monitor follicular growth and ovarian reserve function. AMH is a glycoprotein secreted by primary follicles, preantral follicles, and antral follicular granulosa cells that can inhibit the activation of primordial follicles and slow the rate of ovarian reserve depletion. Because early follicular secretion of AMH is not regulated by FSH and the level of AMH is relatively stable throughout the menstrual cycle, AMH is used as a relatively objective index for evaluation of ovarian function. FSH is a sex hormone secreted by the pituitary under stimulation of hypothalamic gonadotropin-releasing hormone, which is regulated by negative feedback of E2 and inhibin B. Increases FSH levels can lead to early collection of follicles and shortening of the menstrual cycle. In this study, we found that kuntai capsules combined with FMT regulated endocrine function in the treatment of decreased ovarian reserve function, as demonstrated by detection of the above hormone indexes. These findings provided important insights into the mechanisms through which kuntai capsules and FMT improved ovarian reserve function.

**CONCLUSION**

In this study, we found that kuntai capsules combined with FMT for the treatment of decreased ovarian reserve function promoted uterine artery blood circulation, improved menstruation, alleviated symptoms, regulated endocrine function, and improved curative effects. However, we only included patients with decreased ovarian reserve function, and not all patients had fertility problems. Therefore, we did not observe pregnancy and delivery rates for the patients after treatment. Therefore, in future clinical studies, patients with fertility problems can be screened to further explore whether kuntai capsules combined with FMT could increase fertility rates in the treatment of ovarian reserve function decline.

**ARTICLE HIGHLIGHTS**

***Research background***

Decreased ovarian reserve function, also known as premature ovarian failure, is characterized by a decrease in the level of estrogen in the body, resulting in a series of low-estrogen symptoms that adversely affect the physical and mental health of patients.

***Research motivation***

From the direction of traditional Chinese medicine (TCM) to find ways to treat the decline of ovarian reserve.

***Research objectives***

This study aimed to observe the clinical manifestations of Kuntai capsule combined with Fenmotong in treating decline of ovarian reserve function.

***Research methods***

Patients (130) with decreased ovarian reserve function, were divided into two groups: The FMT group, and the observation group, in which patients were treated with kuntai capsules. The clinical indexes including TCM symptom score and uterine artery blood flow parameters were recorded, and the total effective rate of the two groups was counted.

***Research results***

The total effective rate in the observation group was higher than that in the FMT group (*P* < 0.05). Secondary symptoms decreased in both groups, and the scores of primary and secondary symptoms in the observation group were lower than those in the femoston group (*P* < 0.05).The observation group was more conducive to promoting uterine artery blood circulation, improving ovarian blood supply, preventing ovarian atrophy, and facilitating follicular formation.

***Research conclusions***

Effect of Kuntai capsule combined with femoston on ovarian reserve function decline is better than that of femoston alone.

***Research perspectives***

Therefore, we did not observe pregnancy and delivery rates for the patients after treatment. Therefore, in future clinical studies, patients with fertility problems can be screened to further explore whether kuntai capsules combined with FMT could increase fertility rates in the treatment of ovarian reserve function decline.

**REFERENCES**

1 **Zhou Q**, Tao J, Song H, Chen A, Yang H, Zuo M, Li H. Chinese herbal medicine Kuntai capsule for treatment of menopausal syndrome: a systematic review of randomized clinical trials. *Complement Ther Med* 2016; **29**: 63-71 [PMID: 27912959 DOI: 10.1016/j.ctim.2016.09.011]

2 **Zhang J**, Fang L, Shi L, Lai Z, Lu Z, Xiong J, Wu M, Luo A, Wang S. Protective effects and mechanisms investigation of Kuntai capsule on the ovarian function of a novel model with accelerated aging ovaries. *J Ethnopharmacol* 2017; **195**: 173-181 [PMID: 27845267 DOI: 10.1016/j.jep.2016.11.014]

3 **Xue W**, Sun AJ, Zheng TP, Jiang JF, Wang YP, Zhang Y, Chen FL, Deng Y, Wang YF. [Analysis of the effects on menopausal symptoms, quality of Life, and cardiovascular risk factors of five different therapy in women at early stage of menopause]. *Zhonghua Yi Xue Za Zhi* 2016; **96**: 2327-2311 [PMID: 27524190 DOI: 10.3760/cma.j.issn.0376-2491.2016.29.009]

4 **Chen JM**, Gao HY, Ding Y, Yuan X, Wang Q, Li Q, Jiang GH. Efficacy and safety investigation of Kuntai capsule for the add-back therapy of gonadotropin releasing hormone agonist administration to endometriosis patients: a randomized, double-blind, blank- and tibolone-controlled study. *Chin Med J (Engl)* 2015; **128**: 427-432 [PMID: 25673440 DOI: 10.4103/0366-6999.151057]

5 **Liu YN**, Zhang S, Xu D, Liu B, Shan JJ, Xu JY, Zhou HF. [Meta-analysis of Kuntai Capsules combined with GnRH-a in treatment of endometriosis]. *Zhongguo Zhong Yao Za Zhi* 2020; **45**: 1933-1941 [PMID: 32489080 DOI: 10.19540/j.cnki.cjcmm.20191127.502]

6 **Ma Q**, Tan Y, Mo G. Effectiveness of Cotreatment with Kuntai Capsule and Climen for Premature Ovarian Failure: A Meta-Analysis. *Evid Based Complement Alternat Med* 2020; **2020**: 4367359 [PMID: 32215038 DOI: 10.1155/2020/4367359]

7 **Qi X**, Guo Y, Sun L. Effects of Kuntai capsule on breast pain and vaginal bleeding in postmenopausal women. *Pak J Pharm Sci* 2019; **32**: 2471-2476 [PMID: 31894037]

8 **Liu W**, Nguyen TN, Tran Thi TV, Zhou S. Kuntai Capsule plus Hormone Therapy vs. Hormone Therapy Alone in Patients with Premature Ovarian Failure: A Systematic Review and Meta-Analysis. *Evid Based Complement Alternat Med* 2019; **2019**: 2085804 [PMID: 31346337 DOI: 10.1155/2019/2085804]

9 **Zhang H**, Qin F, Liu A, Sun Q, Wang Q, Li Q, Lu S, Zhang D, Lu Z. Kuntai capsule attenuates premature ovarian failure through the PI3K/AKT/mTOR pathway. *J Ethnopharmacol* 2019; **239**: 111885 [PMID: 31009706 DOI: 10.1016/j.jep.2019.111885]

10 **Du X**, Xu L, Wang L, Heng M, Bu H, Hao Y, Tian J. Comparison of the effect and safety of Kuntai capsule and hormone replacement therapy in patients with perimenopausal syndrome: a systematic review and Meta-analysis. *J Tradit Chin Med* 2017; **37**: 279-285 [PMID: 31682369 DOI: 10.1016/S0254-6272(17)30062-6]

11 **Wang MY**, Wang YX, Li-Ling J, Xie HQ. Adult Stem Cell Therapy for Premature Ovarian Failure: From Bench to Bedside. *Tissue Eng Part B Rev* 2021 [PMID: 33427039 DOI: 10.1089/ten.TEB.2020.0205]

12 **Mashayekhi M**, Mirzadeh E, Chekini Z, Ahmadi F, Eftekhari-Yazdi P, Vesali S, Madani T, Aghdami N. Evaluation of safety, feasibility and efficacy of intra-ovarian transplantation of autologous adipose derived mesenchymal stromal cells in idiopathic premature ovarian failure patients: non-randomized clinical trial, phase I, first in human. *J Ovarian Res* 2021; **14**: 5 [PMID: 33407794 DOI: 10.1186/s13048-020-00743-3]

13 **Lin D**, Quan H, Chen K, Lin L, Lin L, Ji Q. An adolescent girl with premature ovarian failure, Graves' disease, and chronic urticaria: a case report. *J Med Case Rep* 2020; **14**: 184 [PMID: 33038927 DOI: 10.1186/s13256-020-02491-w]

14 **Bahrehbar K**, Rezazadeh Valojerdi M, Esfandiari F, Fathi R, Hassani SN, Baharvand H. Human embryonic stem cell-derived mesenchymal stem cells improved premature ovarian failure. *World J Stem Cells* 2020; **12**: 857-878 [PMID: 32952863 DOI: 10.4252/wjsc.v12.i8.857]

15 **Chen H**, Liu C, Zhu S, Li S, Zhang Q, Song L, Liang X. The therapeutic effect of stem cells on chemotherapy-induced premature ovarian failure. *Curr Mol Med* 2020 [PMID: 32888266 DOI: 10.2174/1566524020666200905113907]

16 **Park J**, Park Y, Koh I, Kim NK, Baek KH, Yun BS, Lee KJ, Song JY, Lee E, Kwack K. Association of an *APBA3* Missense Variant with Risk of Premature Ovarian Failure in the Korean Female Population. *J Pers Med* 2020; **10** [PMID: 33114509 DOI: 10.3390/jpm10040193]

17 **Jin H**, Ahn J, Park Y, Sim J, Park HS, Ryu CS, Kim NK, Kwack K. Identification of potential causal variants for premature ovarian failure by whole exome sequencing. *BMC Med Genomics* 2020; **13**: 159 [PMID: 33109206 DOI: 10.1186/s12920-020-00813-x]

18 **Cao LB**, Leung CK, Law PW, Lv Y, Ng CH, Liu HB, Lu G, Ma JL, Chan WY. Systemic changes in a mouse model of VCD-induced premature ovarian failure. *Life Sci* 2020; **262**: 118543 [PMID: 33038381 DOI: 10.1016/j.lfs.2020.118543]

19 **Abrahami N**, Izhaki I, Younis JS. Do young women with unexplained infertility show manifestations of decreased ovarian reserve? *J Assist Reprod Genet* 2019; **36**: 1143-1152 [PMID: 31115740 DOI: 10.1007/s10815-019-01467-0]

20 **Yücel B**, Kelekci S, Demirel E. Decline in ovarian reserve may be an undiagnosed reason for unexplained infertility: a cohort study. *Arch Med Sci* 2018; **14**: 527-531 [PMID: 29765438 DOI: 10.5114/aoms.2016.58843]

21 **Leeangkoonsathian E**, Pantasri T, Chaovisitseree S, Morakot N. The effect of different progestogens on sleep in postmenopausal women: a randomized trial. *Gynecol Endocrinol* 2017; **33**: 933-936 [PMID: 28609128 DOI: 10.1080/09513590.2017.1333094]

**Footnotes**

**Institutional review board statement:** This manuscript wasapproved by the Medical Ethics Committee of Zhanjiang Central Hospital.

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

**Conflict-of-interest statement:** The authors declared that there is no conflict of interest between them.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/Licenses/by-nc/4.0/

**Manuscript source:** Unsolicited manuscript

**Peer-review started:** May 27, 2021

**First decision:** June 24, 2021

**Article in press:** August 5, 2021

**Specialty type:** Pharmacology and pharmacy

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Arif N, Reyna-Villasmil E **S-Editor:** Ma YJ **L-Editor:** A **P-Editor:** Yuan YY

**Table 1 Comparison of two groups of general data (*n* = 65)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Group** | **Age** | **Course of disease** | **Number of pregnancies** | **Pregnancy times (times)** | **BMI (kg/m2)** |
| Fenmatong group | 34.02 ± 3.89 | 3.45 ± 0.61 | 2.05 ± 0.36 | 1.32 ± 0.28 | 23.17 ± 1.24 |
| Observation group | 33.74 ± 4.29 | 3.38 ± 0.57 | 1.98 ± 0.45 | 1.37 ± 0.26 | 23.06 ± 1.48 |
| *t* | 0.390 | 0.676 | 0.979 | 1.055 | 0.459 |
| *P* value | 0.697 | 0.500 | 0.329 | 0.293 | 0.647 |

BMI: Body mass index.

**Table 2 Comparison of curative effects between the two groups [*n* = 65, *n* (%)]**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **Significant effect** | **Effective** | **Invalid** | **Total efficiency** |
| Fenmatong group | 32 (49.23) | 21 (32.31) | 12 (18.46) | 53 (81.54) |
| Observation group | 47 (72.31) | 14 (21.54) | 4 (6.15) | 61 (93.85) |
| *χ*2 |  |  |  | 4.561 |
| *P* value |  |  |  | 0.033 |

**Table 3 Comparison of traditional Chinese medicine syndrome scores between the two groups (mean ± sd, scores)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Group** | ***n*** | **Less menstruation** | | **Delayed menstruation** | | **The color is red and thick** | | **Dizziness and palpitations** | |
| **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** |
| Fenmatong group | 65 | 4.63 ± 1.14 | 2.03 ± 0.75 | 4.37 ± 1.23 | 1.89 ± 0.64 | 4.12 ± 1.05 | 1.95 ± 0.54 | 2.36 ± 0.54 | 1.32 ± 0.39 |
| Observation group | 65 | 4.59 ± 1.07 | 1.27 ± 0.59 | 4.39 ± 1.21 | 1.04 ± 0.37 | 4.18 ± 0.97 | 1.12 ± 0.38 | 2.41 ± 0.47 | 0.87 ± 0.31 |
| *t* |  | 0.206 | 6.421 | 0.093 | 9.270 | 0.338 | 10.134 | 0.563 | 7.282 |
| *P* value |  | 0.837 | 0.000 | 0.426 | 0.000 | 0.736 | 0.000 | 0.574 | 0.000 |
| **Group** | ***n*** | **Sore waist and knees** | | **Insomnia and dreaminess** | | **Irritable** | | **Pudendal dryness** | |
| **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** |
| Fenmatong group | 65 | 2.27 ± 0.43 | 1.37 ± 0.37 | 1.97 ± 0.37 | 1.21 ± 0.29 | 2.08 ± 0.35 | 1.09 ± 0.28 | 1.86 ± 0.44 | 1.03 ± 0.32 |
| Observation group | 65 | 2.31 ± 0.37 | 0.87 ± 0.49 | 2.03 ± 0.41 | 0.74 ± 0.23 | 2.11 ± 0.37 | 0.79 ± 0.25 | 1.81 ± 0.46 | 0.58 ± 0.27 |
| *t* |  | 0.568 | 6.565 | 0.876 | 10.238 | 0.475 | 6.444 | 0.633 | 8.665 |
| *P* value |  | 0.571 | 0.000 | 0.383 | 0.000 | 0.636 | 0.000 | 0.528 | 0.000 |

**Table 4 Comparison of uterine artery blood flow parameters between the two groups (*n* = 65, mean ± sd)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **PSV (cm/s)** | | **EDV (cm/s)** | | **RI** | |
| **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** |
| Fenmatong group | 30.85 ± 3.14 | 35.42 ± 3.36 | 5.24 ± 1.14 | 12.19 ± 1.45 | 0.87 ± 0.10 | 0.81 ± 0.08 |
| Observation group | 30.41 ± 3.52 | 38.96 ± 3.11 | 5.30 ± 1.07 | 15.89 ± 1.57 | 0.86 ± 0.13 | 0.73 ± 0.10 |
| *t* | 0.752 | 6.234 | 0.309 | 13.958 | 0.492 | 5.036 |
| *P* value | 0.453 | 0.000 | 0.758 | 0.000 | 0.624 | 0.000 |

PSV: systolic peak flow rate; EDV: end-diastolic flow rate.

**Table 5 Comparison of ultrasonic detection indexes of ovaries between the two groups (*n* = 65, mean ± sd)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Group** | **Ovarian diameter(cm)** | | **Antral follicle count** | |
| **Before treatment** | **After treatment** | **Before treatment** | **After treatment** |
| Fenmatong group | 2.56 ± 0.12 | 2.60 ± 0.10 | 3.08 ± 0.57 | 4.64 ± 0.51 |
| Observation group | 2.57 ± 0.13 | 2.64 ± 0.14 | 3.12 ± 0.53 | 4.91 ± 0.43 |
| *t* | 0.456 | 1.874 | 0.414 | 3.263 |
| *P* value | 0.649 | 0.063 | 0.679 | 0.001 |

**Table 6 Comparison of pictorial blood loss assessment chart scores between the two groups (*n* = 65, mean ± sD)**

|  |  |  |
| --- | --- | --- |
| **Group** | **PBAC score** | |
| **Before treatment** | **After treatment** |
| Fenmatong group | 18.14 ± 2.98 | 21.74 ± 3.06 |
| Observation group | 17.95 ± 3.15 | 23.45 ± 2.77 |
| *t* | 0.353 | 3.340 |
| *P* value | 0.724 | 0.001 |

PBAC: Pictorial blood loss assessment chart.

**Table 7 Comparison of hormone levels between the two groups (*n* = 65)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **FSH (IU/L)** | | **E2 (pg/mL)** | | **AMH (ng/mL)** | |
| **Before treatment** | **After treatment** | **Before treatment** | **After treatment** | **Before treatment** | **After treatment** |
| Fenmatong group | 18.21 ± 2.44 | 13.78 ± 2.06 | 25.38 ± 3.24 | 44.23 ± 4.05 | 0.22 ± 0.05 | 0.26 ± 0.07 |
| Observation group | 18.14 ± 2.26 | 10.14 ± 1.57 | 24.89 ± 4.77 | 57.96 ± 5.17 | 0.21 ± 0.08 | 0.29 ± 0.09 |
| *t* | 0.170 | 11.330 | 0.685 | 16.855 | 0.855 | 2.121 |
| *P* value | 0.866 | 0.000 | 0.495 | 0.000 | 0.394 | 0.036 |

FSH: follicle-stimulating hormone; E2: estradiol; AMH: anti-mullerian hormone.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2021 Baishideng Publishing Group Inc. All rights reserved.**