Impact analysis of femoston on endocrine function in women with menopausal symptoms

Zhang Lijun
Maternal and Child Health Division, Ningbo Women and Children Hospital, Ningbo, Zhejiang, 315000, CHINA

Abstract
Objective To study impact of femoston on endocrine function in women with menopausal symptoms. Methods Clinical data of 38 hospital women with menopausal symptoms for the period September 2013-August 2015 were retrospectively reviewed. These patients were assigned to observation group. Each patient in observation group took one femoston tablet each time. Patients with fear or contraindication to hormones at the same period were assigned to control group. These patients were administered two oryzanol tablets each time. For all the patients, treatment course was 3 months. Changes in blood lipid levels and sex hormone levels prior to and post treatment were compared.

The therapeutic effects and adverse reactions were observed in patients of the two groups. Results Triglyceride (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels in observation group were significantly lower than those in control group. (3.82±0.35) mmol/L, (2.56±0.31) mmol/L, (1.21±0.15) mmol/L vs (4.96±0.73) mmol/L, (3.15±0.29) mmol/L, (1.73±0.25) mmol/L] (P<0.05). Estradiol level was higher in observation group compared with control group [(56.32±7.13) ng/ml vs (32.43±4.66) ng/ml]. Follicle-stimulating hormone and luteinizing hormone levels were lower in observation group than in control group [(15.03±1.42) mIU/ml, (9.67±1.36) mIU/ml vs (26.32±2.53) mIU/ml, (15.32±2.04) mIU/ml] which showed significant differences between the two groups. The total response rate was 92.10% (35/38) in observation group, which was higher than the 68.42% (26/38) in control group (P<0.05). Conclusion Femoston has good therapeutic effects and safety in adjusting endocrine function and reducing blood lipid levels in women with menopausal symptoms.

Keywords: Femoston; Menopausal symptoms; Endocrine.

Introduction

The main clinical manifestations of menopausal are a series of psychological and physical symptoms including dizziness, tinnitus, insomnia, irritability, hot flashes, sweating by low estrogen levels and declined ovary function. experience was estimated for 13% of men.[2] For this, multidrug regimen drugs and delivery systems have been reported to improve the osteoporosis treatment.

It has serious impacts on the quality of life of patients [1, 2].

Relevant researches show that hormone replacement therapy can be adopted in order to effectively ease clinical symptoms. It is beneficial for this special group to go through the stage of menopause syndrome safely and smoothly and also effective in preventing cardiovascular disease and osteoporosis [3-6]. Femoston is a new hormone replacement therapy drug in the treatment of menopausal syndrome. A retrospective analysis was conducted on women with menopausal symptoms treating by femoston with observation of its effects on endocrine function to provide clinical reference.

Material and Methods

Study design: A retrospective study design was adopted.

Patient selection: A retrospective analysis was conducted on 38 hospital women with menopausal symptoms for the period September 2013-August 2015. All the patients and their families signed informed consent forms.

Diagnostic criteria for inclusion:[7] 1) patients do not receive hormone therapy in the past three months; 2) patients are not administered protective food (antidepressive drugs, soybean isoflavones and sleep-improving drugs) and therapeutic drugs for treating menopausal symptoms; 3) patients without endometrial cancer and breast cancer.

Exclusion criteria: 1) patients with abnormal test results in kidney, liver, heart, blood and urine routine diagnostics; 2) patients with diabetes, coronary heart disease or hypertension which are hard to control; 3) patients with contraindication to hormone drugs.

Oryzanol, specification: 10mg*100s, batch No.: 20130204, manufacturer: Sichuan Otsuka Pharmaceutical Co. Ltd.

Femoston, specification: estradiol and dydrogesterone tablet containing 10 mg of dydrogesterone and 1 mg of estradiol, estradiol tablet containing 1 mg of estradiol, batch No.: 20130522, manufacturer: Abbott Biologicals B.V.

H60 ultrasonic diagnostic apparatus, manufacturer: Samsung Medison; Automatic biochemical analyzer, Beckman Coulter, Inc.; DxI 800 immunoassay analyzer, Beckman Coulter, Inc.; Blood analyzer, manufacturer: Chengdu Icansensing Co. Ltd.

Grouping and therapeutic method: Clinical data of 38 hospital women with menopausal symptoms for the period September 2013-August 2015 were retrospectively reviewed. These patients were assigned to observation group. Patients with fear or contraindication to hormones at the same period were assigned to control group. Prior to treatment, women with menopausal symptoms were explained of the purpose, precautions, methods, effects and adverse reactions of the treatment. Relevant checks such as breast ultrasound, liver and kidney function, blood routine, urine routine, endoscopic color doppler ultrasonography, triglyceride, low density lipoprotein, high density lipoprotein, estradiol, follicle-stimulating hormone were performed in patients when they consent to treatment. Patients in control group received conventional treatment with two oryzanol tablets each time for three consecutive months. Patients in control group were administered one femoston tablet each time for three consecutive months. All the patients kept their way of life unchanged prior to and after treatment.

Observation criteria and efficacy evaluation: Changes in blood lipid levels (TG, LDL and HDL) and sex hormone levels (estradiol, follicle-stimulating hormone, progesterone, luteinizing hormone, lactation hormone and testosterone) prior to and three months post treatment were compared. Prior to treatment, all the patients were banned from smoking and alcohol for half a month and fasted for over 10 hours. 6mL of venous blood was drawn from patients in both groups before and within treatment. The serum was separated from the blood within one hour and placed in the cryogenic box at -50℃. Sex hormone levels were measured by homogenous enzyme immunoassay.

Clinical efficacy was analyzed and compared. Complete response: Clinical symptoms disappear. Marked response: Clinical symptoms showed significant remission with the remaining symptoms having no significant influence on life and work. Partial response: Clinical symptoms showed a trend of remission with the remaining symptoms having influence on life and work. However, remission is classified as partial response compared with complete response. No response: Clinical symptoms are not relieved or even worse [8-11]. The total response is the sum of complete response, marked response and partial response.

Statistical analysis: Data was analyzed using software SPSS 18.0. Quantitative data were expressed as average±standard deviation (x±s). T-test was used. Count data were expressed as percentage (n, %) and chi-square test was performed. Rank sum test was used for comparison of ranked data and there is difference when P<0.05.

Result

General information: The difference in general information such as age, BMI and clinical symptoms between the two groups had no statistical significance (P>0.05). The two groups were comparable (Table 1).

Table 1
Comparison of general information in two groups
($\bar{\chi}$±s)

Item	Experiment (n=38)	Control(n=38)
Age （year）	45.41±4.14	45.52±3.98
Weight(kg)	63.21±5.32	63.19±5.28
Height(cm)	160.21±1.24	159.87±1.25
BMI(kg/m^2)	23.45±1.21	23.46±1.24
Clinical symptoms Insomnia	14(36.84)	15(39.47)
Night sweats, hot flashes	11(28.95)	10(26.32)
Fatigue	13(34.21)	12(31.58)
Headache	12(31.58)	13(34.21)
Palpitation	10(26.31)	9(23.68)
Irritability	9(23.68)	8(21.05)

BMI: Body mass index;
Control group: 20 mg of vitamin B6 and 20 mg oryzanol drug; Observation group: Femoston

Comparison of changes in blood lipid levels of two groups prior to and post treatment: Prior to treatment, the difference in blood lipid levels between the two groups had no significance difference (P>0.05). In comparison with those before treatment, TG, LDL and HDL levels declined in observation group (P<0.05), whereas in control group these levels had no significant difference (P>0.05) after treatment. Therefore, TG, LDL and HDL levels in observation group were significantly lower than those in control group after treatment (P<0.05) (Table 1).

Table 2
Comparison of blood lipid level changes before and after treatment in two groups($\bar{\chi}$±s, mmol/L)

Item	Time	Experiment (n=38)	Control (n=38)
TC	Before treatment	5.01±0.87	5.07±0.84
	After three months treatment	3.82±0.35*	4.96±0.73
LDL	Before treatment	3.28±0.56	3.27±0.58
	After three months treatment	2.56±0.31*	3.15±0.29
HDL	Before treatment	1.74±0.24	1.78±0.28
	After three months treatment	1.21±0.15*	1.73±0.25

TC: Total cholesterol; LDL: Low density lipoprotein; HDL: high-density lipoprotein
Compared with control group, *P<0.05

Comparison of changes in sex hormone levels of two groups prior to and post treatment: Prior to treatment, the difference in sex hormone levels between the two groups had no significance difference (P>0.05). In comparison with those before treatment, estradiol level increased (P<0.05), whereas follicle-stimulating hormone and luteinizing hormone levels declined (P<0.05) in both groups after treatment. In observation group, estradiol level was higher, whereas follicle-stimulating hormone and luteinizing hormone levels were lower than those in control group. The difference was statistically significant (P<0.05). However, progesterone, lactation hormone and testosterone levels had no significant difference in both groups after treatment (P>0.05) (Table 3).

Table 3
Comparison of sex hormone levels changes before and after treatment in two groups ($\bar{\chi}$ ±s)

Item	Time	Experiment (n=38)	Control (n=38)
E2(ng/ml)	Before treatment	18.43±2.41	18.59±2.45
	After three months treatment	56.32±7.13[ab]	32.43±4.66[a]
FSH (mIU/ml)	Before treatment	31.42±7.31	31.46±7.41
	After three months treatment	15.03±1.42[ab]	26.32±2.53[a]

E2: Estradiol; FSH: Follicle-Stimulating Hormone; P: Progesterone; LH: luteinizing hormone; PRL: Prolactin; T: Testosterone
Compared with before treatment,[a]P<0.05;Compared with control group,[b]P<0.05

Comparison of clinical effect of patients in both groups: After treatment, the total response rate was 92.10% (35/38) which was higher than the 68.42% (26/38) in the control group. The difference has statically significance (P<0.05) (Table 4).

Safety assessment: In the observation group, one patient developed headache after administration and the symptom relieved a week later. Two patients experienced mild mammary swelling pain. However, no abnormal phenomenon was found after detection by ultrasonic diagnostic apparatus. No severe adverse reactions were observed in control group.

Table 4
Clinical efficacy comparison of patients in two groups (*n*, %)

Item	Experiment (n=38)	Control (n=38)
Recovery	20(52.63)	10(26.32)
Excellent	9(23.68)	2(5.26)
Effective	6(15.79)	14(36.84)
Invalid	3(7.89)	12(31.58)
The total effective	35(92.10)*	26(68.42)

Compared with control group, *P*<0.05

Discussion

Progressive loss of ovarian function is frequently found in menopausal women that appeared as sex hormone changes in a fluctuating way. It brought about a series of changes to the mentality, spirit and trunk which resulted in a series of complications at the early, middle and late stages of menopause [12-14]. Relevant studies manifest that appearance and development of menopausal symptoms are largely related to low estrogen levels. It is mainly generated as levels rise of follicle-stimulating hormone and luteinizing hormone and decrease of estradiol levels [15-17]. Therefore, estrogen replacement is important for women with menopausal symptoms. The most common treatment measure is hormone replacement therapy which can significantly alleviate menopausal symptoms and improve quality of life of patients. Relevant studies show that immune system has a direct or indirect impact on atresia and development of ovarian follicle [18-21].

Femoston is the combination of dydrogesterone and oestradiol. Each tablet contains 1mg oestradiol and 10mg dydrogesterone. Its biological properties and chemical composition are identical with human endogenous estradiol. It is often classified into the human estrogen [22-23]. After administration of micronized estradiol orally, it is easy to be absorbed and metabolized widely in the body. Metabolites are generally non-binding and binding type of estrogen and estrone sulfate. After being converted to estradiol, it has estrogenic activity [24-25]. Dydrogesterone effectively completely metabolized in the body and its metabolite is usually 20α- dihydrodydrogesterone.

The study manifests that after treatment by femoston, estradiol levels increase markedly and follicle-stimulating hormone and luteinizing hormone levels decrease correspondingly. It also significant changes the overall regulatory function of women with menopause syndrome and favors recovery of partial endocrine function and ovulation of failed ovarian. Changes in sex hormone levels of women with menopause syndrome play a role in improving neuroendocrine function and lipid levels. The study finds that femoston can preferably eliminate “foreign matter” from the body, repair the atrophic or damaged endometrium and regulate the body's various pathological

states. Its clinical effect has increased to 92.10% with low rate of adverse reactions and high safety.

Femoston has a good therapeutic effect and safety in adjusting endocrine function and reducing blood lipid levels in women with menopausal symptoms.

References

1. Wu Fan, Yin Lirong and Guo Sujie, Study on Quality of Life in Perimenopausal Women after Different Surgical Procedures of Uterus and Ovary, *Tianjin Medical Journal*, **40(7)**, 666-668 **(2012)**

2. Wang Yanjun, Influence on Quality of Life for Premenopausal Women after Different Operations of Hysterectomy, *Chinese Journal of Coal Industry Medicine*, **7**, 1075-1077 **(2015)**

3. Sang Haili and Sang Yuting, Clinical Observation on Qianjin Yikang Tablets Combined with Auricular Therapy for 100 Cases of Menopausal Syndrome, *Journal of Traditional Chinese Medicine*, **54(23)**, 2015-2017 **(2015)**

4. Yu Hongjun, Clinical Study on Yikun oral liquid in Treating Climacteric Syndrome of Yin Deficiency of Liver and Kidney, *Chinese Journal of Information on Traditional Chinese M*edicine, **16(04)**, 16-18 **(2009)**

5. Cao Jing, Clinical observation of Yixinshu combination with Zuoguiwan in treating menopause syndrome, *Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease*, **10(08)**, 1010-1011 **(2012)**

6. Yao Li, Huang Wei and Liu Ying, Therapeutic effect of hormone replacement therapy on periodontitis combined with postmenopausal osteoporosis, *Chinese Journal of Osteoporosis*, **2**, 196-198 **(2015)**

7. Wan Xia, Chen Jiaxu and Hu Lisheng, TCM symptom weighted score method for syndrome diagnosis of perimenopausal period syndrome, *Journal of Beijing University of Traditional Chinese Medicine*, **29(9)**, 603-606 **(2006)**

8. Gong Jian and Lu Huizhen, Observation of Curative Effect of Angeliq Hormone Replacement Therapy on Postmenopausal Women, *Maternal & Child Health Care of China*, **30(10)**, 1607-1610 **(2015)**

9. Sood R., Faubion S.S. and Kuhle C.L., Prescribing menopausal hormone therapy: an evidence-based approach, *International Journal of Womens Health*, **6(1)**, 47-57 **(2014)**

10. Liu Yan and Liu Xiaoai, Clinic evaluation of Conjugated Estrogen for Postoperative Menopausal Women, *Clinical Medical Journal of China*, **7(01)**, 49-51 **(2000)**

11. Wu Qiulin and Liu Huifang, Clinical observation of hormone replacement therapy for Menopausal Women, *Shananxi Medical Journal*, **34(06)**, 761-762 **(2005)**

12. Mu Huaying, Study on risk factors of cardiovascular disease and the status of bone mineral density by hypoestrogenism in menopausal woman, *Maternal & Child Health Care of China*, **29(27)**, 4447-4449 **(2014)**

13. Li Lan, Zhou Ti and Shao Jinkang, Effect of hormone replacement therapy on postmenopausal osteoporosis, *Chinese Journal of Osteoporosis*, **06(02)**, 48-51 **(2000)**

14. Liu Donge, The physiological and pathological changes of women in perimenopausal period, *Chinese Journal of Practical Gynecologe and Obstetrics*, **20(08)**, 473-474 **(2004)**

15. Yang Lan, Liu Baogeng and Zhang Peihao, Clinical observation on treatment of 60 cases with climacteric depression by Tiaogengjieyu Decoction, *Chinese Journal of Experimental Traditional Medical Formulae*, **21(12)**,182-185 **(2015)**

16. Zhao Yonghou and Zhao Yuping, Clinical Observation of Tiaojing Jieyu Decoction in Treating Depression Following Perimenopausal Syndrome, *Shanghai Journal of Traditional Chinese Medicine*, **39(06)**, 34-35 **(2005)**

17. Guo Xiyong, Wang Yue and Wu Fei, Occurrence actuality of menopause women's gloomy symptom and its related factors, *Maternal and Child Health Care of China*, **17(02)**, 100-102 **(2002)**

18. Wu Hongjin, Zhang Xiaodan and Dai Weiwei, Influence of Ziyang Ganshen Formula on expression of ET-1, NO and sex hormone in menopausal rats, *China Journal of Traditional Chinese Medicine and Pharmacy*, **13(07)**, 2560-2563 **(2015)**

19. Meeta, Digumarti Leela and Agarwal Neelam, Clinical practice guidelines on menopause: An executive summary and recommendations, *J Midlife Health*, **4(2)**, 77–106 **(2013)**

20. Jeprentice R., Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause, *Digest of the World Core Medical Journals*, **297(13)**, 1465-77 **(2007)**

21. Jeprentice R., Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause, *Digest of the World Core Medical Journals*, **297(13)**, 1465-77 **(2007)**

22. Li Weiei, An Lihong and Zhang Ge, Application of femoston combined with Kuntai capsule in poor ovarian responders receiving vitro fertilization, *The Journal of Practical Medicine*, **11(14)**, 2308-2310 **(2014)**

23. Lu Xiang, Xi Ji and Jiang Shan, Effects of estradiol pretreatment at luteal phase on outcome of in vitro fertilization and embryo transfer treatment of antagonist protocol for patients with poor ovarian responder, *Journal of Shanghai Jiaotong University (Medical Science)*, **36(2)**, 248-251 **(2016)**

24. Wang Haiyan and Bai Hongyan, Study on vaginal administration of femoston combined with clomiphene citrate in ovulation induction of sterility due to anovulation, *Maternal & Child Health Care of China*, **30(24)**, 4173-4175 **(2015)**

25. Yue Xiaoling, The clinical study on CC and HMG for 21 cases inhibited ovulation infertility, *Maternal and Child Health Care of China*, **21(18)**, 2584-2585 **(2006)**.