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Effect of self prescription for nourishing liver and kidney combined with tibolone on hormone levels, lipid metabolism and immune response in women with menopausal syndrome

Ming−Xi Zhu✉, Yu−Ling Chen

Department of Obstetrics and Gynecology, Hebei Weichang County Hospital, Chengde City, Hebei Province, 068450

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ABSTRACT

Objective: To study the effect of self prescription for nourishing liver and kidney combined with tibolone on hormone levels, lipid metabolism and immune response in women with menopausal syndrome. **Methods:** Patients with menopausal syndrome who were admitted in Hebei Weichang County Hospital between April 2014 and March 2017 were selected as the research subjects and randomly divided into to the combined group who accepted self prescription for nourishing liver and kidney combined with tibolone therapy and the control group who accepted tibolone monotherapy. The serum levels of sex hormones, lipid metabolism and immune cytokines were detected before treatment and3 months after treatment. **Results:** 3 months after treatment, serum E2, HDL-C, Omentin-1, VaspinC, IL-4 and IL-10 levels of both groups of patients were significantly higher than those before treatment while LH, FSH, TC, TG, LDL-C, Rsistin, IFN-γ and IL-2 levels were significantly lower than those before treatment, E2, LH and FSH levels were not significantly different between the two groups, serum TC, TG, LDL-C, Rsistin, IFN-γ and IL-2 levels of combined group were significantly lower than those of control group while HDL-C, Omentin-1, VaspinC, IL-4 and IL-10 levels were significantly higher than those of control group. **Conclusion:** Self prescription for nourishing liver and kidney combined with tibolone is equivalent to tibolone monotherapy in regulating the sex hormones, and more significant than tibolone monotherapy in improving the lipid metabolism and immune response in patients with menopausal syndrome.

1. Introduction

Menopausal syndrome, also known as perimenopausal syndrome, refers to a series of psychical and psychological symptoms caused by sex hormone decrease before and after menopause, and the ovarian function decline and reduction in estrogen secretion are the main causes of clinical symptoms[1,2]. Hormone replacement therapy is the main western medicine treatment of menopausal syndrome, it can effectively supplement estrogen and improve clinical symptoms, but the exogenous estrogen may increase the occurrence risk of breast cancer, endometrial cancer and other hormone-dependent malignant tumors. In addition, there are also lipid metabolism disorder and immune response imbalance in patients with menopausal syndrome, they will further increase the occurrence risk of a variety of cardiovascular and cerebrovascular diseases, but hormone replacement therapy alone cannot effectively regulate the lipid metabolism and immune response. In recent years, TCM drugs have been increasingly used in the treatment of endocrine diseases. Deficiency of kidney Yin is the main TCM pathogenesis of menopausal syndrome, and nourishing liver and kidney is the main therapeutic idea of TCM[3]. The prescription for nourishing liver and kidney was made by out hospital for menopausal syndrome, and the effect of self prescription for nourishing liver and kidney combined with tibolone on hormone levels, lipid metabolism and immune response in women with menopausal syndrome was specifically analyzed in the following research.

✉Corresponding author: Ming-Xi Zhu, Department of Obstetrics and Gynecology, Hebei Weichang County Hospital, Chengde City, Hebei Province, 068450.
Tel: 03147568535; 13831423831
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2. Case information and research methods

2.1 General case information

Patients with menopausal syndrome who were admitted in Hebei Weichang County Hospital between April 2014 and March 2017 were selected as the research subjects, and all patients

had the symptoms such as facies frontalis flushing, palpitation, dizziness, emotional lability, impatience and easily excited, and were in accordance with the western medical diagnostic criteria for menopause syndrome and the standard of TCM liver-kidney Yin deficiency type of menopause. Patients who had received hormone replacement therapy and patients combined with gynecologic tumors were excluded. A total of 88 patients were enrolled in the study and divided into two groups by random number table, each with 44 cases. Combined group were 42-51 years old, and the menstrual change time was 4-9 months; control group were 41-50 years old and the menstrual change time was 4-10 months. There was no statistically significant difference in general information between the two groups (P>0.05).

2.2 Therapy

Control group received tibolone therapy as follows: tibolone tablets, 1 tablet, oral administration, 1 time/d. Combined group received self prescription for nourishing liver and kidney combined with tibolone therapy as follows: cooked rehmannia root 30 g, processed tortoise shell 30 g (predecoction), cornus 15 g, medlar 15 g, mulberry 15 g, prepared fleeceflower root 20 g, glossy privet fruit 15 g, stir-fried white peony 15 g, moutan bark 12 g, rhizoma anemarrhenae 12 g, cortex phellodendri 12 g, seed of wild jujube 30 g and Angelica sinensis 15 g were decocted with water, 1 dose each day; tibolone tablet, 1 tablet, oral administration, 1 time/day.

2.3 Serum index detection

Before treatment and 3 months after treatment, 3 mL of peripheral venous blood was collected from two groups of patients and centrifuged to separate serum, then electrochemiluminescence was used to determine E2, LH and FSH, enzyme-linked immunosorbent assay kit was used to determine IFN-γ, IL-2, IL-4, IL-10, Rsistin, Omentin-1 and Vaspin contents, and automatic biochemical analyzer was used to determine the contents of TC, TG, LDL-C and HDL-C.

2.4 Statistical methods

SPSS 20.0 software was used to input and analyze data, differences in data between two groups were by t test and $P<0.05$ indicated statistical significance in differences.

3. Results

3.1 Serum sex hormone levels

Before treatment and 3 months after treatment, analysis of serum sex hormones E2 (pg/mL), LH (U/L) and FSH (U/L) levels between two groups of patients was as follows: serum E2, LH and FSH levels were not significantly different between two groups of patients before treatment (P>0.05); 3 months after treatment, serum E2 levels of both groups of patients were significantly higher than those before treatment while LH and FSH levels were significantly lower than those before treatment (P<0.05), and E2, LH and FSH levels were not significantly different between the two groups (P>0.05).

3.2 Serum lipid metabolism indexes

Before treatment and 3 months after treatment, analysis of blood lipid indexes TC, TG, LDL-C and HDL-C levels between two groups of patients was as follows: serum TC, TG, LDL-C and HDL-C levels were not significantly different between two groups of patients before treatment (P>0.05); 3 months after treatment, serum TC, TG and LDL-C levels of both groups of patients were significantly lower than those before treatment while HDL-C levels were significantly higher than those before treatment (P<0.05), and serum TC, TG and LDL-C levels of combined group were significantly lower than those of control group while HDL-C level was significantly higher than that of control group (P>0.05).

Before treatment and 3 months after treatment, analysis of serum adipocytokines Rsistin, Omentin-1 and Vaspin levels between two groups of patients was as follows: serum Rsistin, Omentin-1 and Vaspin levels were not significantly different between two groups of patients before treatment (P>0.05); 3 months after treatment, serum Rsistin levels of both groups of patients were significantly lower than those before treatment while Omentin-1 and VaspinC levels were significantly higher than those before treatment (P<0.05), and serum Rsistin level of combined group was significantly lower than that of control group while Omentin-1 and VaspinC levels were significantly higher than those of control group (P>0.05).

Table 1.
Serum sex hormone levels before and after treatment.

Groups	n	Time	E2	LH	FSH
Combined group	44	Before treatment	42.5±7.6	49.5±6.2	62.5±9.5
		After treatment	62.1±7.9*#	27.5±3.6*#	33.2±5.7*#
Control group	44	Before treatment	43.1±7.7	50.1±6.6	63.1±8.8
		After treatment	63.0±8.5*	28.3±3.8*	33.7±4.9*

*: comparison of index between before and after treatment within group, $P<0.05$; #: comparison of index between combined group and control group after treatment, $P<0.05$.

Table 2.
Blood lipid index levels before and after treatment (mmol/L).

Groups	n	Time	TG	TC	LDL-C	HDL-C
Combined group	44	Before treatment	2.05±0.27	6.25±0.77	3.62±0.52	0.83±0.10
		After treatment	1.42±0.18*#	4.12±0.57*#	2.32±0.31*#	1.15±0.12*#
Control group	44	Before treatment	2.11±0.28	6.31±0.82	3.66±0.47	0.85±0.11
		After treatment	1.73±0.22*	5.23±0.67*	3.03±0.38*	1.03±0.15*

*: comparison of index between before and after treatment within group, $P<0.05$; #: comparison of index between combined group and control group after treatment, $P<0.05$.

Table 3.
Serum adipocytokine levels before and after treatment (ng/mL).

Groups	*n*	Time	Resistin	Omentin-1	Vaspin
Combined group	44	Before treatment	33.2±4.9	21.6±3.2	1.98±0.25
		After treatment	19.3±2.2*#	33.4±3.9*#	3.15±0.41*#
Control group	44	Before treatment	33.6±4.5	20.8±3.2	2.02±0.33
		After treatment	23.1±3.7*	26.4±3.5*	2.67±0.31*

*: comparison of index between before and after treatment within group, $P<0.05$; #: comparison of index between combined group and control group after treatment, $P<0.05$.

Table 4.
Serum Th1/Th2 cytokines before and after treatment (pg/mL).

Groups	*n*	Time	IFN-γ	IL-2	IL-4	IL-10
Combined group	44	Before treatment	24.2±3.2	19.3±2.5	13.1±1.7	22.5±2.9
		After treatment	11.3±1.4*#	9.2±1.0*#	20.3±2.7*#	34.1±3.6*#
Control group	44	Before treatment	24.6±3.5	19.7±2.3	12.8±1.6	22.1±2.6
		After treatment	17.2±2.0*	14.2±1.8*	15.6±2.2*	26.5±3.2*

*: comparison of index between before and after treatment within group, $P<0.05$; #: comparison of index between combined group and control group after treatment, $P<0.05$.

3.3 Serum immune response indexes

Before treatment and 3 months after treatment, analysis of serum Th1 cytokines IFN-γ and IL-2 as well as Th2 cytokines IL-4 and IL-10 levels between two groups of patients was as follows: serum IFN-γ, IL-2, IL-4 and IL-10 levels were not significantly different between two groups of patients before treatment ($P>0.05$); 3 months after treatment, serum IFN-γ and IL-2 levels of both groups of patients were significantly lower than those before treatment while IL-4 and IL-10 levels were significantly higher than those before treatment ($P<0.05$), and serum IFN-γ and IL-2 levels of combined group were significantly lower than those of control group while IL-4 and IL-10 levels were significantly higher than those of control group ($P>0.05$).

4. Discussion

Estrogen replacement therapy is the main western medicine therapy for menopausal syndrome, which can effectively replenish estrogen levels and improve the clinical symptoms caused by ovarian function decline. But exogenous estrogen may increase the occurrence risk of various hormone-dependent malignant tumors, and estrogen complement alone cannot adjust the perimenopausal lipid metabolism and immune stress[4,5]. Traditional Chinese medicine decoction has been increasingly used in recent years for the treatment of female endocrine metabolism disorder, and the traditional Chinese medicine theory holds that the pathogenesis of menopausal syndrome is deficiency of kidney yin, so the prescription for nourishing liver and kidney was made in our hospital according to the pathogenesis. Declined ovarian function decline, decreased estrogen secretion and increased compensatory pituitary gonadotropic hormone secretion are the basic characteristics of patients with menopausal syndrome. In order to confirm the value of self prescription for nourishing liver and kidney combined with tibolone therapy for menopausal syndrome, the changes of serum sex hormone levels before and after the treatment were analyzed in the study, and the results showed that serum E2 levels of both groups of patients significantly increased while LH and FSH levels significantly decreased after treatment, and serum sex hormone levels were not significantly different between the two groups after treatment. It means that both tibolone monotherapy and self prescription for nourishing liver and kidney combined with tibolone therapy can effectively improve the sex hormone levels in patients with menopausal syndrome and have definite hormone replacement effect, and the combination of traditional Chinese medicine decoction will not affect the hormone replacement effect of tibolone. Menopausal women and postmenopausal women are with relatively increased risk of various cardiovascular and cerebrovascular diseases, estrogen has significant protective effect on cardiocerebral vascular system, and the decrease of estrogen levels caused by ovarian function decline will weaken its protective effect on cardiocerebral vascular system[6,7]. Studies have confirmed that lipid metabolism disorder is associated with the increased risk of cardiovascular and cerebrovascular diseases in menopausal women, TG and TC are the important elements of the body blood fat, and the TG and TC levels abnormally increase in the case of blood lipid metabolism disorder, which will increase the risk of atherosclerosis as well as cardiovascular and cerebrovascular diseases[8,9]. LDL-C is the main form of cholesterol transport in the body, it can transport the cholesterol to peripheral vessels and other tissues, it participates in the formation process of foam cells and atheromatous plaque after being oxidized into ox-LDL, and the elevated LDL-C is also seen as an independent risk factor for cardiovascular and cerebrovascular diseases; HDL-C is the main form of reverse cholesterol transportation in the body and can also transport the cholesterol from peripheral tissues to the liver, and then be excreted to the outside of the body through the bioconversion of the liver, and HDL-C is regarded as a protective factor of cardiovascular and cerebrovascular diseases. In the study, analysis of the changes of blood lipid indexes before and after treatment showed that serum TC, TG and LDL-C levels of both groups of patients significantly decreased while HDL-C levels significantly increased after treatment, and serum TC, TG and LDL-C levels of combined group were significantly lower than those of control group while HDL-C level was significantly higher than that of control group. It means that both tibolone monotherapy and self-prescription for nourishing liver and kidney combined with tibolone therapy can effectively improve blood lipid metabolism in patients with menopausal syndrome and the combination of traditional Chinese medicine decoction can be more effective than tibolone hormone replacement therapy alone in improving blood lipid metabolism.

In recent years, research on lipid metabolism disorder shows that adipose tissue has strong endocrine function, and lipid metabolism disorder is not only characterized by abnormal blood lipid composition, but also the abnormal secretion of a variety of adipocytokines. Rsistin is an adipocytokine with proinflammatory effect, which can cause endothelial function injury and promote the infiltration of macrophages in vascular endothelium, thus accelerating the formation of atherosclerosis[10]. Omentin-1 and Vaspin are the adipocytokines with cardiovascular protective effect, which can improve lipid metabolism and rectify lipid metabolism disorder, and can also inhibit endothelial damage, plaque deposition and other pathological processes in the process of atherosclerosis[11,12]. In the study, analysis of the changes of the adipocytokine levels before and after the treatment showed that serum Rsistin levels of both groups of patients significantly decreased while Omentin-1 and VaspinC levels significantly increased after treatment, and serum Rsistin level of combined group was significantly lower than that of control group while Omentin-1 and VaspinC levels were significantly higher than those of control group. It means that both tibolone monotherapy and self-prescription for nourishing liver and kidney combined with tibolone therapy can effectively improve the secretion of adipocytokines in patients with menopausal syndrome and the combination of traditional Chinese medicine decoction is more effective than tibolone hormone replacement therapy alone in improving the secretion of adipocytokines in patients with menopausal syndrome.

The increased risk of cardiovascular and cerebrovascular diseases in menopausal women is not only related to lipid metabolism disorder, but also to immune response imbalance. Th1 cells and Th2 cells are important T cell subgroups that regulate the immune response in vivo and they are in dynamic equilibrium under physiological conditions. When the ovarian function declines, the change in estrogen levels will cause the Th1/Th2 balance to shift to Th1. The cytokine IFN-γ and IL-2 secreted by Th1 cells have strong pro-inflammatory activity, which can mediate the amplification activation of inflammatory response and increase the risk of cardiovascular diseases[13,14]; the cytokines IL-4 and IL-10 secreted by Th2 cells have significant anti-inflammatory activity, which can inhibit the secretion of multiple inflammatory mediators and reduce the risk of cardiovascular diseases[15,16]. In the study, analysis of the changes of serum Th1/Th2 cytokine levels before and after treatment showed that serum IFN-γ and IL-2 levels of both groups of patients significantly decreased while IL-4 and IL-10 levels significantly increased after treatment, and serum IFN-γ and IL-2 levels of combined group were significantly lower than those of control group while IL-4 and IL-10 levels were significantly higher than those of control group after treatment. It means that both tibolone monotherapy and self-prescription for nourishing liver and kidney combined with tibolone therapy can effectively improve the Th1/Th2 immune response in patients with menopausal syndrome, and the combination of traditional Chinese medicine decoction is more effective than tibolone hormone replacement therapy alone in regulating the Th1/Th2 immune response balance in patients with menopausal syndrome, and can more significantly inhibit the differentiation of Th1 cells and promote the differentiation of Th2 cells.

The value of self-prescription for nourishing liver and kidney for menopausal syndrome was mainly analyzed in this research, and analysis of the above results shows that self-prescription for nourishing liver and kidney combined with tibolone is equivalent to tibolone monotherapy in regulating the sex hormones, and more significant than tibolone monotherapy in improving the lipid metabolism and immune response in patients with menopausal syndrome.

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