

Research Progress of Traditional Chinese Medicine in the Treatment of Premature Ovarian Failure

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Abstract: Premature ovarian failure refers to a disease in which women usually present with amenorrhea, infertility, decreased estrogen secretion, and increased gonadotropin before the age of 40. It seriously endangers women's health, making them prone to various endocrine reproductive and even systemic disorders. Its pathogenesis remains unclear; however, it may be related to genetic, immune, enzyme deficiency, iatrogenic, cyclin, psychology, and other factors. Traditional Chinese medicine believes that its etiology is related to the kidney, liver, and spleen. It can be divided into kidney deficiency and liver depression syndrome, liver and kidney Yin deficiency syndrome, spleen and kidney Yang deficiency syndrome, and so on. Traditional Chinese medicine is mainly made up of oral Chinese medicine, acupuncture, and other therapies. Through literature research, this paper discusses the etiology, pathological mechanism, and treatment of premature ovarian failure in the field of traditional Chinese medicine.

Keywords: Premature ovarian failure (POF); Traditional Chinese medicine (TCM)

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1. Introduction

Premature ovarian failure (POF) refers to the occurrence of hypergonadotropic hypogonadism, amenorrhea, and infertility in females less than 40 years of age^[1]. Ovarian atrophy leads to a reduction in follicle reserve, resulting in menstrual irregularities, ovarian dysfunction, and infertility^[2]. POF affects up to 1% of women of reproductive age^[3], and the known causes of this condition include genetic aberrations, autoimmune ovarian damage, and iatrogenic or environmental factors^[4]. However, the underlying mechanisms have not been fully elucidated, and insights into both, disease etiology and targeted intervention are needed.

In recent years, the incidence rate of premature ovarian failure has been increasing, accounting for 1% to 3% of women and affecting those of younger age. As the causes of POF and its physiological and pathological mechanisms are unknown, the treatment for POF is often not very clear. Western medicine mostly uses hormone replacement therapy (HRT), but the long-term use of HRT increases the incidence of endometrial carcinoma and breast cancer; in addition, its long-term effect is not very satisfactory^[5]. Traditional Chinese medicine believes that the main cause of premature ovarian failure lies in kidney deficiency. Therefore, the treatment for this condition is mainly to nourish kidney Yin and kidney Yang,

while considering the situation of the patient ^[6]. In terms of treatment, traditional Chinese medicine follows the principle of symptomatic treatment. For one thing, it has been well acknowledged that the diagnosis and treatment must be based on an overall analysis of the illness and the patient's condition. For another, regulation of menstruation, acupuncture, ointment, and other therapies related to TCM emphasize on psychological counseling and the theory of preventing diseases. Clinically, it has achieved remarkable results and has been accepted as well as recognized by patients.

2. The concept of traditional Chinese medicine and history of POF

Ancient Chinese medicine has long known about premature aging. In *Su Wen*, concerning Yin and Yang, it is stated, "The emperor said: How can you adjust the two? Qi Bo replied: If you know the seven losses and the eight benefits, then the two can be adjusted. If you don't know how to use it, it will be the festival of premature aging. When you are 40 years old, the Yin Qi is half, and your daily life is declining." It put forward the condition of premature aging. There is also a record of breaking through the water before getting old in *Fu Qing's* main female department – *Tiaojing*. The book records that the onset characteristic of breaking through the water before reaching the age of 77 are consistent with premature ovarian failure. However, there is no independent record of premature ovarian failure in traditional Chinese medical books. According to its clinical symptoms, TCM symptoms such as amenorrhea, infertility, women's visceral irritability, and premenopausal and postmenopausal syndromes are similar to this disease. Therefore, this disease can be classified into several categories: amenorrhea, infertility, women's visceral irritability, and premenopausal and postmenopausal syndromes ^[7].

3. Etiology and pathogenesis of POF in Chinese medicine

There is no related concept of POF in ancient books. According to its clinical manifestations, it can be classified as amenorrhea, blood blight, infertility, premature menopause, and several others.

At present, there are five common clinical causes: kidney deficiency, Chong-Ren imbalance, liver depression, spleen deficiency, and blood stasis ^[8-10]. Among them, kidney deficiency is the root cause, along with kidney essence deficiency, early exhaustion of *Tianguai*, damage to Chong-Ren, and the premature aging of human reproductive function. Liver and kidney are of the same origin, while essence and blood grow together. If the kidney essence is insufficient, the liver loses nourishment, liver Qi becomes stagnant, the discharge becomes abnormal, and the operation of Qi and blood is not smooth, thus affecting the normal physiological function of the ovary; with deficiency of Yang Qi in the kidney, there will be weak promotion, endogenous Yin-cold, stagnation of blood collaterals, obstruction of blood stasis, and the inability of menstrual blood to meet the current situation; the kidney Yang cannot warm the spleen Yang, the spleen and stomach are weak, and the Qi and blood are insufficient to nourish the uterus. In addition, some studies have pointed out that the disease is closely related to cardiopulmonary dysfunction ^[11]. The heart hides the spirit and commands human life activities; the sealing and storage of kidney essence and catharsis are closely related to the heart and spirit; the physiological function of the cell palace is also regulated by the heart and spirit; if the heart and spirit are out of balance, the cell palace catharsis is out of order. The Yin and Yang of lung and kidney complement each other. The deficiency of Yin and Yang of lung as well as the deficiency of Yin and Yang of kidney can be seen at the same time, and they can affect each other. Eventually, this will lead to the deficiency of lung and kidney as well as the imbalance of the treatment of lung and kidney.

4. Progress of traditional Chinese medicine in the treatment of POF

In this study, it is found that the etiology and pathogenesis of premature ovarian failure are complex and changeable. Due to that and the course of disease, the treatment philosophy of traditional Chinese medicine

is very diverse. In syndrome differentiation and treatment, the simultaneous treatment of multiple viscera and syndromes is often considered. In terms of methods, in addition to the use of traditional Chinese medicine, there is also no lack of cooperation with the use of Chinese proprietary medicine. Traditional Chinese medicine includes acupuncture, ointment, massage, emotional therapy, and even the combination of traditional Chinese medicine and western medicine.

4.1. Traditional Chinese medicine

The principle of treatment of traditional Chinese medicine is based on tonifying the kidney, supplemented by regulating menstruation and soothing the liver according to the actual situation, which provides a strong scientific basis and theoretical support for the clinical treatment of menstrual diseases by traditional Chinese medicine. Zhao and other TCM practitioners used the modified Gan Mai Da Zao decoction to treat POF from the heart and spleen to reconcile the heart and spleen, and there was good clinical curative effect [12]. From a study [13], it has been suggested that the main pathogenesis of POF is the deficiency of kidney Yang and the obstruction of Qi and blood stasis. Therefore, the suggested treatment is to promote blood circulation and remove blood stasis as well as warm and tonify kidney Yang. The study came up with their own Wenyang Bushen Huoxue recipe to warm and tonify kidney Qi, tonify the kidney and essence, as well as strengthen the spleen and stomach; it showed good curative effect on premature ovarian failure of spleen and kidney Yang deficiency type, and it can effectively improve TCM syndromes as well as reduce the level of serum FSH in patients. The effect of Bushen Huoxue recipe (amethyst, psoralen, dodder, etc.) on the protein expressions of transforming growth factor in granulosa cells at the follicular wall of autoimmune premature ovarian failure mice was studied [14]; the study demonstrated that Bushen Huoxue recipe improves ovarian function by upregulating TGF- β 1, TGF- β R2, and Smad2/3 in granulosa cells.

Traditional Chinese medicine believes that the menstrual cycle can be divided into four periods: menstrual period, late menstrual period, intermenstrual period, and premenstrual period, in which each period circulates in an orderly manner. In traditional Chinese medicine, the clinical treatment of regulating menstruation takes this as the basis and adopts periodic sequential therapy to promote blood circulation, regulate menstruation, and tonify the kidney. Good results have been achieved from this. In another study [15], Xu and other researchers observed the clinical effect of Bushen Tiaojing ointment on premature ovarian failure with kidney deficiency and the level of sex hormone; they found that Bushen Tiaojing ointment has the advantages of high drug concentration, stable, mild and lasting effect, as well as convenient for carrying and taking; besides, it has a definite curative effect on POF of kidney deficiency type, and it can effectively alleviate clinical symptoms, restore normal menstruation, and regulate the level of sex hormone. Research has shown that Bushen Tiaojing ointment has a significant clinical effect in the treatment of PFO with kidney deficiency, effectively improving the clinical symptoms of patients, regulating the levels of sex hormone and immune function, and improving the prognosis of pregnancy [16]. Several researchers have explored the potential mechanism of Zigui Yijing decoction in the treatment of POF using TCM network pharmacology, which showed that quercetin, luteolin, and kaempferol are the main active components in Zigui Yijing decoction that could activate the PI3K/Akt, HIF-1, FOXO, and p53 signaling pathways by acting on targets, such as IL6, AKT1, and PTEN [17].

4.2. Acupuncture

Using acupuncture to treat patients with premature ovarian failure has been a hotspot in recent years. The principle of acupoint selection is mainly to tonify the kidney and essence, soothe the liver and regulate Qi, strengthen the spleen and blood, as well as regulate Chong-Ren. By analyzing the acupoint selection in previous literatures, Guan Yuan, Shenshu, Sanyinjiao, Zhongji, Zusanli, uterus, and other commonly used acupoints are selected for modern clinical treatment of premature ovarian failure [18], reflecting the overall

idea of acupuncture and moxibustion in the treatment of premature ovarian failure based on the principles of regulating Chong-Ren, dredging meridians, and activating blood circulation. In another study ^[19], acupuncture on Zusanli and Guan Yuan combined with ginger-separated moxibustion at Badao point were used, revealing a significant effect on improving FSH/LH, the peak systolic velocity (PSV) of ovarian blood flow, and the number of follicles. Guided by the theory of Yin rising and Yang falling, several researchers used acupuncture before and after ovulation and found that it can promote menstruation and improve the expression levels of IFN- γ and TNF- α in patients with POF ^[20]. Another study used acupuncture and moxibustion to treat patients with premature ovarian failure, suggesting that the calming effect of acupuncture and moxibustion has obvious advantages of improving perimenopausal discomfort symptoms ^[21]. In addition, umbilical acupuncture combined with mixed yuan moxibustion ^[22], acupoint catgut embedding ^[23], and other methods of treatment can also improve the levels of sex hormone in patients.

5. Conclusion

In recent years, the incidence rate of premature ovarian failure has been on the rise, gaining more attention from researchers and clinicians. Research has shown that Chinese medicine and western medicine have significant therapeutic effect on premature ovarian failure; however, the treatment used in western medicine increases the risk of breast cancer, endometrial cancer, thrombosis, and other diseases. Compared with western medicine, the treatment used in traditional Chinese medicine has minimal side effects, a wide range of beneficiaries, and can be added or subtracted with the syndrome, which is conducive to syndrome differentiation treatment. More importantly, the philosophy of “prevention before disease” in traditional Chinese medicine can be applied to POF to prevent its occurrence and strengthen ovarian function in the early stage, so as to reduce the probability of disease development.

Disclosure statement

The authors declare no conflict of interest.

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