

# Research Progress on the Combination of Acupuncture and Medicine in the Treatment of Premature Ovarian Failure

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**Abstract:** Premature ovarian failure (POF) is a condition in which the ovarian reserve function decreases due to a variety of factors, resulting in menstrual irregularities, amenorrhea, and decreased fertility before the age of 40. POF is a common reproductive endocrine disorder in gynecology that seriously affects the physical and mental health of women of appropriate age. Western medicine mostly uses hormone replacement and assisted reproduction techniques in clinical treatment, but in the long run, the side effects are large. With the development of Chinese medicine in recent years, the efficacy of Chinese medicine in the treatment of POF has been recognized. A large number of studies have shown that the combined effect of Chinese and Western medicine in the treatment of POF is better than that of Chinese medicine alone. The treatment methods mainly include Chinese medicine combined with Western medicine therapy, Chinese medicine combined with acupuncture therapy, Western medicine combined with acupuncture therapy treatment and Chinese medicine - Western medicine - acupuncture triple therapy. It is found that the combined effect of Chinese and Western medicine is better than the treatment of Chinese medicine or Western medicine alone, with significant clinical effect, which can effectively improve the endocrine level of the body, restore normal menstruation and improve fertility.

**Keywords:** Premature Ovarian Failure, Etiology and Pathogenesis, Combination of Acupuncture and Medicine, Review

## 1. Introduction

Premature ovarian failure (POF), also known as premature ovarian insufficiency (POI), is a gynecological disease caused by various factors that lead to the development of ovarian dysfunction or even failure before the age of 40. POF is characterized by menstrual cycle disorders, amenorrhea, decreased fertility, and even infertility, with varying degrees of perimenopausal symptoms such as hot flashes, night sweats, insomnia, anxiety and depression, sexual dysfunction, etc. Hormone measurements show high gonadotropin (FSH>40IU/L) and low estrogen<sup>[1]</sup>. With the increase of social pressure, the incidence of this disease has been increasing year by year in recent years with a trend of rejuvenation, according to statistics, the incidence of premature ovarian failure in the general population is about 1% to 3.8%<sup>[2]</sup>. POF is clinically highly heterogeneous, and the exact cause of its development is still unclear. Modern medicine generally believes that its occurrence is closely related to genetic factors, medical factors, autoimmune diseases, environmental factors, psychological factors, and congenital enzyme deficiency<sup>[3]</sup>. Most of the symptoms of POF are related to low estrogen levels, therefore, western medicine uses hormone replacement therapy, which is effective in relieving perimenopausal symptoms, but also increases the risk of endometrial cancer and breast cancer<sup>[4]</sup>. It has been found that the combination of Chinese and Western medicine and acupuncture and drug therapy is better than Western medicine alone or Chinese medicine alone for this disease, which can reduce the adverse effects of Western medicine and also improve the disadvantages of slow onset of Chinese medicine to achieve the ideal treatment effect.

## 2. Etiology and Pathogenesis

Modern medicine classifies POF as "amenorrhea, infertility, symptoms before and after menstruation break, blood withering, blood isolation" according to its clinical manifestations. In the

"Female Medicine of Fu Qingzhu", it is discussed that "menstrual flow is broken before old age" is most relevant to the manifestation of POF. Chinese medicine believes that the cause of POF is mainly due to kidney deficiency. The kidneys are the foundation of the innate nature, harboring the innate essence, dominating reproduction. The physiological activities of women throughout their lives are closely related to the function of kidney energy. Su Wen - Shang Gu Tian Zhen Lun" cloud "women two seven, Tian Gui to, Ren pulse through, Tai Chong pulse is abundant, menstruation came on time, so ..... seven seven Ren pulse deficiency, Tai Chong pulse decay less, Tian Gui exhausted menstruation stop,so the body decline, unable to breed". The above statements all indicate that the decline in female reproductive function is related to the gradual exhaustion of kidney energy. According to traditional Chinese medicine, the production and development of the ovum is based on the kidney essence, and the discharge of the mature ovum depends on the promotion of kidney qi. If the kidney qi is full, it will produce Tian Gui, and if Tai Chong pulse is smooth and Ren pulse is full, then menstruation will reach the uterus on time and have reproductive function.If the kidney qi is weak, the Tian Gui is exhausted, Tai Chong pulse and Ren pulse fail, and menopause cannot be pregnant. The spleen and stomach are the acquired foundation and the source of qi and blood, and it is the material basis for the production of menstruation.If the spleen and stomach are damaged, the subtlety of the water valley cannot be transported and absorbed, the biochemical source of qi and blood is lacking, the internal organs lose nourishment, and the uterus has no menstrual filling;Or cause retention of water, gather dampness become phlegm, coagulation of sputum leads to poor flow of qi and blood, sputum and stasis coagulate each other, blocking blood veins, which will also lead to the occurrence of amenorrhea and infertility.On the basis of the previous understanding, modern medical practitioners have more detailed insights into the etiology and pathogenesis of the disease and have further supplemented them. Ma KUN et al. [5] considered that the main pathogenesis of POF is kidney deficiency and blood stasis.Jin Jing et al. [6] based on the principle of "the menses is Yin Blood , which organ does not have it" believe that the root cause of premature ovarian failure is yin blood deficiency, and its occurrence is closely related to the five internal organs. In conclusion, the cause of POF is either lack or excess, or deficiency-excess mixing. Although doctors have different opinions about the cause, most of them agree that kidney deficiency is the root cause of the disease. Although medical practitioners have different views on the etiology, most of them agree that kidney deficiency is the root cause of the disease.

### 3. Traditional Chinese Medicine Treatment

#### 3.1. Identification and Typing Treatment

However, in the fundamental analysis, the main pathogenesis of the disease lies in the kidney and is closely related to the heart, liver, and spleen.

Liu, T.Y., et al. [7] divided 40 POF patients into three types through TCM differentiation, namely kidney yang deficiency, liver depression and kidney deficiency, and blood deficiency, and used the "Liu's Bu Shen Gu Yuan Jian" (composition: Huai Shan Yao, Tu Si Zi, Ji Nei Jin, etc.) as the basic formula for the treatment of this disease. For the evidence of kidney yang deficiency, Erxian Tang was added to the original formula; for the evidence of kidney deficiency and liver stagnation, Chai Hu Shu Gan San was added to the original formula; for the evidence of blood deficiency and fire stronger, Chai Hu Siwu Tang was added to the original formula. The results showed that the total effective rate was up to 90.00%, and the patient's sex hormone level and adverse symptoms were significantly improved. Jiao Qinghua [8] The control group was treated with sequential estrogen and progesterone therapy, while the observation group was treated with TCM evidence-based therapy, i.e., The liver and kidney yin deficiency type was treated with Zuo Gui Yin plus and minus, and the spleen and kidney yang deficiency type was treated with You gui Wan and Er Xian Tang plus and minus treatment; For those with liver qi depression, it is treated with Xiao Yao San. The results showed that the total effective rate of the observation group was 97. 50%, which was higher than that of the control group (80. 00%). Zhan Jinyu et al. [9]. In clinical practice, they found that the pathogenesis of premature ovarian failure is closely related to the heart and kidney, and believed that the deficiency of kidney yin and the hyperactive fire of the heart lead to the disconnection of the heart and kidney, and that the disconnection of the heart and kidney is the pathogenesis of premature ovarian failure, so the treatment was based on tonifying the kidney, nourishing yin, clearing fire and nourishing the heart. They used their own formula "Zi Shen Qing Xin Tang" to treat POF ( composition: Sheng Di Huang, Shu Di Huang, Lian Zi Xin, Huang Lian,Chao Bai Shao,Huai Shan Yao,Wu Zhu Yu, etc.).The combination of various medicines nourishes the kidney yin, clears the heart and fire, and communicates the heart and

kidney.

### 3.2. Chinese Medicine Cycle Therapy

Chinese medicine cycle therapy is based on the physiological characteristics of the internal organs, Qi and blood, and the Yin and Yang of the human body during the menstrual cycle, and the corresponding treatment methods are used at different stages of the menstrual cycle to achieve the purpose of restoring the normal menstrual cycle and ovulation. In the late menstrual period, the blood is deficient, and yin grows, and yang subsides, so the treatment is to nourish yin and blood, tonify the liver and kidney, and promote follicle development and endometrial growth. In the intermenstrual period, the emphasis is on changing yin to yang and promoting follicle discharge. In the premenstrual period, the qi and blood in the uterus are abundant, yang grows and yin subsides, so the treatment is to tonify the kidney and help yang and promote endometrial shedding. Zhang Lixia et al. [10] used traditional Chinese medicine cycle therapy combined with traditional Chinese medicine emotional therapy to treat 40 patients with POF and gave Self-created formula "Bu Shen Huo Xue Tang" during menstruation; In the late menstrual period, giving Self-created formula "Bu Shen Shu Gan Yang Xue Tang"; Giving Self-created formula "Bu Shen Shu Gan Tiao Chong Tang" during the intermenstrual period. In the premenstrual period, the self-created formula "Bu Shen Shu Gan Gu Chong Tang" and combined with emotional therapy on the basis of traditional Chinese medicine treatment, achieved good therapeutic results. Yan Erxia [11] Observed the effect of herbal cycle therapy on sex hormone levels and endometrial thickness in patients with POF. The results showed significant improvement in symptoms, thickening of endometrium, increase in estradiol ( $E_2$ ) level and decrease in follicle stimulating hormone (FSH) level. Prof. Weili Li [12] It is believed that the main etiology of this disease is deficiency of essence and blood in the kidney, liver qi stagnation, and lack of intercourse between the heart and kidney. In the treatment, according to the characteristics of female menstrual cycle, during menstruation, the main thing is to activate blood circulation and remove stasis and give the self-created formula Tao Hong Si Wu Tang with addition and subtraction to treatment. In the late menstrual period, by tonifying the kidney and promoting sperm to promote the growth of the yin, to promote the repair of the endometrium, give the self-created formula Bu Shen Tiao Jing Tang plus or minus. In the intermenstrual period, it is advisable to warm up the kidney yang, regulate qi and activate the blood, and give self-created formula Bu Shen Zhu Yun Fang. The premenstrual period is equivalent to the luteal phase of Western medicine, during which the sea of blood is filled, and the yang qi is gradually filled. So, it is advisable to warm the kidneys and strengthen the spleen and give self-created formula Bu Shen Yang Chong Tang. Professor Han Yanhua [13] believed that kidney deficiency is the root of the disease and is closely related to the malfunction of the liver, therefore, in the treatment of kidney deficiency and liver depression type POF, Han's self-created formula "Bu Shen Huo Xue Tiao Chong Tang" was added and reduced, and the patient's symptoms improved significantly and the hormone level returned to normal. After treatment, the patient's symptoms improved significantly and hormone levels returned to normal.

### 3.3. Traditional Chinese Medicines Compound Treatment

Chinese medicine compound formula is an agent formed by the combination of two or more drugs, which is based on the pathogenesis of the disease and administered through clinical evidence, with significant clinical effects. Chen Fengrong et al. [14] researched the effect of Er Zhi Wan on mice in the POF model group caused by Tripterygium Glycosides. 42 female rats were randomly divided into six groups, including blank group, Er Zhi Wan high, medium and low dose group and estradiol group. The results showed that the serum luteinizing hormone (LH) and FSH levels decreased,  $E_2$  and progesterone (P) levels increased, estrogen receptor expression tended to increase, and follicular and uterine glands increased in the Er Zhi Wan group. Therefore, Er Zhi Wan has a significant effect on the protection and improvement of premature ovarian failure. Chen Junmei et al. [15] 80 patients with POI were divided into 2 groups according to the patients' wishes, 30 cases in the control group were treated with hormone replacement therapy and 50 cases in the treatment group were treated with the formula of Qi Zi Luan Shen Yu Luan Tang (composition: Nu Zhen Zi, Mo Han Lian, Tu Si Zi, Gou Qi Zi, Fu Pen Zi, Chong Wei Zi, Wu Wei Zi, Shi Liu Zi, Huang Dou, Xiao Mai, Dao Gu). The 2 groups were treated separately for 6 weeks. The results showed that the TCM symptom scores, FSH,  $E_2$ , and anti-mullerian hormone (AMH) were effectively improved in the treated group, the endometrial thickness was thicker and the number of sinus follicles increased compared with that before treatment, indicating that Qi Zi Bu Shen Yu Luan Tang was effective in treating premature ovarian failure, effectively regulating the patients' hormone levels and improving ovarian function.

### 3.4. Acupuncture Treatment

Acupuncture treatment is one of the characteristic therapies of Chinese medicine, which has the efficacy of unblocking the meridians and improving the immunity of the body, and its therapeutic scope is wide and can be applied to the treatment of many diseases. In recent years, the efficacy of acupuncture in the treatment of premature ovarian failure has been fully recognized in clinical practice. The principles of acupuncture in the treatment of POF are mainly based on the lesions of internal organs and the doctrine of meridians, which are closely related to the kidney, liver and spleen. Prof. Yigong Fang<sup>[16]</sup> It is believed that the main pathogenesis of POF is the deficiency of kidney essence, dysregulation of Chong and Ren pulse and the discomfort of the emotions. Therefore, in the treatment of POF, "13 needles for regulating menstruation and promoting pregnancy" is used to nourish kidney essence, regulate the two pulses of Chong and Ren, regulate mood, and the acupuncture points of Bai Hui, Shen Ting, Guanyuan, Zhong Wan, Ovary, Zu San li, Shen Shu, San Yin jiao, and Tai Chong are selected for treatment. Wang Qin. et al.<sup>[17]</sup> used abdominal acupuncture combined with moxibustion Du pulse to treat 30 patients with POF and observed their clinical efficacy, hormonal improvement levels, and immune cell improvement levels after 3 and 6 months of treatment. The results showed that E<sub>2</sub> and CD4<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> levels increased significantly after treatment compared with those before treatment, while P, FSH, LH and CD8<sup>+</sup> levels decreased, indicating that abdominal acupuncture combined with moxibustion can effectively improve the adverse symptoms of POF, regulate sex hormone levels and improve immune disorders. Du Xin et al.<sup>[18]</sup> studied the pattern of acupuncture point selection and commonly used acupuncture point combinations in the treatment of premature ovarian failure by data mining methods, and found that acupuncture in the treatment of POF is based on the principle of selecting acupuncture points to tonify the kidneys, detoxify the liver, and strengthen the spleen, and harmonize the Chong pulse and Ren pulse, among which Guan Yuan, San Yinjiao, Shen Shu, and Zi Gong are the most frequently used, and Guan Yuan with San Yinjiao is the commonly used combination. It is well known that the kidney-Tian Gui-Chong pulse and Ren pulse-uterus axis plays a vital role in female reproductive endocrine secretion, and if its function is disrupted, it can lead to menstrual disorders and infertility. The efficacy of acupuncture treatment depends on the selection of acupuncture points and the method of acupuncture, and some scholars have found that<sup>[19]</sup>, the combination of warm acupuncture for Guan Yuan and electroacupuncture for Sanyinjiao can regulate the reproductive axis, improve endocrine secretion and reduce ovarian inflammatory response, which is worthy of clinical promotion.

## 4. Combination of Acupuncture and Medicine Treatment

### 4.1. Acupuncture Combined with Chinese Herbal Medicine for POF

Sun Juan<sup>[20]</sup> selected 50 patients with POF, the control group was treated with Zi Shen Fu Jing Tang; the observation group was treated with Chinese medicine and acupuncture treatment: Guan Yuan, Shen Shu, Zhong Ji, Zi Gong, Da He, etc. The yang deficiency of the spleen and kidneys plus Pi Shu, Ming Men, Di Ji, and Ci Liao, and in case of deficiency of liver and kidney, San Yin jiao, Gan Shu, Yin Xi, Yin Ling Quan, and Fu Liu were added. The total effective rate of treatment in the observation group was 96.00%, which was higher than that in the control group. The FSH and LH levels in both groups were lower than before treatment, E<sub>2</sub> hormone levels were significantly higher than before treatment, and endometrial thickness was higher than before treatment, and the efficacy of the observation group was significantly better than that of the control group, and the difference was statistically significant ( $P < 0.05$ ). Teng Jing et al.<sup>[21]</sup> selected fifty-six patients with POF of spleen and kidney deficiency, and randomly divided into two groups, and the control group was treated with kelimong, while the observation group was treated with self-created formula Bu Shen Nuan Chong Tang (drug composition: Sha Shen, Bai He, Tu Si Zi, Lu Jiaojiao, Dang Gui, Bai Shao, Chai Hu, Sang Jisheng, etc.) and acupuncture, with acupuncture points selected: Zhong Ji, Xue Hai, Guan Yuan, Gui Lai, Qi Hai, Yao Yangguan, Ming Men, Pi Shu, San Yinjiao, Shen Shu, and Ci Liao points. The results showed that the total efficiency of the observation group was better than that of the control group, and the sex hormone level was significantly improved. The treatment of POF with acupuncture and moxibustion combined with traditional Chinese medicine was significantly better than that with Western medicine alone, which is worthy of clinical application. Wu Yan et al.<sup>[22]</sup> The control group was treated with estradiol valerate tablets and progesterone, while the observation group was given Xian Tu He Che formula with electro-acupuncture treatment, and the acupoints were selected: Qi Hai, Guan Yuan, Qi Men, Uterus, San Yin Jiao (double), Tai Chong and Tai Xi. Both groups were treated for 3 months, and the results

showed that the observation group was better than the control group in terms of reducing FSH and LH levels, increasing endometrial thickness, and improving POF symptoms, but the increase in E<sub>2</sub> was not as significant as that of the control group.

#### **4.2. Acupuncture Combined with Western Medicine for POF**

Xie, Ying et al. [23] selected 60 patients with liver and kidney yin deficiency type POF, they were randomly divided into treatment group and control group, and both groups were treated with kelimong, and the treatment group was treated with acupuncture combined with Du pulse moxibustion on the basis of the control group, and the acupoints were selected: prescription 1 selected acupoints: scalp acupuncture, five visceral points (Xin Shu, Gan Shu, Pi Shu, and Shen Shu ),Ming Men , Ge Shu, and TaiXi; prescription 2: scalp acupuncture, Qi Hai, Guang Yuan, Da He, and Gui Lai. The acupuncture points in both groups were alternately performed 5 times a week. After 3 months of treatment in both groups, it was found that the efficiency of acupuncture combined with western medicine treatment was better than that of western medicine treatment alone, and the decrease in serum FSH level and increase in E<sub>2</sub> level were significantly better than that of western medicine treatment alone, with fewer adverse effects. Liu Wenxia et al. [24] In 128 patients with POF, the control group was treated with estradiol valerate combined with didrogestrel, and the observation group was treated with acupuncture on the basis of the control group, with acupuncture points selected: Baihui, Ben Shen, Guan Yuan, Luan Chao, San Yinjiao, Tai Xi, and Tai Chong, etc., three times a week. The results of the study showed that the ovarian function of the patients who received western medicine combined with acupuncture treatment group improved significantly and their sex hormone levels recovered to a higher degree. It indicates that combining acupuncture treatment with the application of western medicine for POF can effectively enhance the efficacy of western medicine and reduce the occurrence of adverse effects.

#### **4.3. Triple Therapy for POF**

Shi Yange et al. [25] selected 105 patients with POF , and the control group was treated with estrogen sequential therapy, while the treatment group was given Yulin Tang and Du Ren Moxibustion on the basis of the control group. The results showed that the total effective rate of the treatment group reached 96.23%, which was higher than that of the control group, and effectively improved the hormone level, endometrial thickness and blood flow of the patients without adverse effects, which is worthy of clinical promotion. Wei Dongmei et al. [26] selected 68 patients with POF and randomly divided into two groups, the control group used hormone replacement therapy combined with warm acupuncture, and the observation group was given Yikun Tiao Jing Tang on the basis of the control group, selected acupoints: Baihui, Shenting, Ben Shen, Zu Sanli, Tianshu, Zhongwan, Guan Yuan, Dahe, and Luanchao, etc. After 3 months of treatment, the results showed that the total effective rate of treatment in the observation group was 94.12%, and patients with hot flashes, insomnia and dreaminess, and The symptoms such as hot flashes, insomnia, dizziness, etc. were significantly improved, and the serum FSH and LH levels decreased, E<sub>2</sub> levels increased, and ovarian blood flow status was improved compared with that of the control group before treatment, and all of them were better than that of the control group. Hu Julan et al. [27] Selected 60 patients with POF, the control group was treated with sex hormone sequential therapy and the observation was treated with estrogen and progestin sequential therapy combined with kidney and liver nourishing herbs and acupuncture, the result was that the total effective rate of treatment in the observation group reached 83.3% and the serum hormone levels improved significantly, which was significantly better than that of hormone therapy alone. Li Yu [28] randomly divided 122 POF patients into two groups, and both groups were given Kuntai capsule combined with estrogen and progestin sequential treatment, and the observation group was treated with acupuncture on the basis of the control group, and both groups were treated continuously for 3 menstrual cycles. The results showed that the overall efficiency of the acupuncture and medicine group was higher than that of the control group, and the LH and FSH levels were significantly lower and the E<sub>2</sub> and AMH expression levels were significantly higher in the two groups. This indicates that acupuncture combined with Chinese and Western medicine has significant advantages in the treatment of POF and is worthy of wide clinical application.

### **5. Summary and Prospect**

Currently, the prevalence of POF is increasing year by year and is gradually becoming younger, so how to effectively prevent and improve the fertility of patients has become a major challenge for the

future. This paper summarizes the current status of POF treatment with Chinese herbal medicine, Chinese herbal medicine combined with western medicine, Chinese herbal medicine combined with acupuncture, western medicine combined with acupuncture and the triple therapy of Chinese herbal medicine - western medicine - acupuncture, each of which has its own advantages. The combination of acupuncture and medicine has the best effect in treating this disease because it reduces the adverse effects of western medicine, reduces the amount of hormones, makes up for the slow onset of Chinese medicine and acupuncture, greatly shortens the treatment cycle, improves the ovarian function of the patient, and increases the conception rate. However, because of the small sample size, human variability and complexity of the combination of acupuncture and medicine in the treatment of POF, the therapeutic effect is not yet uniform. Therefore, a large number of experimental studies and clinical data should be provided to support this treatment and to more comprehensively elucidate the treatment mechanism of needle-drug combination. Only by choosing the optimal needle-drug combination can we obtain better clinical efficacy.

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