

Clinical study of traditional Chinese medicine in the treatment of decreased ovarian reserve function

Juanjuan Zhang^{1,a}, Xiaoping Cui^{1,b,*}

¹Shaanxi University of Chinese Medicine, Xianyang, 712046, Shaanxi, China
^a1962421712@qq.com, ^b13892079999@163.com
*Corresponding author

Abstract: The decline of ovarian reserve function refers to the decline of ovarian reproductive function and endocrine function, which is reflected by the decline of the quantity and quality of ovarian follicles. The occurrence of this disease directly leads to the decline of female fertility and the lack of sex hormones, and further can develop into premature ovarian failure. The effect of traditional Chinese medicine in the treatment of this disease is quite significant. We will make a brief introduction to the understanding and treatment of this disease in traditional Chinese medicine, so that our later research can be more specific and serve the majority of patients.

Keywords: Traditional Chinese medicine; Decreased ovarian reserve; Clinical Research

1. Introduction

Ovarian reserve function is used to evaluate the function of the ovary, the decline of ovarian reserve function refers to the decline of ovarian reproductive function and endocrine function, which is reflected by the decline in the quantity and quality of ovarian follicles. The occurrence of this disease directly leads to the weakening of female fertility and the lack of sex hormones. Most of the clinical symptoms are oligomenorrhea, oligomenorrhea, amenorrhea and infertility in women of childbearing age before the age of 40, which can progress to premature ovarian failure [1].

2. Understanding of low ovarian reserve in traditional Chinese medicine

The name of this disease is not recorded in ancient Chinese medical books. According to its clinical symptoms, it can be classified as "dry blood", "menstrual closure", "non-month", "month after less infertility", "young age after water deprivation" and so on.

The relationship between kidney and menstruation is close, and the root of qi is the true Yang in kidney. The root of blood is the true Yin in the kidney, so the kidney is the root of qi and blood and the material basis of menstruation. This disease is discussed in Fu Qingzhu Nuke·Tiaojing (Regulating the Classics). Women take seven as a cycle, and in the year of Seven weeks, kidney qi failure occurs, the heaven and decubrate, and menstruation is broken, which is a normal physiological performance. If not in the year of Seven weeks, the water failure should be given priority to tonifying kidney qi, and the depression of heart, liver, and spleen should be removed, then the kidney essence is sufficient and the water comes from them.(See Figure 1)

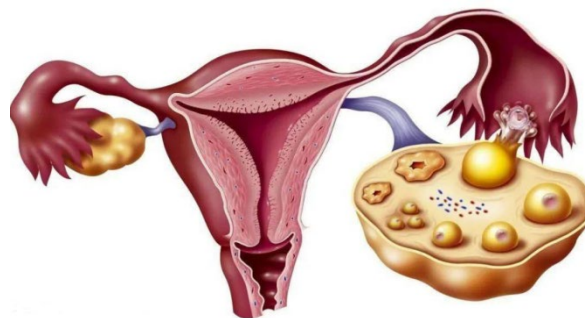


Figure 1: The ovarian reserve was low

3. Understanding of the etiology and pathogenesis of impaired ovarian reserve in traditional Chinese medicine

3.1. Kidney deficiency is the root

In the discussion of women's life in the Ancient Days of Plain Questions, it is pointed out that the rise and fall of kidney essence, the exhaustion of heaven and decuple and the rise and fall of Taichong pulse are related to the growth and reproduction of women's life. In Qi bing Lun pian of Plain Questions, it is believed that the bao collateral is closely related to the kidney. The main opening and closing of the kidney are related to the accumulation and diarrhea of the uterus, and are related to the uterus. The kidney is the root of reproduction, and the function of reproduction has a great relationship with menstruation. The essence and blood in the kidney are sufficient, and the menstruation comes on schedule. If the function of kidney Yang is normal, it can run normally. If the kidney Yang is insufficient, the qi is insufficient and the warming function is abnormal, resulting in the block of qi and blood in the uterus and the palace cold. If the kidney Yin is insufficient, the blood is insufficient, and the zangfu uterus is lost, resulting in the emptiness of the blood sea. In Fu Qing Zhu Nu Ke, it is mentioned that the meridians come from all the kidneys. If the kidney water is exhausted and the kidney qi is deficient, how can the meridians overflow and the tide come? Woman to blood for congenital, sperm and blood homologous. The essence of the kidney is the foundation of human growth and development and reproduction, Yin and essence are also dependent on the nourishment of qi and blood, and zangfu are also closely related to qi and blood. Therefore, the pathogenesis of this disease is mainly responsible for kidney deficiency, and there are also pathological changes of liver depression, spleen deficiency and blood stasis.

Modern doctors also believe that the main pathogenesis of this disease is kidney deficiency. Xu Xiaofeng et al. [2] believed that the basic pathological mechanism of decreased ovarian reserve function is mainly kidney deficiency, women are born with blood for use, and pregnancy and childbirth lead to blood damage, causing blood deficiency, qi and blood deficiency and inability to promote blood circulation, leading to blood stasis, and blood deficiency and blood stasis are the main link in the pathogenesis of this disease. Cong Huifang [3] believes that kidney deficiency is the root of the disease, so the treatment of kidney tonifying is the basis of implementation, and most of it is used in clinical practice. She also believed that the disease was caused by early exhaustion of kidney water, and the treatment was often mainly to nourishing the kidney and nourishing the Yin. Teng Xiuxiang [4] believes that the occurrence of this disease is mainly due to the failure of Yin and essence in the kidney, which leads to the gradual decrease of Tian-Gu, the deficiency of Taichong vessels, the sea of blood cannot be full on time, and the menstruation cannot be as usual, resulting in amenorrhea. (See Figure 2)

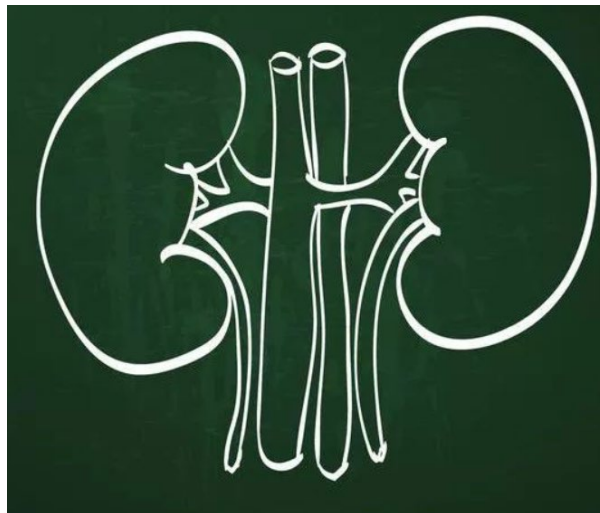


Figure 2: Kidney deficiency is the root

3.2. The lesions involved the heart, liver and spleen

Kidney essence is sufficient, Tiangui arrives as scheduled, Taichong pulse is full; The liver and blood are vigorous, the distribution is as usual, the qi is smooth, and the qi and blood are smooth; The heart is the main blood vessel, the heart is handed over to the kidney, the heart is full of qi, and the

blood vessel is unobstructed. The spleen biochemistry was normal, the blood sea was active, the solid uptake was strong, and the blood circulation was regular.

Stagnation of liver qi is qi stagnation, qi stagnation is not blood, blood stasis cannot make the menstrual blood, leading to menstruation delay, even amenorrhea. In addition to the fierce competition in today's society, women's family and work pressure is gradually increasing, which is easy to cause psychological depression, pessimism, anxiety, impatience and irritability, and other emotions. Over time, it leads to stagnation of liver qi, disorder of distribution, affecting physiological health, resulting in menstruation cannot be normal.

The deficiency of heart qi cannot be transmitted to the kidney, which affects the physiological function of the kidney. At the same time, the deficiency of heart qi can lead to the abnormal operation of the blood vessels. Excessive long-term thinking, staying up late, etc., can consume the qi and blood of the heart, resulting in insufficient heart qi.

Qi and blood biochemistry is weak, so that the basic qi and blood of menstruation is insufficient, causing blood deficiency, no blood can be under, at the same time the uterus lost in Ruyang and cause menstruation cannot be as usual. Long-term ingestion of fatty, spicy, cold and cool food, and overeating can damage the function of the spleen and stomach, resulting in the loss of spleen and stomach transportation.

Therefore, the pathogenesis of this disease is mainly responsible for the kidney, mainly kidney deficiency, and also the dysfunction of the heart, liver and spleen.

4. TCM (traditional Chinese medicine) therapy

The treatment of this disease in Fu Qingzhen Nuke Tiaojing (Regulating the Classics) is described as "However, the water is cut off early, it seems that the kidney water has dried up..." Fu Qingzhu believed that the treatment of this disease not only lies in the method of tonifying the kidney, but also must relieve the depression of the heart, liver and spleen, and finally the overflow of kidney essence will be unobstructed by water. Prescription with Yijing decoction (prescription has cooked rehmannia, fried atractylodes, fried yam, wine angelica, fried peony, jujube kernel, salvia miltiorrhiza, salvia miltiorrhiza, bupleurum, fried Eucommia, ginseng). The four meridians of heart, liver, spleen and kidney are treated together, and the meridians are self-channeled by supplementing and dispersing stagnation. Aim to make up for. The clinical curative effect is quite remarkable.

In the clinical treatment of this disease, Professor Luo Songping mainly uses supplements. The treatment of Shenzhiguishen pill with alkali and combined with the overall conditioning of Chinese herbal ointment, focusing on the treatment of tonifying kidney and filling essence, activating blood circulation and dredging collaterals, the curative effect is remarkable, the symptoms are significantly improved, the serum follicle-stimulating hormone level is basically reduced to normal, and the menstruation and cycle return to normal after treatment, and even successful pregnancy.(See Figure3)



Figure 3: Chinese ointment prescription

Professor He Jialin^[5] believes that kidney deficiency is the basic pathogenesis of the disease, and clinically divides the disease into two syndrome types, namely spleen and kidney Yang deficiency, heart deficiency and zang-zang dryness, and liver and kidney Yin deficiency, heart deficiency and nourishment. Long-term observation has found that liver and kidney Yin deficiency and heart deficiency and nourishment are more common in clinical practice. If Yin deficiency and Yang hyperactivity, heart and kidney do not cross, then add Huanglian Ejiao decoction. For those with

spleen-kidney Yang deficiency and heart deficiency and zang-zang dryness, the treatment principles were tonifying the kidney and strengthening the spleen, nourishing blood and replenishing qi. The Yijing decoction of Fuqingzhu and Ganmai Dazao decoction of Zhang Zhongjing were added or subtracted. For those with phlegm dampness block and heart-kidney failure, Dingzhi pill from Wai tai Mi Yao was added.

Professor Li Zhiyuan ^[6] believes that the pathogenesis of this disease is kidney deficiency as the root, blood stasis as the standard, combined with stagnation of liver qi and depression of mood for a long time, so the clinical treatment of liver disease is the starting point, and puts forward the method of soothing the liver and removing blood stasis (mainly using Xuefu Zhuyu decoction), and the method of regulating the liver and nourish the heart (mainly using Angelica sinensis, raw rehmanniae radix, Radix paeoniae alba, anemarrhiza rhizoma, raw Longmu, chrysanthemum, mother-of-pearl, and Tribulus terrestris and other drugs). Soothing liver and dissolving phlegm method (use Cangfu Dao phlegm pills combined Buddha Hand powder addition and subtraction), soothing liver and spleen method (use Xiaoyao powder and Sijunzi decoction addition and subtraction), nourishing liver and kidney method (use Zuogui Yichong decoction or Guishen pill addition and subtraction), warm and nourishing liver. Kidney method (selection of Codonopsis, Angelica, Cistanche, Curculipia, Morinda officinalis, raspberry, Wolfberry, osthole, litchi and other drugs) six methods.

Hu Guohua ^[7] attributed the pathogenesis of the disease to kidney deficiency, and believed that kidney deficiency was the root. At the same time, he believed that the liver and kidney were homologous, the imbalance of Yin and Yang of kidney damaged other viscera over time, and blood stasis was the main cause of the disease. Thus, he proposed that "flushing and conception is the key to promoting prosperity". The treatment was based on nourishing the liver and nourishing the kidney, regulating and tonifying the blood vessels, and self-made Hu's premature aging prescription. The curative effect was satisfactory. In the long-term clinical experience, Professor Wang Jin-quan has proved that the basic pathogenesis of this disease is kidney deficiency. At the same time, Professor Wang believes that the liver and kidney are homologous. Kidney-yin deficiency is the main syndrome type. Wang's Yijing decoction, a self-made empirical prescription, is effective. (See Figure 4)



Figure 4: Traditional Chinese medicine compound

5. Modern pharmacological research

A number of studies have shown that ovarian oxidative stress (OS) may be the main reason for poor pregnancy outcomes in women of advanced age. OS is a state of excessive expression of oxidative free radicals (ROS) produced by the body, which leads to an imbalance between ROS and the body's antioxidant system (SOD, GSH-Px, etc.). ROS play a central role in cell signaling and in the regulation of major pathways of apoptosis mediated by mitochondria, death receptors, and endoplasmic reticulum. Based on the theory of "kidney-dominated reproduction", antioxidant therapy can be classified into the category of strengthening and tonifying deficiency in traditional Chinese medicine. Modern studies have shown that traditional Chinese medicine for tonifying kidney can regulate the balance of oxidation and antioxidant system of the body, enhance the antioxidant capacity of the body, reduce oxidative damage, and thus protect ovarian function ^[8]. Zhang Yan ^[9] observed that the levels of SOD, CAT and other antioxidant factors in DOR patients decreased significantly, and the levels of MDA and other

oxidative factors increased significantly. It suggests that OS is involved in the pathological process of DOR. After treatment with Bushen Huoxue Decoction, the contents of SOD and CAT increased, and the content of MDA decreased, indicating that Bushen Huoxue decoction can improve the antioxidant stress ability of patients with DOR, thereby improving the ovarian reserve function. Chen Yanxia^[10] showed that Bushen ovulation promotion formula could protect primordial follicle pool and growing follicle, inhibit oxidative damage and reduce excessive apoptosis of granulosa cells by regulating PI3K/AKT/mTOR signaling pathway, so as to protect ovarian function. Wang Qian et al.^[11] selected Shenshu points and Guanyuan points to observe the effect of acupuncture on Nrf2 / HO-1 protein signaling pathway in rats with ovarian dysfunction. The results showed that after acupuncture treatment, FSH, LH, AMH and E2 were significantly improved, SOD content was increased, and MDA content was decreased. Nrf2 and HO-1 protein levels were increased, and compared with the hormone treatment group, the differences were not statistically significant.

Traditional Chinese medicine (TCM) has a long history of treating subfertility in the elderly. Based on the theory of "kidney controlling reproduction", traditional Chinese medicine (TCM) takes invigorating spleen and tonifying kidney, regulating and tonifying the circulation and conception as the treatment method, and adopts the combination of traditional Chinese medicine compound, Chinese patent medicine, enema, acupoint catgut embedding and other traditional Chinese medicine characteristic therapies. It can significantly improve the clinical symptoms of patients, and the clinical objective indications are also significantly improved. In addition, ART has been widely used in recent years, but it only uses hormones to establish artificial cycles and induce ovulation, which cannot be ignored, and it is time-consuming and expensive, and also increases the mental burden of patients. Studies have shown^[12-13] that the "multi-stage and multi-form" participation of traditional Chinese medicine in ART has a clear clinical effect on improving the clinical transfer rate, pregnancy rate and embryo live birth rate.

In conclusion, the therapeutic effect of traditional Chinese medicine (TCM) on this disease has been clinically verified. Not only Chinese medicine syndrome differentiation and treatment, Chinese medicine empirical prescription and traditional Chinese medicine, but also Chinese medicine plus acupuncture, Chinese medicine plus moxibustion, Chinese medicine plus acupoint application (See Figure 5), Chinese medicine plus auricular point, Chinese medicine plus western medicine are widely used in clinical practice, and the application rate is high, and the treatment effect of modern doctors is also quite significant. For the decline of ovarian function, the most important thing for us is to strengthen the function of the ovary, prevent the progress of the disease, especially for women who have fertility needs to preserve their fertility, improve the quantity and quality of follicles, and restore ovarian endocrine function. Therefore, in the future research, we should strengthen the basic research and explore the way of improving ovarian function with traditional Chinese medicine. To better serve clinical patients.



Figure 5: Acupoint application

References

- [1] Menopause Group of Chinese Society of Obstetrics and Gynecology. Expert consensus on hormone replacement therapy for premature ovarian insufficiency [J]. *Chin J Obstetrics and Gynecology*, 2016, 51 (12) :881-886.
- [2] Xu Xiaofeng, Tan Yong, Chen Xuanyi. *Chinese Medicine Information Journal*, 2009, 16 (12): 492-497. (in Chinese)
- [3] Han Lanxiang, Du Juan, Guo Yangzhi. *Cong Hui'fang's experience in treating premature ovarian*

failure. *Sichuan TCM*, 2012, 30 (2) :16-17.

[4] Liu Wei-ping, LI Peipei. *Chinese Journal of Traditional Chinese Medicine Information*, 2015, 22 (10) :97-99.

[5] Zhao Hongli, Zhang Qin, Ma Jing. *Experience of He Jialin in the treatment of premature ovarian failure [J]. Zhejiang Journal of Traditional Chinese Medicine*, 2012, 47(4):240-241.

[6] Yuan Ailing, Wang Fang, Yang Xianhai. *Li Zhiyuan's experience in the treatment of premature ovarian failure from the liver [J]. Seeking Medical Advice*, 2012, 10(7):82-83.

[7] Chen Jing, Wang Chunyan. *Professor Hu Guo-hua's experience in the treatment of premature ovarian failure and low ovarian reserve function. World Journal of Integrated Chinese and Western Medicine*, 2013, 8(10):988-990.

[8] Ma Huirong, Du Huilan, Song Cuimiao, Yang Xiufang, Cao Gang, Li Qingxue. *Effects of Bushen Tiaojing Decoction on oxidative damage, antioxidant capacity and ovarian estrogen level in anovulation rats induced by androgen [J]. Chinese Materia Medica Pharmacology & Clinic*, 2004, 20(5):34-36.

[9] Zhang Y. *The clinical study of Bushen Huoxue prescription regulating oxidative stress to improve ovarian reserve function in patients with kidney deficiency and blood stasis [D]. Nanjing University of Chinese Medicine*, 2020.

[10] Chen Yanxia. *Study on the mechanism of Bushen Huo decoction regulating PI3K and Nrf2 signaling pathway to protect low ovarian reserve function [D]. China Academy of Chinese Medical Sciences*, 2020.

[11] Wang Qian, LU Ge, Xie Zijing, et al. *Effect of moxibustion on Nrf2/HO-1 signaling pathway in rats with decreased ovarian reserve [J]. Chinese Acupuncture and Moxibustion*, 2021, 41(1):6.

[12] CAI Liang, Li Li, Zhao Yilin, et al. *Effect of Bushen Jianpi acupuncture on ovulation induction with antagonist protocol in infertility patients undergoing IVF-ET treatment [J]. Shanghai Journal of Acupuncture and Moxibustion*, 2021, 40(1):5.

[13] Wang F H , Tan Y , Yin Y Y , et al. *Effects of Ziyin Buyang Sequential Formula combined antagonist on the outcome of poor ovarian response in vitro fertilization[J]. China Journal of Traditional Chinese Medicine and Pharmacy*, 2019.