Advances in Clinical Research in Chinese Medicine for Decreased Ovarian Reserve Function

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Abstract: Decreased ovarian reserve function (DOR) is a pre-disease state of premature ovarian failure (POF), the pathogenesis of which is not well understood and the disease is insidious, so early detection and active treatment can save adverse outcomes. In recent years, the incidence of DOR has become younger, which seriously affects women's physical and mental health. In this paper, we analyze the etiology and clinical treatment methods from relevant experimental studies and clinical observations in the past 5 years, in order to provide theoretical support and treatment ideas for female reproductive health.

Keywords: Decreased Ovarian Reserve Function, Etiology and Pathogenesis, Chinese Medicine Treatment, Review

Decreased ovarian reserve function (DOR) refers to the decrease in quality of oocytes in the ovarian cortex before the age of 40 years, reduced ability of follicles to grow, develop and form fertilizable follicles, decreased AMH level, increased FSH and FSH/LH ratio, and decreased AFC, which are reliable serological indicators of ovarian reserve function, mainly manifesting as menstrual disorders or even amenorrhea, lack of sex hormones and decreased fertility, and accompanied by a series of perimenopausal symptoms, seriously affecting women's work and life[1]. The progression of DOR to POF is a gradual process that can develop into irreversible lesions in about 1-6 years without intervention. Therefore, intervention and treatment in the early and middle stages of the disease to reverse the decline of ovarian function and improve fertility outcomes reflects the idea of "treating the disease before it occurs" in Chinese medicine, and is also a hot issue in reproductive medicine today. Current Western medical treatments are limited and mostly target clinical symptoms such as scanty and late menstruation for symptomatic treatment and restoration of normal cycles. The commonly used treatment is estrogen and progestin replacement therapy (HRT) with sequential treatment, such as estradiol valerate, progesterone capsules, Clomid, and fenomycin, in order to form a negative feedback mechanism to reduce serum levels of FSH and LH and FSH/LH ratio and increase E2, which leads to follicular recovery and ovulation, and patients can have regular menstrual-like withdrawal bleeding every month during the drug administration [2]. The clinical efficacy is obvious, but the adverse effects should not be ignored. 10-year follow-up studies suggest that the overall treatment efficiency is less than 75% after prolonged application, and the risk of breast cancer and endometrial cancer is increased by 30% and 40% in some patients compared with the normal population, which tends to increase the risk of hormone-dependent neoplastic diseases [3,4].

According to its clinical symptoms, it is classified as "late menstruation", "irregular menstrual flow", "menstrual disorders", "infertility" and other gynecological diseases. According to its clinical symptoms, it is classified as "late menstruation", "irregular menstrual flow", "infertility", and "menstrual flow breaking before old age" in the category of gynecological diseases. Chinese medicine has rich clinical experience in the treatment of gynecological diseases, and has a variety of protocols to regulate the patient's body as a whole by adjusting the hypothalamic-pituitary-ovarian axis and enhancing the body's immune function under the guidance of evidence-based treatment and holistic concept, with very few adverse effects. In this paper, we have collected relevant literature in the past five years to provide a comprehensive description of the etiology and mechanism of this hot issue of DOR and TCM treatment, in order to provide reference for clinical practice.

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1. Modern Research Advances in the Pathogenesis of DOR

The causes of most patients are not fully understood, but modern medical findings are mainly related to the following factors: (1) genetic factors: genetic abnormalities such as abnormal X chromosome number, autosomal abnormalities and genetic mutations can cause impaired follicular development in the ovary, leading to the occurrence of DOR. (2) Enzyme defects: deficiencies of related enzymes such as galactose-1-phosphate uridyltransferase (GALT), 17α-hydroxylase, 17,20-cleavage enzyme, and steroid hormone dehydrogenase can alter gonadotropin activity, elevate FSH in a negative feedback mechanism, and accelerate follicular atresia [5,6]. (3) Autoimmune factors: such as anti-ovarian antibodies (AoAb), anti-nuclear antibodies (AnAb), anti-cardiolipin antibodies (AcAb), anti-thyroglobulin antibodies (TG-Ab) and thyroid peroxidase antibodies (TPoAb), anti-ovarian zona pellucida antibodies, anti-nuclear antibodies and other antibody positivity often lead to abnormal ovarian blood supply and induce the body to produce anti The presence of ovarian autoantibodies in turn accelerates DOR and premature ovarian failure [7,8]. (4) Medical factors: one of the common factors leading to acquired ovarian reserve hypofunction. Surgery on ovaries and surrounding tissues damages ovarian tissues and causes local inflammation, which reduces ovarian blood supply; radiotherapy can induce loss of oocyte or granulosa cell function. (5) Environmental pollution, poor lifestyle, and psychological factors: at present, environmental pollution is serious, and the massive use of life such as pesticides, indoor formaldehyde, and chemicals such as cadmium, arsenic, and mercury can also damage ovarian function [9].

Current research results show that excessive obesity, underweight and improper diet, smoking, excessive exercise, alcohol consumption, caffeine intake, drug use and even mental stress have particularly significant effects on the female reproductive system [10].

2 TCM Etiology and Pathogenesis

According to the results of a study exploring the distribution of TCM evidence of DOR, the TCM evidence of DOR can be divided into five main types: kidney deficiency and liver depression, spleen and kidney deficiency, liver and kidney yin deficiency, kidney deficiency and blood stasis, and kidney yin and yang deficiency [11]. 5 main types of evidence include kidney deficiency, which shows that kidney essence failure is the main pathogenesis of DOR, which is consistent with the main view of current scholars.

2.1 Kidney Deficiency and Liver Depression

The "Medical Zong must read" cloud: "the same source of B and Dec, liver and kidney with the same treatment." Liver belongs to "B wood" and kidney belongs to "Kui water". On the one hand, kidney is the mother of liver, liver is the son of kidney, liver and kidney are of the same origin, the essence and blood are mutually transformed, the collection and drainage are mutually used, the yin and yang are mutually nourished and controlled, kidney yin nourishes liver yin and controls liver yang together, kidney yang finances liver yang and warms liver veins together. The two complement each other physiologically, and together regulate the uterus Tibetan drainage function, so that it opens and closes the degree, so that the female menstrual flow and reproductive function, the pathology of mutual influence, liver blood and kidney essence due to female menstruation and maternity breast easy to lose, "Medical Zong Jin Jian" cloud: "women from the human Therefore, menstrual disease due to the seven emotions are mostly." [12] Modern women need to balance career and family, tension, fatigue and other adverse emotions are prone to liver qi stagnation, the symptoms of kidney deficiency and liver depression manifestations.

2.2 Deficiency of both Spleen and Kidney

The kidneys are the main innate, the spleen is the main posterior, the spleen and stomach, the water and grain essence into blood, both to nourish the kidney essence, but also through the meridian infusion uterus, as the main menstrual flow. Currently many women follow the trend of "thin for beauty", more and more women use controlled diet to achieve the purpose of slimming, in the long run will damage the spleen and stomach function, biochemical lack of source of qi and blood, punching the uterus without blood can be down. Many women choose to take oral diet pills to lose weight by interfering with nutrient metabolism and absorption, which can cause endocrine disorders and, in severe cases, liver and kidney function damage and kidney essence deficiency [13,14].

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2.3 Liver and Kidney Yin Deficiency

The kidney collects essence, the liver collects blood, and the essence and blood nourish each other so that the menstrual blood springs inexhaustible. If the kidney essence deficiency, liver blood deficiency, liver depression, Qi stagnation, dysregulation of the two veins, the uterus is not moistened, it will cause menstrual disorders. Poor lifestyle, such as staying up late and sleeping late, prolonged vision, and overexertion consume the essence and blood, resulting in low menstrual flow or even withering of the blood and menstrual closure; while deficiency of essence and blood in the liver and kidney can easily lead to loss of control of liver yang, which turns into fire and consumes fluids, resulting in thick blood, causing stasis of the ramus and the uterus, resulting in abnormal menstruation and obstruction of fertility [15,16].

2.4 Kidney Deficiency and Blood Stasis

Women take blood as the basis and qi as the use. The deficiency of the kidney leads to deficiency of the kidney, which is caused by the depletion of the kidney essence due to the lack of blood vessels, stagnation of the veins, and poor blood flow, resulting in stasis [17]; deficiency of yin and blood to control yang, deficiency of heat, and sticky blood, resulting in stasis; and deficiency of kidney qi, which is unable to promote blood flow [18]. Therefore, kidney deficiency is the main cause of the disease, and blood stasis is the symptom of the disease.

2.5 Kidney Yin and Yang deficiency

The kidneys contain essence, and the essence in the kidneys is divided into kidney yin and kidney yang. The kidney yin nourishes and moistens the internal organs, and the kidney yang can promote the warmth of the internal organs, just like the water and fire, so the cloud "kidney for the water and fire of the house, the true yin and contain the true yang." Water and fire loss of its system, true water deficiency, lack of source, menstrual blood deficiency to moisten the uterus; or yin deficiency, burning fluid, flushing also its disturbance; if the kidney yang deficiency, the vital fire failure is flushing the uterus loss of warmth, blood vessels are not smooth, can affect the woman normal pregnancy.

3 Chinese Medicine Treatment

3.1 The Idea of "Treating the Untreated"

Zhang Zhongjing, the sage of medicine, proposed that "the best work is to treat the untreated". In the Shen Jian - Miscellaneous Words, it is said that "prevention is the first priority, rescue is the second, and precaution is the next." The basic elements of the idea of treating the untreated disease include: prevention before illness (diet and regular physical examination), prevention after illness (early treatment and prevention of gradual changes), and prevention of recurrence after disease (consolidation of treatment and regulation of emotions). In other words, in the different processes of disease development, different treatments are used to slow down the process. As the Su Wen - Shang Gu Tian Zhen Lun said: "Harmonize with the arts and figures, and the method of Yin and Yang And the end of his heavenly life, to the extent of a hundred years before leaving." To prevent the occurrence of diseases, firstly, we should regulate our lives, maintain a peaceful state of mind, make our body function in accordance with the laws of nature, exercise appropriately, and maintain the harmony and unity between the body and the external environment. delay disease progression and reduce the occurrence of complications [19].

3.2 Dialectical Treatment in Chinese Medicine

3.2.1 Tonifying the Kidney and Draining the Liver

Liu Yanfeng[20] showed that the self-designed formula of tonifying the kidney and regulating the liver could effectively improve ovarian reserve function and chronic psychological stress. The mechanism of this formula in animal studies was related to the upregulation of PI3K/AKT/m TOR signaling pathway in the ovary and hippocampus, which can promote vascular renewal, improve hippocampal blood circulation, and participate in the regulation of cell proliferation, metabolism, apoptosis and a series of other vital phenomena. Yang Qingqing [21] et al. selected 50 outpatients with kidney deficiency and liver depression and gave the observation group Zhi Kidney and Liver Tonics,

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adding fried white peony, Chai Hu, neem, incense stick and green calyx plum to the kidney tonifying formula to soften the liver and detoxify the liver, and confirmed that it could improve the clinical symptoms and sex hormone levels of DOR patients; Huang Ziwei et al [22] studied the endometrial tolerance in mice with chronic stress and liver depression evidence model, and the results showed that the liver tonifying and kidney tonics The results showed that the herbs could improve the levels of E2, P and HCG in the model mice, increase the content of estrogen and progesterone receptors in the endometrium, increase the affinity of estrogen receptors in target tissues, improve endometrial proliferation and secretion, improve endometrial tolerance and increase the number of implantations.

3.2.2 Nourishing the Spleen and Kidneys

Liu Kaiya et al [23,24] used Chinese herbal medicine in combination with electro-acupuncture to treat DOR with the principle of strengthening the spleen and tonifying the kidneys, harmonizing yin and yang, and activating blood circulation and resolving blood stasis with remarkable efficacy. Luo Songping[25] inherited the academic experience of Luo's gynaecology in Lingnan and considered DOR to be a common occurrence among the "five and seven" people, and used Shou Fetus Pill minus Agaricus and Si Jun Zi Tang to restore and improve ovarian function. Wang Daqing [26] used tonifying kidney and spleen soup combined with hormone therapy to treat osteoporosis in patients with DOR. Estrogen supplementation promoted bone densification, increased osteocalcin, decreased calcitonin, and significantly increased the levels of bone metabolic indexes compared to the previous levels, and the CT levels of bone metabolic indexes were higher than those of the control group.

3.2.3 Nourishing the Kidney and Nourishing the Liver

Yao Wei et al[27] formulated a series of formulas to regulate the menstrual cycle and improve the endocrine function, and found that they effectively lowered the serum hormone levels. Guo Lixuan et al [28] showed that the daily consumption of Qiyue Yue tea for the treatment of liver and kidney yin deficiency type of DOR was similar to the effect of fenmodong, but more convenient and without adverse effects, which also laid the foundation for the clinical development of Chinese health products for the treatment of DOR.

3.2.4 Tonifying the Kidney and Invigorating the Blood

Li Wei [29] et al. concluded from a retrospective analysis of 80 cases of DOR patients with kidney deficiency and blood stasis admitted to outpatient clinics that the results showed that the serum FSH and LH levels of patients in the treatment group were lower than those in the control group, and the serum E2 level was higher than that in the control group, and that the formula for nourishing the kidney and invigorating blood had the effect of nourishing kidney yin, nourishing blood and resolving blood stasis, accelerating ovarian angiogenesis, promoting ovarian release of follicles and corpus luteum, and improving blood supply. Zeng Fuling [30] concluded that in the clinical efficacy of the Revitalizing Blood and Invigorating Blood formula and Clonimax in treating patients with immune POF and DOR, both of them could increase ovarian volume to some extent, increase the number of sinus follicles, decrease the ovarian stromal blood flow resistance index and pulsatile index, and thicken the endometrial thickness, but the Revitalizing Blood and Invigorating Blood formula was more effective.

3.2.5 Tonifying the Kidney Essence

Geng Jian et al [31] treated 66 patients with kidney deficiency type DOR with Gui Kidney Pill plus reduction. The sex hormones in the treatment group improved, the ovulation rate and pregnancy rate increased, and the TCM symptom score was lower than that of the control group, which was statistically significant. Xu Bihong [32] et al. formulated their own formula for tonifying the kidney and regulating menstruation with an effective rate of 78.26% in the treatment of DOR, and the rate of improvement of menstruation and the time of improvement of menstruation were significantly better than that of the Western medicine group.

3.3 Acupuncture Treatment

Modern research has shown that acupuncture activates the dopamine system in the brain, stimulates the meridians to regulate the neuro-immuno-endocrine network, adjusts the function of the hypothalamic-pituitary-ovarian reproductive axis itself, regulates the immune balance and the release of relevant neurotransmitters, and promotes the gradual recovery of reproductive endocrine function. Li Chen et al [33] analysed the pattern of acupuncture point selection for DOR treatment based on data mining, and the most frequently used meridian was the Ren meridian, and the most effective and commonly used acupuncture points were "Guan Yuan, Kidney Yu and San Yin Jiao", "San Yin Jiao, Zi

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Gong and Foot San Li". In a study by Fang Intergong et al [34], 13 acupuncture points were used to regulate menstruation and promote pregnancy, including Zhi Yu, Guan Yuan, Da He, Ovary, Sanyin Jiao and Foot San Li, in order to tonify the kidney essence, regulate Chong Ren and calm the mind. The experiment showed that acupuncture can reduce FSH value, increase AFC, reduce SAS score, and improve ovarian function and anxiety in DOR patients. Feng Xiaoling [35] used Yuyin pill with electroacupuncture to stimulate the acupoints of Sanyinjiao, Taixi, Taichong and Zi Gong to tonify the liver and kidney and nourish yin, to regulate the Chong Ren, and to nourish the blood and activate the blood.

3.4 Embedding of Acupuncture Points

Acupuncture point embedding, also known as TCM protein embedding, is an extension and development of acupuncture needle retention and embedding methods, and is a long-acting acupoint stimulation therapy [36]. Zhang Linyun et al [37] selected 60 patients with DOR and used Qihai, Guanyuan, Zhongji, Zigong, Fusanli and Sanyinjiao as the main acupoints based on the theory of "Ren is the main twin". The results showed that the overall efficiency of the observation group was 93.10% better than that of the control group (76.67%). Zhang Jiajia et al [38] selected Yin Du, Shi Guan, Zhi Yu, Qi Chong, Qi Hai, Guan Yuan and Zhong Ji for the buried threads. The results of the study showed that the FSH, FSH/LH and TCM symptom scores of DOR patients decreased significantly after the buried threads treatment at the Chong Ren meridian points compared with those before the treatment.

3.5 Ear Point Bean Press

Liang Jing et al[39] applied Wang Bu Liu Xing seeds to ear points, selecting the heart, kidney and ovary corresponding ear points, and then selecting the sympathetic, subcortical, Shen Men and hypothalamus ear points, fixed with adhesive tape, pressing 6-8 times/d, combined with Chinese medicine cycle therapy, after treatment, the efficiency reached 95%, the perimenopausal symptoms were relieved, and the pregnancy success rate was improved.

4. Conclusion

The pathogenesis of DOR is still unclear and the insidious nature of the disease is a growing concern. In terms of prevention and treatment, women aged 35 years and above should have relevant biochemical tests and ultrasound examinations, regular medical check-ups and real-time monitoring of ovarian status; for established disease, the cause should be identified and therapeutic interventions should be made to prevent progression to premature ovarian failure. In terms of treatment, Western medicine is based on hormone replacement therapy, which is clinically effective but costly, has high side effects and is highly dependent. In contrast, Chinese medicine has a wealth of experience in treating DOR, which is tailored to the individual and has good long-term efficacy with few side effects, and can be regulated holistically with multiple systems, links and targets. Through the hormone-like effects of Chinese medicine, HPOA is regulated, the endocrine environment is adjusted and the patient's physical condition is improved. It is also combined with acupuncture, acupuncture point buried thread, auricular pressure bean and other Chinese medicine characteristics, combined with the patient's own characteristics to choose the best plan, clinical application and good results. At present, the classification of DOR Chinese medical evidence is complicated and not yet unified. With the strong support of the state for the development of motherland medicine, we should actively generalize and explore the etiology and pathogenesis, classification of symptoms and treatment of reduced ovarian reserve function to promote the further development of Chinese medicine, with a view to achieving more satisfactory clinical treatment results.

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