

Progress in Diagnosis and Treatment of Polycystic Ovary Syndrome with Traditional Chinese and Western Medicine

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Abstract: *Polycystic ovary syndrome is a common multifactorial and complex endocrine disorder disease in gynecology. The pathogenesis is not clear, its clinical manifestations are diverse, and the treatment schemes are also diverse. It is a hot and difficult point in the field of reproductive medicine. This article reviews the current progress in the diagnosis and treatment of polycystic ovary syndrome with traditional Chinese and Western medicine.*

Keywords: Etiology of polycystic ovary syndrome treated with Chinese and Western Medicine.

1. Introduction

Polycystic ovary syndrome (P-COS) is the most common gynecological endocrine disorder in adolescent and reproductive age women. It is a disorder of hypothalamic pituitary ovarian axis function, menstrual disorder (menorrhagia, amenorrhea), infertility, hirsutism, obesity, acanthosis nigra and ovarian polycystic changes caused by multiple genetic, polygenic and environmental factors. Its endocrine characteristics are mainly LH elevation, E1/E2>1, hyperandrogenism, hyperinsulinemia, and the long-term complications caused by it, including insulin resistance, abnormal glucose and lipid metabolism Cardiovascular disease, breast cancer, endometrial cancer[1]. It is reported that the prevalence of PCOS among people of childbearing age in China is 5.61%[2], Thin and infertile patients account for 80%[3]. The prevalence of infertility is 7%~10%, infertility caused by ovulation disorders accounts for 25%~35%[4], among which P-COS accounts for 50%~70% of anovulatory infertility, and 50% of women who use assisted reproductive technology to help pregnancy have P-COS[5]. The condition has been reported that androgenic alopecia, sleep apnea, depression, pregnancy induced hypertension, preeclampsia, nonalcoholic fatty liver disease caused by lipid metabolism, etc. can also be complicated[6]. It seriously affects the health of women throughout their lives. In this paper, the etiology, pathogenesis and clinical research progress of traditional Chinese and Western medicine of P-COS are summarized as follows.

2. Etiology of P-COS

2.1 Genetic Factors

Polycystic ovary syndrome is hereditary, and the prevalence of P-COS in female immediate relatives of the patient is increased. Compared with normal people, the sisters of P-COS patients are more likely to have menstrual disorders, hyperandrogenemia and polycystic ovary, and the probability is 4 times that of normal people. The heritability of PCOS patients and their incidence rate in identical twins are significantly higher than that in non-identical twins. Norman et al.[7] found that P-COS is hereditary, and monozygotic

twins cannot all be sick, suggesting that PCOS is not caused by a single genetic gene. Therefore, some scholars believe that it is caused by multiple genes and gene polymorphisms, including androgen, insulin, chronic inflammatory response related genes, etc.

2.2 Insulin Resistance

Insulin resistance refers to the decrease of peripheral tissue sensitivity to insulin, which makes the biological efficiency of insulin lower than normal. Insulin exerts its effects on ovaries through intracellular signal transduction pathways, including the pro metabolic pathway that regulates glucose metabolism and the pro mitotic pathway that causes ovarian cell division and proliferation. The probability of occurrence in women with polycystic ovary is more than 50%. The ratio of hyperinsulinemia and insulin resistance in P-COS patients is 50%-70%[8]. Some scholars believe that insulin resistance is the main reason for the occurrence and development of P-COS. Insulin resistance leads to the impairment of the metabolic pathway, the compensatory increase of insulin, the formation of hyperinsulinemia, and the amplification of the function of the mitogenic pathway of insulin/insulin-like growth factor in cells, which leads to the excessive proliferation of theca cells and stromal cells, secretes more androgens, and further aggravates hyperandrogenemia. Hyperinsulinemia also inhibits the synthesis of sex hormone binding globulin in the liver. Increase free sex hormones in the body and promote their biological effects. In addition, androgen is converted into E1 in the peripheral tissue, which increases the secretion of LH in the pituitary gland. Excessive LH and insulin jointly stimulate theca cells and stromal cells of the ovary. The recruitment of follicles with mitogenic effect increases, while the relative deficiency of FSH leads to the stagnation of follicular development and follicular stage, which eventually leads to ovulation disorder and the formation of polycystic ovary.

2.3 Inflammatory Factors

The inflammatory factors in patients with PCOS were significantly higher than those in normal people, including interleukin-6 (IL-6) and IL-1 β . Tumor necrosis factor- α

(TNF- α) and inflammatory factors such as C-reactive protein (CRP) may play an important role[9]. Inflammatory factors affect normal ovulation by increasing the level of androgen metabolism and interfering with the hypothalamic pituitary adrenal axis, affecting the normal growth and development of follicles. Popovic et al.[10] found that a variety of inflammatory factors in the serum of patients with P-COS are higher than those of normal people, and this phenomenon is more significant in patients with insulin resistance, suggesting that inflammatory factors are related to insulin resistance in patients with P-COS, and inflammatory factors may indirectly lead to polycystic ovary syndrome by increasing insulin resistance.

2.4 Environmental Factors

Environmental factors: women who consume too much fat and sugar, lack of sleep, work, economy and competition are prone to mental tension and P-COS, which are high-risk factors for the occurrence of P-COS. Obese P-COS patients usually have unhealthy lifestyles such as excessive food intake, incorrect eating patterns (irregular eating, partial eating, eating too fast, etc.) and lack of exercise. Obese P-COS patients have higher blood pressure, cholesterol, triglyceride, blood glucose and insulin levels than normal people, and are more prone to metabolic disorder syndrome. Some studies have pointed out from the analysis of the relationship between family environment and children's spirit that children with disharmonious families, low education level and poor family economic conditions are prone to mental stress, while long-term mental stress can cause the imbalance of endocrine system, and the typical manifestation will be menstrual disorders (sparse menstruation, amenorrhea), which is a high-risk factor causing P-COS [11].

3. H-P-O Axis Adjustment Function Disorder

Due to the dysfunction of h-p-o axis, the vertical body has increased sensitivity to hypothalamic gonadotropin releasing hormone, secreted excessive luteinizing hormone (LH), and stimulated ovarian stroma and theca cells to secrete androgens[10]. High androgens in the ovary inhibit follicular maturation and cannot form dominant follicles, but multiple small follicles in the ovary can still secrete low levels of estradiol; In addition, the increased androstenedione is converted into estrone in the periphery, forming hyperestrinemia[11]. In the peripheral circulation, this abnormally secreted estrogen acts on the hypothalamus and pituitary, giving a negative feedback on the secretion of FSH, causing a relative decrease in the level of FSH and an increase in the proportion of LH/FSH. High levels of LH also promote the secretion of androgens by the ovaries. Continuous FSH stimulation stops the development of small follicles in the ovaries, thus forming a vicious cycle of excessive androgens and continuous anovulation, and finally forming ovarian polycystic changes.

4. TCM Understanding of Polycystic Ovary Syndrome

Traditional Chinese medicine has no exact disease name corresponding to P-COS. According to its clinical symptoms

and characteristics, this disease can be classified into the categories of "late menstruation", "amenorrhea" and "infertility", and P-COS is the syndrome of deficiency and excess, and the dysfunction of kidney, liver and spleen is the main cause of its occurrence.

4.1 Kidney

Kidney deficiency: medical Zhuan Zheng says: "menstruation is all based on kidney water. If kidney water is scarce, menstrual blood is increasingly dried up"; Another "annotation of a woman's good prescription - seeking heirs" says: "a woman has no children, because of lack of Chong Ren and weak kidney qi, so it is also.". Kidney is the origin of congenital, the root of vitality, the source of acquired biochemistry, and it is mainly responsible for reproduction, uterus and essence storage. Therefore, the deficiency of kidney yin and kidney yang leads to menstrual disorder, Chong Ren pulse failure, cell loss of nourishment and infertility.

4.2 Spleen

The spleen is the acquired foundation and the biochemical source of Qi and blood. The secret collection of the orchid room says: "a woman's spleen and stomach are deficient for a long time, or her body is weak in both qi and blood, resulting in the disconnection of menstruation and water." Spleen deficiency leads to biochemical passivity of Qi and blood, and Qi and blood deficiency, which cannot nourish the uterus, leads to late menstruation; "Medical school Jian Jin" said: "because the body is full of phlegm, the lipid membrane is blocked in the cell and cannot be pregnant." Professor Bing Sun[12] believes that if the spleen is deficient and dysfunctional and cannot transport water, the water dampness will stop, the phlegm dampness will be accumulated, and the cellular collaterals will be blocked, resulting in menstrual disorders, rare episodes, amenorrhea, and even obesity.

4.3 Liver

QingFu governs women's science" said: "a woman has intermittent menstruation, or no regular period before or after, people think that the Qi and blood is also empty, but who knows it is the stagnation of liver Qi! The husband's menstrual fluid flows out of the kidneys, and the liver is the son of the kidney, and liver depression is also the stagnation of the kidney". The liver likes and dislikes depression, poor mood, abnormal liver Qi catharsis, disharmony of Qi and blood, and imbalance of Chong Ren cause amenorrhea or infertility.

5. Treatment Plan

5.1 Western Medicine Treatment Plan

5.1.1 Lifestyle intervention

The basic treatment of P-COS patients is to improve their bad living habits, especially for obese P-COS patients. Lifestyle intervention includes diet control, exercise and behavior intervention. Adjusting bad living habits can increase insulin sensitivity and reduce insulin and testosterone levels, so as to

restore ovulation and reproductive function[13].

3.1.2 Regulating menstrual cycle

Drugs should be used regularly and reasonably to regulate menstrual cycle. It is very traditional Chinese medicine for controlling menstrual cycle, especially for patients with menstrual disorder and menstrual cycle greater than 2 months. P-COS patients whose endometrium is stimulated by estrogen for a long time are prone to endometrial hyperplasia and endometrial cancer. According to different physiological stages and the level of sex hormones in the body, periodic progesterone therapy, short acting compound oral contraceptive (COC) and periodic sequential therapy of estrogen and progesterone can be considered. The compound oral contraceptive is composed of synthetic estrogen and progesterone. Commonly used are ethinylestradiol, cyproterone tablets (Diane-35), spironone ethinylestradiol tablets (ursamine), etc. Ethinylestradiol cyproterone is the preferred drug. Its mechanism of action is mainly to inhibit dihydrotestosterone by combining with dihydrotestosterone receptor, and inhibit the activity of 5- α reductase, so as to inhibit the secretion of sex hormones in the hypothalamus and reduce the production of androgens in the ovary; In addition, the resistant gland effect of ethinylestradiol cycloacetone is further enhanced by ethinylestradiol, which improves the synthesis of blood sex hormone binding globulin, and can be rapidly absorbed and metabolized by the body[14].

5.1.3 Reduce androgen levels

Hyperandrogenemia or hyperandrogen is the main endocrine feature of PCOS, which is mainly manifested in acne, hirsutism, acanthosis nigricans, etc. short acting compound oral contraceptives are the first choice for treatment. Estrogen can increase the production of SHBG in the liver and reduce free androgens in the blood; Progesterone can inhibit LH secretion and ovarian androgen synthesis; The combination of estrogen and progesterone can reduce the synthesis of adrenal derived androgens. Spironolactone and glucocorticosteroids can also be used for patients with poor contraceptive treatment, taboo or intolerable hyperandrogens.

5.1.4 Improve insulin resistance

Insulin resistance is an important factor in the occurrence of P-COS. The current guidelines believe that the primary treatment of insulin resistance is to adjust lifestyle, followed by the use of insulin sensitizers. Metformin is the most commonly used insulin sensitizer, which can inhibit the synthesis of glucose in the liver, increase the utilization of glucose in peripheral tissues, improve the sensitivity of peripheral tissues to insulin, correct the patient's hyperandrogen state by reducing the blood insulin level, so as to regulate menstruation and resume ovulation[15].

5.1.5 Induced ovulation

For those who have fertility requirements, ovulation induction treatment should be carried out after basic treatment such as lifestyle adjustment, anti-androgen and improvement of insulin resistance. (1) Clomiphene is a traditional first-line ovulation inducing drug, with an ovulation rate of 73%~87%.

The drug is cheap, and the method is simple, safe and effective, but its half-life is long, the peripheral anti estrogen effect affects cervical mucus, as well as ovarian hyperstimulation syndrome, and the multiple pregnancy rate is high; (2) Letrozole; As a P-COS ovulation inducing drug, compared with clomiphene, it does not affect endometrium and cervical mucus, and is conducive to embryo implantation. Its single follicle rate is high, reducing multiple pregnancy and ovarian hyperstimulation syndrome[16].

5.1.6 Assisted reproduction

Assisted reproductive technology is a third-line treatment for polycystic ovary syndrome. When ovulation induction treatment fails, IVF is recommended to help pregnancy. Studies have shown that patients with P-COS and non P-COS who undergo IVF assisted pregnancy have similar clinical pregnancy rate and live birth rate. The purpose is to obtain more high-quality oocytes, improve fertilization rate, pregnancy rate and reduce the incidence of ovarian hyperstimulation syndrome.

5.2 TCM Treatment Plan

5.2.1 Traditional Chinese medicine periodic therapy

Periodic therapy is a treatment method that uses drugs by stages according to the law of kidney yin, kidney yang transformation, growth and decline rhythm and the change of Qi and blood profit and loss in different periods of menstrual cycle, combined with the pathogenesis characteristics of gynecological diseases, in order to adjust the function of kidney Tiangui Chongren uterine axis. Yuting Yang[17] and others began to use yulinzhu from the third day of withdrawal bleeding. Tiaogan decoction was used during ovulation, and Taohong Siwu Decoction was added or subtracted during luteal phase. Combined with acupuncture treatment, the number of ovulation, the number of dominant follicles and the thickness of endometrium during ovulation after 6 months of treatment were better than those in the control group daying-35. YongTan [18] believes that the sequential treatment of nourishing yin and yang can reduce the incidence of ovarian hyperstimulation syndrome, increase endometrial thickness, improve endometrial receptivity, and improve pregnancy rate.

5.2.2 Syndrome differentiation and treatment

Traditional Chinese medicine believes that the pathogenesis of infertility caused by PCOS is based on kidney deficiency, dysfunction of kidney, liver and spleen, phlegm dampness and blood stasis, which destroys the yin-yang balance between the reproductive axis of kidney - Tiangui - Chong Ren - uterus, resulting in infertility. Modern doctors often treat polycystic ovary syndrome from the kidney, spleen and liver. Professor Juan Wang[19] believes that the disease is mainly responsible for the kidney and spleen. The deficiency of Yang in the spleen and kidney is the core pathogenesis of the disease, and the endogenous phlegm and dampness is the standard. On the basis of the classic prescription Yougui Pill, it is combined with addition and subtraction, which has the effect of warming the kidney and strengthening the spleen, resolving phlegm and removing dampness. Professor Xin Xu[20]

attaches importance to tonifying the kidney in the treatment of polycystic kidney disease. It is often used by *Dipsacus asper*, parasitic mulberry and dodder. They all enter the liver and kidney meridians, and have the effect of Tonifying the liver and kidney. At the same time, they are flexibly compatible with Liver Soothing drugs, Qi tonifying drugs, blood nourishing drugs, dampness diuretics, stasis removing drugs, etc.

5.2.3 Acupuncture Therapy

Acupuncture therapy can regulate the body environment as a whole, has small adverse reactions, has good curative effect in the treatment of P-COS, and has unique advantages in preventing and reducing complications. Dun Jingjing et al.[21] observed the therapeutic effect of acupuncture and drug artificial cycle combined with letrozole in the treatment of P-COS ovulation disorder infertility with kidney yang deficiency syndrome. On the basis of oral letrozole ovulation induction, the treatment group adopted traditional Chinese medicine and acupuncture cycle therapy in the follicular phase, ovulation phase and corpus luteum phase respectively, Traditional Chinese medicines are used to replenish kidney yang, nourish kidney yin and soothe the liver, such as antler cream, dodder, raspberry, *Cyperus*, angelica, *Dipsacus*, *Eucommia ulmoides*, astragalus, etc. acupuncture points such as Guanyuan, Qihai, uterus, ovary, Zhongji, Wushu, blood sea, etc; After 3 months of treatment, the TCM symptom score of the treatment group was lower than that of the control group (3 months of oral letrozole treatment), the number of ovulation cycles was higher than that of the control group ($P<0.01$), and the levels of luteinizing hormone, luteinizing hormone/follicle stimulating hormone and testosterone were lower than that of the control group ($P<0.05$ or $P<0.01$); The thickness of endometrium was thicker than that of the control group ($P<0.05$), and the pregnancy rate (60%) was significantly higher than that of the control group (32%, $P<0.05$).

6. Summary and Outlook

P-COS is a disease caused by many factors, and its treatment is still difficult and hot. Although western medicine treatment can improve the hormone level in patients and increase the ovulation rate and pregnancy rate, it is difficult to overcome its adverse reactions such as low ovulation or "high ovulation and low pregnancy" and ovarian hyperstimulation syndrome. While the curative effect of traditional Chinese medicine is positive and the occurrence of adverse reactions is less, most of its literatures have problems such as too few samples. The combination of traditional Chinese and Western medicine in the treatment of P-COS infertility, traditional Chinese medicine and acupuncture combined with western medicine, acupuncture combined with western medicine, and traditional Chinese medicine combined with modern assisted reproductive technology have achieved remarkable results, which proves that traditional Chinese medicine treatment can not only improve patients' clinical symptoms and endocrine levels, promote ovarian function recovery and follicular development, optimize pregnancy outcomes, but also reduce the incidence of multiple pregnancy and LUFs and other complications, It can be used as an important treatment for P-COS infertility.

Due to the lack of relevant basic research, whether the method of integrated traditional Chinese and Western medicine can be more accurately applied to the clinical treatment of P-COS infertility still needs to be supported by relevant pharmacological research and large sample data, so as to obtain a more comprehensive and reliable evidence-based basis.

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