

Research Progress of Chinese and Western Medicine in Non-obese Polycystic Ovary Syndrome

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Abstract: *In recent years, the number of patients with non-obese polycystic disease has gradually increased. Its clinical manifestations are different from those of obese polycystic disease, and the treatment should also be different from those of obese polycystic disease. This paper summarizes the endocrine and metabolic characteristics and TCM syndromes of non-obese PCOS patients in order to provide ideas for the systematic treatment of non-obese PCOS based on syndrome differentiation of traditional Chinese and Western medicine in the future.*

Keywords: Non-obese type, Polycystic ovary syndrome, Traditional Chinese and western medicine, Diagnosis, summary.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases in gynecology. Most patients have metabolic disorders and reproductive dysfunction at the same time. Short-term clinical manifestations include amenorrhea, less menstruation, infertility, ovarian enlargement, obesity and so on. From the perspective of long-term clinical manifestations, it can be complicated by diabetes and even Xie syndrome [1]. However, in recent years, according to the author's observation, the number of non-obese patients (in accordance with the diagnostic criteria for the diagnosis and treatment of polycystic ovary syndrome in China [2] and BMI<25 [3] issued by the Endocrinology Group of the Chinese Society of Obstetrics and Gynecology and the Guideline expert Group in January 2018) has gradually increased, and the gonadotropin disorder is the main manifestation. Compared with the disorder of glucose and lipid metabolism in obese patients, the treatment of non-obese patients is more complicated. Long-term endocrine disorders will increase the physiological and psychological burden of patients and reduce the quality of life of patients. Therefore, more attention should be paid to non-obese patients with PCOS clinically, timely and accurate detection and systematic treatment should be taken.

2. Advances in Western Medicine Research

2.1 Endocrine

It is generally believed that [4] compared with obese patients, non-obese patients have higher LH value, more obvious LH/FSH>2, and lower E value [5], and the expression level of AMH in non-obese patients is much higher than that of healthy people [6]. Non-obese polycystic patients with high androgen (HA) are mainly manifested as hirsute (sexual hair, black and thick body hair visible on the upper lip and outer ring of the nipple), acne (mostly on the neck and face, and part of the hair can be sent to the chest and back), alopecia (prominent in the hair follicles on the top of the head are easy to produce oil, and the hair is rare and loose in the sex), masculine signs (such as a deeper voice, prominent Adam's apple, etc.). And some patients have a certain degree of

elevated serum testosterone.

Due to the unknown etiology of PCOS and the mutual influence of hormones, for non-obese PCOS patients, it is currently believed that taking the abnormal increase of LH as the starting point, the abnormal increase of LH can cause follicle membrane cells to secrete more androgens, androgens mainly include androstenedione and testosterone. A large amount of androstenedione catalyzed by aromatase also increased the amount of estrone transformed in the periphery, resulting in peripheral hyperestronemia. Abnormal estrogen levels in peripheral blood will act on the hypothalamic pituitary gland, causing the pituitary to secrete more LH. At the same time, the abnormal increase of LH can induce the ovary to synthesize insulin-like growth factor IGF-I receptor and increase its binding amount, which can also induce the proliferation of follicular membrane cells and also secrete more androgens. From the perspective of Western gynecological gonadal axis, the upward impact on pituitary gland, excessive LH can not only prevent follicle development, maturation and exclusion, but also cause negative feedback on FSH, resulting in relatively reduced FSH secretion, follicle development and recruitment disorders. Clinically, patients with B-ultrasound have excessive follicle number (≥ 12 follicles with a diameter of 2-9mm) and no dominant follicles. Downward effect on target organs: Increased androgen levels can inhibit mature follicles, leading to follicle atresia, resulting in ovulation disorders. A series of vicious cycles eventually led to polycystic ovarian changes in non-obese patients.

2.2 Glycolipid Metabolism

Studies have shown that 75% of non-obese PCOS patients are complicated with insulin resistance [9], and studies have shown that AMH level in obese PCOS patients is positively correlated with IR. In recent years, continuous studies have shown [10] that serum AMH level in non-obese PCOS patients is also positively correlated with HOMA-IR. The AMH levels in the combined IR group were higher than those in the PCOS group. Due to long-term abnormal hormone secretion, non-obese patients still have a high risk of metabolic syndrome even if there is no external manifestation of abnormal lipid metabolism [11]. Studies have shown that

non-obese patients have low HDL in body, while obese patients have high LDL [12], which also proves that non-obese patients have great differences in lipid metabolism compared with obese patients.

2.3 Visceral Fat

In recent years, it has also been found that although the BMI and HER (waist-to-hip ratio) of non-obese patients are normal, the harm of visceral fat thickening is often ignored during clinical treatment. Huang Ying Bei [13] found that non-obese patients had a higher risk of visceral fat than non-obese healthy people through ultrasound examination of abdominal subcutaneous fat, prehepatic fat, prehepatic subcutaneous fat and visceral fat, which also suggested that non-obese patients had a certain degree of endogenous obesity. This is consistent with the research results of Satyaraddi et al. [14], who believe that PCOS patients have centering obesity regardless of BMI. Other studies have found [15] that non-obese PCOS patients accumulate more visceral fat, which can secrete cytokines such as leptin, adiponectin and interleukin-6, which can participate in obesity-related insulin resistance and lead to hyperinsulinemia. Interleukin-6 can also affect the adrenal glands, increasing the secretion of androgens, adrenocortical hormones and cortisol, causing hyperandrogenemia.

2.4 Gene Research

Dapas et al. [16] applied (Genome Wide Association Study (GWAS)) to cluster analysis the genes of 893 patients with PCOS, and determined the laboratory evaluation indexes of BMI, reproduction and metabolism of PCOS patients. The clustering results showed two different PCOS subtypes, one of which was reproductive, characterized by high levels of luteinizing hormone (LH) and sex hormone-binding globulin (SHBG). BMI and insulin levels were relatively low; The other is a metabolic subtype characterized by higher BMI, fasting blood glucose and insulin levels, and lower SHBG and LH levels. It can be seen that the BMI of the two subtypes of PCOS patients presents different characteristics. This explains why the two types of polycystic expression differ at the genetic level.

3. Research Progress of Other Related Factors

The incidence of PCOS is closely related to lifestyle, and the incidence of PCOS in non-obese patients is closely related to mood. Nearly 63% [17] of the patients reported that they were under great pressure in study, work and family. In terms of diet, compared with obese patients who liked spicy and stimulating food, non-obese patients preferred to eat sweet and greasy food. In terms of age, in recent years, the incidence of non-obese PCOS has gradually become younger and even many adolescent women will suffer from the disease, so timely diagnosis and treatment can solve more family and social problems caused by persistent ovulation disorders and metabolic problems after entering the reproductive age. In terms of occupation, researchers believe that women who do mental work have a higher risk of developing PCOS than those who do physical work. From a genetic point of view: It has been suggested [18] that patients whose fathers have a history of baldness are more susceptible to the disease than those whose fathers have no history of baldness.

4. Progress in TCM Research

4.1 Etiology and Pathogenesis of TCM

Traditional Chinese medicine does not have the disease name of polycystic ovary syndrome, but according to its clinical manifestations, it can be classified as "late menstruation", "amenorrhea", "leaky", "infertility" and other categories. At present, most people believe that the three viscera of liver, spleen and kidney are mainly responsible for this disease [19]. The main pathological factors were phlegm, dampness and stasis. The vast majority of clinical patients are multi-Zang-fu lesions, and pathological products are also mixed together, so the TCM syndrome differentiation methods included in this paper are mainly based on Zang-fu syndrome differentiation.

Kidney is the congenital, spleen and stomach is the acquired, kidney and spleen, the first talent acquired, the nurture congenital, spleen deficiency is congenital loss in care, kidney essence is insufficient to nourish the cell, Chong Ren disorder, blood sea loss in overflow. The relationship between the liver and the spleen, as "Golden Chamber Synopsis" said: "See the disease of the liver, know that the liver transmits the spleen." The liver qi is excessive and takes the spleen, the spleen is not healthy, the fine matter distribution is abnormal, the spleen can not nourish the limbs, so the body is thin and weak; Chronic liver depression fire, fire inflammation, overflow the skin, and acne. Fully embodies the liver qi too much, weak temper, five elements multiplied principle. Liver storing blood, kidney storing essence, liver and kidney have "ethylene and decyl homology", and "essence and blood homology". Therefore, non-obese PCOS patients are mainly responsible for the mutual influence and mutual transmission of kidney, liver and spleen organs in TCM syndrome differentiation.

4.1.1 Treatment from spleen syndrome differentiation

Non-obesity is a major feature of this type of patients, BMI < 25kg/m², body wasting, blame for the spleen." On the spleen and Stomach" says that "the spleen and stomach are full, then you can eat and fat." If the spleen and stomach are deficient, they cannot eat and are thin." Chinese medicine that women based on blood, blood source in the spleen and stomach, the spleen and stomach water valley and become subtle, Fengxin red and blood, spleen and stomach deficiency water valley is difficult to decay, blood is not born through water, the same "Wan's female branch" that thin body, diet reduction, due to the spleen and stomach weakness, insufficient Qi and blood, so Chong Ren internal injury, menstruation delayed. This type of patients appear "amenorrhea", "late menstruation" and other symptoms. Thin polycystic patients with emaciated body, transport water valley obstacles, spleen can not "central soil to irrigate four along" body emaciation. Although obese patients are more likely to produce moisture than non-obese patients, in recent years, a series of evidences have been found that non-obese patients have a certain amount of visceral fat excess, proving that non-obese patients also have a certain degree of water-wet metabolism disorders. Based on this theory, Li Xiao et al. [20] believed that non-obese PCOS were mainly caused by deficiency of spleen and kidney and obstruction of dampness, and adopted the method of invigorating kidney and spleen to remove dampness to treat it. Compared with the treatment with Daying35 alone, AMH and

INHB levels in the treatment group treated with traditional Chinese medicine combined with Daying35 significantly decreased or even returned to normal levels, and the decrease rate of ovarian volume, ovulation rate, and the reduction rate of ovarian volume were significantly reduced. It was significantly higher than that of western medicine group. This suggests that Chinese medicine can better protect the ovaries of patients in the treatment of non-obese PCOS.

Spleen-qi deficiency, which further develops into spleen-yang deficiency, spleen-yang deficiency, cold from the middle, water dampness stops to gather the middle jiao, and cold dampness evil stops the middle jiao, then excessive visceral fat will also occur. Huang Cancan [21] believes that the main causes of non-obese PCOS are: Spleen Yang is weak, water valley does not transform, difficult to supplement, resulting in endogenous water dampness, cold dampness makes the fire of liver and kidney difficult to calm its position, so the fire of liver and kidney up, in addition to "thin people fire", this physiological characteristics cause non-obese patients, there are clinical manifestations of upper cold and lower heat, specifically: On the top is thirsty dry throat, facial acne, greasy skin, frequent hair loss, on the bottom is amenorrhea, dark red menstrual color, waist cold. The method of warming spleen and tonifying kidney has achieved good curative effect.

4.1.2 Differentiation and treatment of liver

Women are blood-based, the liver stores blood, the body uses Yin and Yang, and women's milk production with fetuses uses blood. Traditional Chinese medicine believes that the main tone of the liver is smooth emotion, but not depression. In modern society, with the increasing pressure of women's life and work and the excessive concentration of spirit, emotional factors have gradually become an important factor of PCOS. As the "Women's Prescription" says: "Feeling angry and not speaking, many have the danger of amenorrhea." Mental pressure increases, emotional frustration, to the liver qi is not sparse, Qi is not smooth, block Chong Ren two pulse, resulting in abnormal menstruation. Fu Jialin [22] et al. analyzed and observed the frequency of clinical symptoms, pulse and tongue of 300 non-obese PCOS patients, and concluded that the distribution of syndrome types was as follows: Qi stagnation (245 cases, 81.7%) and liver depression (212 cases, 70.7%). TCM treatment should focus on soothing liver depression and regulating qi mechanism, and be supplemented with methods of eliminating phlegm and dampness, promoting blood circulation and removing blood stasis. Dredging qi, Qi smooth, then phlegm and dampness, blood stasis self-removal, Chong Ren two pulse regulation, then the water regulation, menstruation as usual. This is consistent with the research results of 180 non-obese PCOS patients selected by Chen Qiang [23]. Through questionnaire survey and cluster analysis, the TCM syndrome with the highest proportion is liver-qi stagnation syndrome.

The Inner Classic: "A woman's life is insufficient in blood", long-term mental tension, the loss of Yin blood, coupled with the loss of Yin blood through fetal birth, so that the lack of Yin blood, and even delayed menstruation or amenorrhea. Jiang Wenna [24] found that the main syndrome type of non-obese PCOS patients was kidney deficiency and liver

depression. This study shows that non-obese patients engage in more mental workers than obese patients, such as heads of state organs, party and mass organizations, enterprises, institutions and professional and technical personnel, whose work nature determines that they often need to use brain power to analyze, think and remember. Chinese medicine believes that "the brain is the sea of marrow, and all pith belong to the brain." Pulp is the kidney master", "essence does not leak, return to the liver and clear blood". Kidney stores essence, essence produces pulp, and pulp gathers to form brain; Kidney essence is full, then the liver has nourishing, blood has produced. Long-term mental labor consumes the kidney's essence and blood, mother's disease and son, water does not contain wood, so it can cause kidney deficiency and liver depression. Modern research also shows that mental workers not only increase the consumption of qi and blood, but also generally have a relatively serious degree of occupational tension, which is easy to cause the imbalance of psychological state, which is also consistent with the cause of this syndrome type. This is consistent with the modern medical people believe that long-term mental tension will lead to endocrine disorders in women, so the treatment from liver syndrome differentiation is also an important direction of syndrome differentiation.

4.1.3 Differentiation and treatment of kidney

Kidney master reproduction, kidney is the root of reproduction, kidney qi filling and regulating is the basis of menstruation regularity, female kidney qi filling, TianGui can overflow, Chong Ren regulating Chang, the month to the present. Kidney qi deficiency, or due to congenital deficiency, or due to the acquired room labor productivity damage kidney qi, qi is not filled, there will be reproductive dysfunction ovulation disorders, and even amenorrhea infertility. Therefore, the treatment of polycystic syndrome from kidney differentiation has a very important position in TCM gynecology. Kidney tonifying prescriptions [25] can increase the secretion of gonadotropin to a certain extent, especially follicle-stimulating hormone (FSH), which can not only promote the growth and development of egg cells, but also induce the formation of luteinizing hormone receptors in follicles and promote the elimination of follicles, thus improving ovulation disorders in patients with polycystic disease. Sun Yahui et al. [26] believed that non-obese PCOS patients were mainly characterized by kidney deficiency. However, due to the complicated disease and mechanism of non-obese patients with PCOS and the large individual differences, the syndrome types in TCM syndrome differentiation are mostly complex syndrome types, and it is required to take other syndrome types into account in syndrome differentiation. Therefore, the treatment of pathological products such as blood stasis and phlegm dampness should be taken into account in the differentiation of syndromes. Similarly, Professor Chen Xia [27] also believed that kidney deficiency was the root of the disease, combined with phlegm dampness and blood stasis, etc., the treatment was mainly focused on invigorating kidney and clearing liver, and liver Wang blood stasis was the standard, and the Zishen-qingan prescription was self-designed to treat the disease, providing a novel and effective treatment idea for clinical pregnancy assistance for non-obese PCOS infertility patients. Based on Professor Xia GuiCheng's theory of heart

(brain) -kidney - uterus axis, Zhou Huifang [28] proposed tonifying kidney and Ningxin combined with regulating Zhou method to treat non-obese polycystic disease, and proposed that Gu Jiao Di Huang Decoction should be used to tonifying kidney and ningxin and promoting blood circulation in the late menstrual period. In the early stage of treatment, Yi Shen Zhu yang prescription (Liu Wei Di Huang pill plus or minus amethyst and other tonifying drugs for kidney-yang) was adopted. During ovulation, choose the drugs that benefit kidney and promote excretion. Good clinical effect was obtained.

5. Heal

5.1 Western Medicine Treatment

At present, Western medicine mainly focuses on symptomatic treatment in the treatment of non-obese PCOS. For patients with no family planning, short-acting oral contraceptives can improve menstrual conditions. For high androgen, Datin 35 is mainly used as the first-line drug. For insulin resistance, metformin and thiazolidinediones are mainly used to increase insulin sensitivity in patients, the former mainly includes metformin, the latter includes pioglitazone and rosiglitazone. Patients with fertility requirements take clomiphene or letrozole to promote ovulation, although it has played a great role in the treatment, but these drugs also have some drawbacks, the current simple western medicine treatment, in the long term, its therapeutic effect and clinical cure has appeared a bottleneck, the side effects of drugs are obvious, with easy to repeat the situation, the patient's compliance is poor and other shortcomings.

5.2 TCM Treatment

With the vigorous development of traditional Chinese medicine, Chinese medicine has gradually shown its therapeutic advantages in the treatment of the motherland. In the treatment of non-obese PCOS, Chinese medicine can improve luteinizing hormone (LH) level, luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio, and testosterone (T) level, and has better therapeutic effect than western medicine alone [29]. A large number of clinical studies have shown that not only Chinese medicine has a significant effect on the treatment of PCOS, but other Chinese medicine therapies also have certain effects, such as moxibustion, acupoint threading, acupuncture, etc., which have significant effects on reducing body weight, improving sex hormone levels and regulating ovarian function in PCOS patients [30].

5.3 General Treatment

Non-obese polycystic disease is a management disease, under the premise of scientific use of drug management, adjustment of lifestyle is also crucial for patients, reasonable diet (mainly low calorie) with appropriate exercise is conducive to the recovery of regular menstrual cycle, reduce androgen levels, improve the performance of high androgen, reduce insulin resistance, and even improve ovarian function. The regular sleep schedule is also helpful to the recovery of patients' conditions, which can alleviate insulin resistance and reduce abnormal glucose and lipid metabolism.

6. Discussion

The prevalence of non-obese polycystic disease (PCOS) is gradually increasing, and scholars from all walks of life are committed to studying its clear pathogenesis and effective clinical treatment. In the case that Western medicine has not given a clear pathogenesis, Chinese medicine should play the advantage of "treating no disease", on the basis of the overall concept and syndrome differentiation, with Zang-fu syndrome differentiation as the core, timely attention to individual differences, and the combination of "disease differentiation - syndrome differentiation - body differentiation" to develop targeted treatment plans. There are certain bottlenecks in the face of patients with simple western medicine treatment or simple Chinese medicine treatment, clinicians choose more integrated Chinese and western medicine treatment, although there is no best plan to cure this disease, but for the patient's menstruation, pregnancy rate, hormone levels can be effectively controlled. The author thinks that the treatment of the disease should be based on the adjustment of life style, and adopt the combination of Chinese and western medicine to actively manage the disease. In addition, positive psychological counseling for women is also essential.

In recent years, non-obese polycystic ovary syndrome (PCOS) has a tendency of younger age. The complexity of non-obese polycystic syndrome and the difficulty in the diagnosis of adolescent polycystic syndrome have led to few studies in this field, and further research and exploration can be conducted in this direction in the future.

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