Research Progress on the Taxonomy of Symptoms of Polycystic Ovary Syndrome

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Abstract: Polycystic ovary syndrome is a common gynecological disorder of reproductive endocrine metabolism. Because of its increasing incidence year by year, it seriously affects the physical and mental health of women. There is a lack of a unified classification of Traditional Chinese Medicine symptoms, and it is crucial to standardize the classification of Traditional Chinese Medicine symptoms. The purpose of this paper is to summarize the literature on Polycystic Ovary Syndrome syndromes in the past 10 years, and to outline the progress of research on the classification of polycystic ovary syndrome syndromes from the perspectives of Chinese medicine pathogenesis theory, medical case experiences, distribution patterns of syndromes and relevant experimental indicators. We also propose issues and suggestions for the promotion of such studies in order to provide a more scientific basis for the further development of the taxonomy of Polycystic Ovary Syndrome symptoms and the characteristic treatment of Traditional Chinese Medicine.

Keywords: Polycystic ovary syndrome, Symptoms, Pathogenesis

Polycystic ovary syndrome is a common gynecological reproductive endocrine metabolic disorder characterized by ovulation disorders, hyperandrogenemia, polycystic ovarian changes and insulin resistance\textsuperscript{[1]}. The incidence of polycystic ovary syndrome in women of childbearing age is about 6\%-12\% in foreign countries and about 6\%-10\% in China, with an increasing trend year by year\textsuperscript{[2][3]}. Polycystic ovary syndrome not only reduces the pregnancy rate and increases the miscarriage rate, but also increases the risk of long-term complications such as diabetes, cardiovascular disease and endometrial cancer, and increases the rate of depression and anxiety compared to healthy women, which seriously affects women's physical and mental health\textsuperscript{[4][5][6]}. Therefore, unified classification of Traditional Chinese Medicine evidence is a strong support for a mature clinical diagnosis and treatment system, and it is crucial to standardize the classification of Traditional Chinese Medicine evidence. At present, mature Traditional Chinese Medicine typing has not yet been established, and there is much room for further refinement of related research. Based on the analysis of the classification of polycystic ovary syndrome symptoms, this paper aims to provide some reference for the standardization and standardization of treatment in Chinese medicine.

1. Theoretical study based on disease mechanism

Polycystic ovary syndrome has no clear Traditional Chinese Medicine name. According to its clinical characteristics, it belongs to the categories of "amenorrhea", "infertility", "late menstruation" and "obstruction". The pathogenesis of polycystic ovary syndrome is mostly deficiency and actuality. Deficiency is the loss of essence and blood, the deficiency of Chong Ren, the sea of blood is empty and there is no blood to go down. The entity is the evil qi stagnates, the uterus is blocked, and the menstrual blood cannot flow down. With the supplement and development of syndrome research, further progress has been made in PCOS pathogenesis and syndrome. Chen Xu\textsuperscript{[7]} proposed that the pathogenesis of PCOS is mainly kidney and spleen deficiency, phlegm and blood stasis. The Kidney governs reproduction, under the nourishment of kidney essence and the agitation of kidney yang, the egg develops and matures and discharges smoothly. If the kidney is deficient, the balance of yin and yang
will be unbalanced, the metaplasia will be insufficient, Chong and Ren will be difficult to fill and the menstruation will be irregular. The spleen is the foundation of acquired, the source of qi and blood biochemical, spleen deficiency of essence and blood is deficient and there is no blood to go down. When the vitality is deficient, the blood is incapable of causing blood stasis, and the spleen, which is in charge of the transport and transformation, will refine the liquid into phlegm and block the uterus. Zhang Yilei et al.\textsuperscript{[9]} believe that in addition to spleen and kidney deficiency, liver stagnation and qi stagnation are also an important pathogenesis of PCOS. Women are born with the liver, their emotions are not satisfied, the liver fails to disperse, and the qi and blood of Chong and Ren are out of balance, resulting in amenorrhea. Chang Jiu et al.\textsuperscript{[9]} emphasized that no matter what type of syndrome it belongs to, chronic illness is prone to phlegm-dampness and blood stasis. It is both a pathological product and a pathogenic factor, thereby blocking the uterine meridians and aggravating the disease. Zhang Wen et al.\textsuperscript{[10]} recognized that the pathogenesis of PCOS is liver, spleen and kidney disorders, phlegm-dampness and blood stasis. And put forward the imbalance of qi, blood, yin and yang, biochemical passive, no blood in the uterus can eventually lead to late menstruation and even amenorrhea. He Huiling and others\textsuperscript{[11]} supplemented the pathogenesis of PCOS and believed that PCOS hirsutism and acne were related to lung failure. Because the lung and kidney meridians belong to the meridian, and the fur belongs to the lung, external evils invade the meridians and blood ducts from the fur, which can cause amenorrhea and infertility. The nourishing qi originates from the lung meridian, circulates back and forth through the twelve meridians, and the branches pass through the Ren and Du meridians, which are injected into the lungs and circulate. Therefore, abnormal lung function can indirectly affect the occurrence of the uterus and even menstruation. Wang Xin et al.\textsuperscript{[12]} believed that the pathogenesis of PCOS is that dampness and heat accumulate in the viscera, and specifically divide it into two categories: heat is superior to dampness and steaming invading the lungs, dampness is superior to heat flow and invading the liver and kidneys, and dampness and heat dwelling for a long time decocts the spleen and stomach. Based on the theory of "circular motion", Xie Lu et al.\textsuperscript{[13]} believe that the pathogenesis of PCOS is "loss of the central axis, loss of wood, and loss of water and temperature". Fat is responsible for spleen deficiency, the spleen is not clear, the stomach is difficult to lower the turbidity, the things are not transformed into the right, the stagnation of the cell arteries. Failure of the kidney to warm the spleen, loss of spleen qi, no source of qi and blood metaplasia, failure of kidney yang to help the growth of wood, and failure of the liver to evacuate and ovulate can lead to late menstruation and even amenorrhea. Chang Hui et al.\textsuperscript{[14]} put forward the theory of reproductive viscera, arguing that the core of the theory is the reproductive axis of the uterus. In reproductive activities, the kidney is in charge of the whole process, Tiangui is the material basis, Chongren is the channel, and the uterus is the "target".Therefore, the pathogenesis of reproductive abnormalities in PCOS is characterized by visceral disorders, disorder of Tiangui, stagnation of Chong and Ren, and phlegm obstructing the uterus. Huang Cancan et al.\textsuperscript{[15]} based on the theory of "fire of dragon and thunder" proposed that "the cold water does not hide the dragon, and the emptiness does not raise the dragon" as the key pathogenesis of PCOS. Deficiency of spleen and kidney yang, yin and cold force the dragon to go out, deficiency of spleen deficiency, insufficiency of spleen and blood, insufficiency of liver blood, and overheating of thunder and fire, upper heat and lower cold lead to amenorrhea and infertility.

2. Syndrome research based on experience and medical records

Only "dialectics" can "discussion", so "dialectics" is very important. Here is a summary of the different types of syndrome differentiation by physicians as follows. Most physicians believe\textsuperscript{[14][16][17]} that the disease has a deficiency at its origin and a real one at its symptoms, with disorders of the kidney, spleen, and liver as the basis and phlegm, dampness, and blood stasis as the symptoms. Therefore, on the basis of this typology, the disease is divided into: spleen and kidney deficiency, kidney deficiency and blood stasis, liver depression and spleen deficiency, kidney deficiency and liver depression, and phlegm and blood stasis. Feng Xiao et al.\textsuperscript{[18]} specifically classified liver-depressed PCOS into four types: liver-depressed qi stagnation evidence, liver-depressed fire evidence, damp-heat evidence in the liver meridian, and liver-depressed kidney deficiency evidence. Based on the different menstrual cycles, Wang Xiuxia\textsuperscript{[19]} emphasized that the disease should be treated in three phases: premenstrual, intermenstrual and postmenstrual. Based on this, Lian Fang\textsuperscript{[20]} innovatively proposed the "eight-stage theory", which refers to the menstrual period, early postmenstrual period, midmenstrual period, late postmenstrual period, intermenstrual period, early premenstrual period, midmenstrual period and late premenstrual period. Hou Lihui\textsuperscript{[21]} has proposed the diagnosis and treatment model of "identification of body - identification of disease - identification of evidence" based on the theory of physical constitution in Chinese medicine and modern medical theory. Treatment with herbs to regulate the cycle and a combination of Western and Chinese medicine during adolescence and reproductive age respectively;

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the classification is based on spleen deficiency and phlegm-dampness, kidney deficiency and blood stasis, kidney deficiency and liver stagnation, and phlegm-stasis interconnection; the disease is treated in four phases: menstrual phase, follicular phase, ovulation phase, and luteal phase. Niu Jianzhao[22] treats the disease by morphological typing, which is divided into obese and wasting PCOS. Xu Xiaofeng[23] believes that infertility patients with this disease are more common with yang deficiency, and the syndrome types are inferred by the treatment method: spleen and kidney yang deficiency, heart and kidney non-communication, yang deficiency and blood stasis, kidney yang deficiency, and yang deficiency orifice closure. According to the characteristics of traditional Chinese medicine constitution, the disease can be classified into phlegm-dampness, qi stagnation, damp-heat and blood stasis[24][25]. Jiang Huizhong[26] believes that the core pathogenesis of the disease is kidney deficiency and liver stagnation. The research concluded that there are four types of kidney deficiency and liver stagnation syndrome, liver and kidney yin deficiency syndrome, kidney deficiency blood stasis syndrome, and liver stagnation and phlegm obstruction syndrome.

3. Research on the distribution law of syndromes

Tang Peipei et al.[27] searched the core literature on the Internet within 5 years and included 2155 cases, and the findings covered 33 PCOS patterns, with kidney deficiency and phlegm-dampness as common evidence. The frequency distribution of the symptom elements was highest for kidney (59.68%), followed by liver (30.65%) and spleen (9.68%), and the pathological symptom elements were phlegm (24.51%), dampness (20.59%), stasis (15.69%), fire/heat (13.73%), and yin deficiency (10.78%) in that order. It can be seen that the distribution of evidence patterns in TCM is relatively discrete, and the standardization of evidence patterns can be studied more accurately by starting from the elements of evidence patterns. Yi Sha et al.[28] studied the distribution pattern of disease location and disease class evidence elements, and added five evidence elements to the four identified with phlegm and dampness, blood stasis, fire/heat, and yin deficiency: qi deficiency, qi stagnation, blood deficiency, yang deficiency, and blood cold. The kidney is most commonly seen in infertile people, blood stasis, phlegm-dampness, qi stagnation and yin deficiency in obese people, spleen and phlegm-dampness in people with high androgen clinical manifestations, fire/heat in people with high LH, and kidney, phlegm-dampness and qi deficiency in people with insulin resistance. Based on literature studies, Li Yaqian et al.[29] summarized the etiology and diagnostic basis to conclude that the main single-evidence syndromes of PCOS are four types: kidney deficiency type, phlegm-damp type, liver-depression type, and blood stasis type, and they are mostly seen in the compound syndromes. On this basis, Liu Xinmin et al.[30] subdivided the kidney deficiency type into kidney yin deficiency type and kidney yang deficiency type. Qiao Shicong et al.[31] classified 469 PCOS patients into 4 categories based on the criteria of TCM evidence types, and found that the highest percentage of patients with phlegm and blood stasis (34.75%) had the most serious endocrine and glucolipid metabolism disorders, while the rest of the evidence types were distributed as spleen deficiency, phlegm and dampness (33.48%), kidney deficiency, liver depression (19.19%), and kidney deficiency, blood stasis (12.58%). Fang Qunying et al.[32] identified the evidence typology of spleen deficiency, kidney deficiency, phlegm-dampness and liver depression, and analyzed the data of 216 PCOS infertility patients with TCM symptoms and body mass index, adding that obesity and insulin resistance were more severe in patients with spleen deficiency and phlegm-dampness, and were the main causative factors in PCOS infertility patients. Ma Jiawen et al.[33] obtained four group formulas for PCOS based on cluster analysis, and the evidence types were inferred from the formulas, which were based on kidney deficiency and blood stasis, spleen deficiency and phlegm obstruction, kidney deficiency, and liver meridian stagnation and heat. Huang Jinzhu et al.[34] collected clinical symptoms from 215 patients with PCOS and used statistical methods such as frequency and cluster analysis to conclude that the common types of the disease were kidney deficiency, liver depression, phlegm-dampness obstruction, kidney deficiency, liver depression, kidney deficiency, liver depression, blood stasis, and kidney deficiency was the highest frequency. According to the analysis of the frequency of deficiency and real symptoms, the disease was dominated by mixed deficiency and real symptoms (92.5%), pure real symptoms (4.70%), and pure deficiency symptoms (2.80%).

4. Studies based on the relationship of relevant laboratory indicators

Tian Lixia et al.[35] investigated the results and found that pro-discharge soup could effectively improve the insulin resistance effect in insulin-resistant PCOS rats, while inflammatory factors tended to increase, which might be related to the improvement of their inflammatory microenvironment. Xu...
Lianwei et al.\textsuperscript{[36]} treated 78 cases of PCOS with the basic formula of tonifying the kidney and invigorating the blood. The results showed that the method of tonifying the kidney and invigorating the blood to regulate the menstrual cycle, promote ovulation and control body weight, improve hirsutism and acne, and also played an important role in regulating glucose metabolism and lipid metabolism in PCOS. Wu Hangfei\textsuperscript{[37]} added Danzhi Xiaoyao capsule to conventional treatment for PCOS. After treatment, endometrial thickness increased significantly, testosterone (T), follicle stimulating hormone (FSH), luteinizing hormone (LH) levels and uterine artery resistance index and pulsatility index decreased, and estradiol (E2) and ovulation rate increased. It can be seen that Danzhi Xiaoyao capsule has the effect of regulating the secretion of sex hormones and improving the microenvironment of uterus and promoting ovulation of ovaries in liver-depression and fire type PCOS. Lu Yan et al.\textsuperscript{[38]} showed that the active ingredients of Kidney Return Pill may treat PCOS through pharmacological effects such as anti-inflammatory response, improvement of insulin resistance, promotion of follicular development, control of glucose homeostasis, and regulation of lipid metabolism and hormone levels. Xiao Cailan et al.\textsuperscript{[39]} showed that tonifying the kidney and invigorating the blood, combined with nourishing the uterus soup, could effectively reduce serum anti-mullerian hormone (AMH), LH, T, and FSH, increase serum sex hormone-binding globulin (SHBG) levels, and improve clinical symptoms such as lumbar and knee weakness, cold form and limbs, and lethargy in the treatment of PCOS with kidney deficiency and blood stasis. Xu Rongqian et al.\textsuperscript{[40]} treated 60 cases of PCOS infertility with kidney yang deficiency and kidney deficiency and blood stasis. The results of the study showed that nourishing kidney and fertility pills significantly reduced serum LH and T, improved clinical symptoms, and increased pregnancy rate and reduced miscarriage rate. Chen Qi et al.\textsuperscript{[41]} treated 72 patients with PCOS with kidney deficiency and phlegm stasis, and the results showed that beneficial kidney prolotherapy could reduce body mass index (BMI), luteinizing hormone to follicle stimulating hormone ratio (LH/FSH), insulin resistance index (HOMA-IR), LH and T, and increase FSH, which could effectively relieve acne and hirsutism. Liu Yuan et al.\textsuperscript{[42]} treated 68 patients with PCOS with spleen deficiency, phlegm and dampness and found that Pu's Plus Flavor Buzhong Yiqi Decoction could significantly reduce LH, T and the number of small follicles, indicating that it could correct the disordered sex hormone status and effectively restore menstruation with significant efficacy.

5. Summary

The incidence of polycystic ovary syndrome is increasing year by year, and many animal experiments and clinical observations have confirmed the effectiveness of TCM treatment. To a certain extent, the treatment based on the identification of evidence has also witnessed the progress and development of its evidence-based research, but there are still some issues that are of major concern for the further promotion of TCM: 1) The quantity and quality of experimental studies related to evidenceology need to be further developed, with a view to having relatively mature pharmacological support for Chinese medicine; 2) There is no unified classification of TCM evidence types, a mature clinical prescription system, and clear criteria for evaluating efficacy; 3) There are few proprietary Chinese medicines for clinical treatment of polycystic ovary syndrome, and it is difficult to meet the different needs of individual differences with a single evidence type and dosage form; 4) The investigation of the factors influencing the disease is not comprehensive, and the influence of work and living environment on the disease is less explored, and there are large gaps in the study of geographical and individual differences. The solution of the established problem should be widely motivated by scientific research to carry out relevant animal and clinical experimental studies; To build a unified standardized expert consensus based on scientific TCM basic theoretical support, and to develop an authoritative diagnosis and treatment evaluation standard system; select a variety of prescriptions mixed according to the main symptoms, increase or decrease them in appropriate amounts, and carry out the promotion of multi-dose proprietary Chinese medicine by taking those with excellent curative effects; we will investigate the impact of regional and individual differences in the treatment of polycystic ovary syndrome and environmental factors on the disease, and develop the path from individual limitations to a high clinical universality of TCM characteristics, so as to provide more scientific basis for the further development of the taxonomy of PCOS symptoms and the characteristic treatment of TCM.

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