

Research Progress of Diane-35 Combined with Traditional Chinese Medicine in the Treatment of Polycystic Ovary Syndrome

Song Li^{1,a,*}, Gao Weihua^{2,b}

¹Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712046, China

²The Second Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, 712046, China

^a2311772536@qq.com, ^b2658499203@qq.com

*Corresponding author

Abstract: Polycystic ovary syndrome is a common gynecological endocrine disease, which is characterized by long-term anovulation and hyperandrogenemia. In recent years, western medicine treatment for polycystic ovary syndrome mostly adopts drug treatment methods, and its preferred drug is Diane-35 (ethinylestradiol cyproterone tablets). Although it can improve the clinical performance of patients, its recurrence is high, and there is a risk of adverse reactions after long-term medication. Traditional Chinese medicine believes that polycystic ovary syndrome belongs to gynecological "infertility", "amenorrhea", "irregular menstruation" and other categories, and puts forward specific dialectical treatment methods, of which the role of Diane-35 is more prominent. This article discusses the treatment of polycystic ovary syndrome by traditional Chinese medicine combined with Diane-35, and summarizes the strategy and research progress of Diane-35 combined with traditional Chinese medicine for polycystic ovary syndrome, so as to provide a certain reference for clinical treatment in the future.

Keywords: Polycystic ovary syndrome; Diane-35; Traditional Chinese Medicine

1. Introduction

Polycystic ovary syndrome (PCOS) is a common gynecologic endocrine disease, with an incidence of only 5% to 10% in women of childbearing age, while the incidence in patients with anovulatory infertility is as high as 30% to 60%. There are also individual differences in clinical manifestations, including menstrual disorders, infertility, polycystic ovarian changes, acanthosis nigricans, androgen excess, acne, obesity, hirsutism, etc. (Figure 1) [1] The key of Western medicine treatment is to adjust the hormone level in the human body, while traditional Chinese medicine treatment can effectively improve the clinical symptoms of patients. The treatment of integrated traditional Chinese and Western medicine can adjust the "kidney anemone Chong Ren uterus axis" and "hypothalamus pituitary gonad axis" at the overall level. By improving the symptoms of endocrine disorders, it can significantly improve the efficiency of dominant follicles, complement each other, and reflect the advantages of the combination of Chinese and Western medicine. This article will review the research progress of Western medicine Diane-35 combined with traditional Chinese medicine in the treatment of polycystic ovary syndrome.

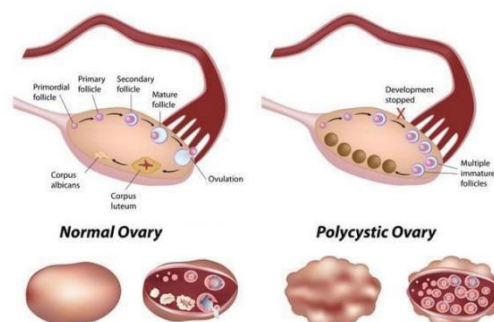


Figure 1: Polycystic ovary syndrome (PCOS)

2. Understanding of polycystic ovary syndrome in Western Medicine

The pathogenesis of polycystic ovary syndrome is complex and variable. It is generally believed that genetic and environmental factors contribute to the occurrence of PCOS. It is closely related to polygenic inheritance, dysfunction of hypothalamus pituitary ovary axis, unhealthy lifestyle and emotional factors, as shown in Figure 2 and Figure 3. Studies have shown that genetic and intestinal microbiota imbalance is also an important reason for its pathogenesis, and long-term chronic inflammation will have many adverse effects on women's reproduction and endocrine [2]. Adverse intrauterine environment during the fetal period or environmental factors after delivery are also involved in its pathogenesis [3]. In terms of treatment, the principle of Western medicine treatment can be divided into basic treatment, complication treatment and pregnancy promotion treatment according to whether there is fertility demand and whether there are complications. Its purpose is to reduce the production of androgen levels in the body. At present, it is generally accepted that the first choice of western medicine is ethinylestradiol cyproterone tablets. Three menstrual cycles are a course of treatment, but it is also prone to adverse reactions such as low menstrual volume, migraine, menstrual breast pain. And long-term medication will also improve the incidence of breast disease, endometrial cancer, and the early recurrence rate is high, long-term hormone stimulation, adding unnecessary adverse reactions for patients.

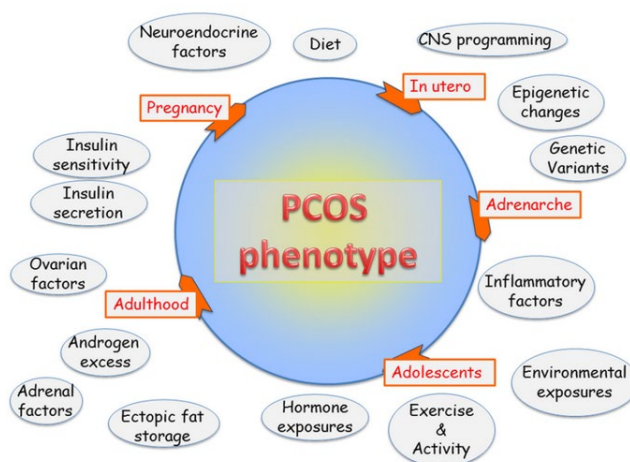


Figure 2: The influencing factors of PCOS

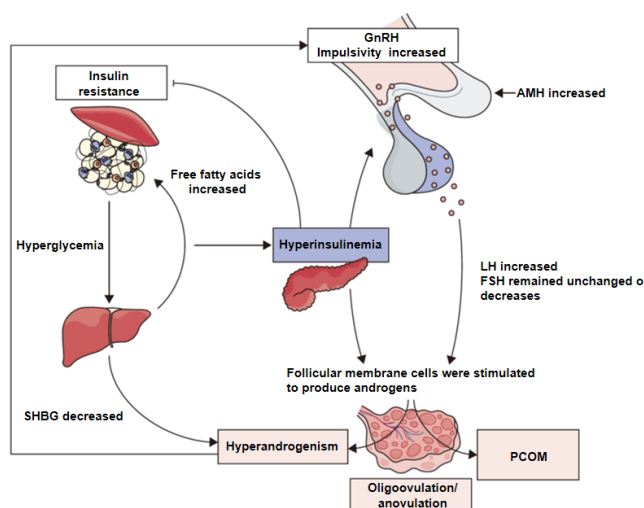


Figure 3: Physiology of PCOS

3. TCM understanding of polycystic ovary syndrome

At present, there is no specific disease name of polycystic ovary syndrome in traditional Chinese medicine, but it is generally attributed to "infertility", "amenorrhea", "metrorrhagia" and so on according

to its clinical manifestations. According to traditional Chinese medicine, PCOS is mainly due to the dysregulation of "kidney anemone Chong Ren cytosolic axis", and its pathogenesis is closely related to the dysfunctions of liver, spleen and kidney, as well as qi stagnation, phlegm dampness, blood stasis and other factors. The main treatment methods are tonifying kidney and regulating menstruation, soothing liver and clearing heat, resolving phlegm and unblocking collaterals, activating blood circulation and removing blood stasis [4]. According to the Yellow Emperor's Canon of internal medicine, "if you are fat and noble, you will get phlegm from the sorghum." It is also recorded in Fuqing dominating women's department that "women are obese, have a lot of phlegm and saliva, and can't conceive... Who knows it's because of dampness". It shows that obesity is mostly related to phlegm dampness, which often leads to infertility, irregular menstruation and even amenorrhea. Traditional Chinese medicine believes that the syndrome of phlegm dampness mostly belongs to the liver and spleen meridians, and the treatment mainly focuses on warming the kidney and strengthening the spleen, removing phlegm and dampness, activating blood circulation and removing blood stasis [5]. According to "Lingshu · Jueqi": "the middle energizer takes juice from Qi, changes, and red is called blood". It can be seen that if the spleen and stomach function is normal, the blood and blood are biochemically active, and the pulse is too strong, then the moon is now in full swing. On the contrary, if the spleen and stomach function is imbalanced, the blood sea is deficient, so the menstrual period and quantity are abnormal. According to Wan's family of women, "only those who are fat and full of cream cannot open the yuan family; those who carry phlegm will have stagnant phlegm and saliva, and the waves of blood will not flow". The spleen and stomach belong to the prefecture of Zhongzhou, regulating the balance of the Qi mechanism between the various viscera. The normal generation and metabolism of human Qi, blood and body fluid are inseparable from the regulation of the spleen and stomach qi mechanism. The spleen is also the "source of phlegm". Once the rise and fall of the spleen and stomach are abnormal, it will damage the existing balance of the Qi mechanism of the human body, accumulate moisture and generate phlegm [1]. Traditional Chinese medicine believes that "the kidney governs reproduction" and "the water flows out of the kidneys". Therefore, diseases related to reproduction and menstruation are usually treated from the kidney, and tonifying the kidney should be taken as the basic treatment for PCOS. Deficiency of kidney qi and weakness of promotion will cause blood stasis due to astringency and stagnation of pulse channels, or kidney deficiency and blood stasis syndrome will occur due to blood stasis caused by long-term illness [6].

4. Current situation of clinical research on Diane-35 combined with traditional Chinese medicine in the treatment of polycystic ovary syndrome

For polycystic ovary syndrome, many researchers have proposed different treatment methods, but generally speaking, it is still based on the principle of traditional Chinese medicine combined with Diane-35 to improve the clinical symptoms of patients and prolong the curative effect. For non obese PCOS patients, Li Xiao and others used the method of invigorating the spleen, removing dampness and tonifying the kidney combined with Diane-35 treatment, which confirmed that it can effectively improve the ovarian function of patients, thereby improving the ability of follicle development and increasing ovulation [7]. Zhang Hongmei et al. Used the "four five" formula (Angelica sinensis, Schisandra chinensis, Curculigo, Achyranthes bidentata, plantain, Paeonia alba, raspberry, epimedium, Ligusticum chuanxiong, Lycium barbarum, rehmannia, Cuscuta chinensis) combined with Diane-35 for three consecutive menstrual cycles in patients with PCOS of kidney deficiency and blood stasis type, which can significantly improve the endometrial receptivity of patients [8]. Chencaiyuan et al. Randomly divided the patients with menstrual disorder caused by PCOS into two groups, who were treated with Diane-35 and Diane-35 combined with Danggui Shaoyao Powder. After 3 months of treatment, the statistical results showed that the effective rate in the combined medication group was higher than that in the simple medication group, which could effectively improve the patient's sex hormone level and adjust the menstrual cycle [9]. Hewenjie and others randomly divided 77 patients with infertility caused by PCOS into control group and treatment group. The control group was only given Diane-35 orally, while the treatment group was given Guizhi Fuling combined with Diane-35. The total effective rate, ovulation rate, pregnancy rate, sex hormone level of the two groups were compared, and the treatment group was better than the control group [10]. Xingxingting et al. Yili qiaotan decoction combined with Diane-35 in the treatment of patients with pcos-ha with phlegm and blood stasis, the total effective rate was 96.67%. It can not only effectively improve the menstrual condition of patients, but also has great advantages in improving the signs of patients, alleviating clinical symptoms and improving sex hormone levels [11]. Lulingyun et al selected patients with phlegm dampness block type PCOS and gave cangchaitiaozhong Decoction plus Diane-35. The total effective rate was as high as 92.5% [12]. Cailimei and others selected infertile patients with PCOS of kidney deficiency and blood stasis type, and gave Zixian Zhuyun

Decoction (Amethyst, Poria cocos, Morinda officinalis, zedoary turmeric, roasted Astragalus, Xianlingpi, angelica, Mitsubishi, bupleurum, Achyrantes bidentata, Cyperus rotundus, Atractylodes macrocephala, Salvia miltiorrhiza, and Rehmannia glutinosa) combined with Diane-35, which can significantly improve the reproductive hormone level of patients [13]. Liu Min et al used Baogui capsule combined with Diane-35 in the treatment of PCOS patients. The results showed that compared with Diane-35 alone, Baogui capsule was more effective in improving menstruation and reducing serum T and AMH levels [14]. Yang Fan et al. Gave Diane-35 treatment combined with cangfu Shenqu Decoction and salt partitioned moxibustion at Shenque point to infertile PCOS patients with spleen deficiency and phlegm dampness syndrome according to the traditional Chinese medicine syndrome. Three consecutive menstrual cycles were a course of treatment. The results showed that it could effectively alleviate the clinical manifestations of patients and increase the probability of pregnancy [15]. Yaoxin used Diane-35 combined with Yishen Qutan Decoction to treat adolescent patients with PCOS. The results showed that it could effectively improve the levels of sex hormones and clinical symptoms of patients [16]. Chenxiaomei and others applied Diane-35 combined with traditional Chinese medicine (Shenqu, Cangzhu, chuanxiong, Pinellia ternata, Xiangfu) to treat PCOS patients. The research results suggested that it could improve the clinical manifestations of patients, improve hormone levels, and help patients ovulate and conceive [17]. Liuchunni and other patients with PCOS were treated with Diane-35 combined with four phase therapy of traditional Chinese medicine: guishaodihuang decoction was added and reduced to nourish yin and blood in the late menstrual period, Bushen zhuovulation decoction was added and reduced to nourish kidney and activate blood in the inter menstrual period, Xiaoyao Powder Combined with cangfu Daotan pill was added and reduced to help Yang and regulate qi in the pre menstrual period, and Wuwei Tiaoqing decoction was added and reduced to activate blood and regulate menstruation in the menstrual period. Results the total effective rate was significantly higher than that of Diane-35 alone [18]. Liyuchang et al took Diane-35 orally and Dingjing Decoction for three consecutive menstrual cycles in patients with PCOS of kidney deficiency type. The results showed that it could significantly improve the level of sex hormones, improve ovarian function, promote menstrual recovery and reduce the recurrence rate [19]. Huangximei used ovulation decoction combined with Diane-35 in the treatment of PCOS. The results showed that the total effective rate was 89.71%, which could significantly improve the clinical treatment effect and improve the level of sex hormones in patients [20]. Tengjing et al used Bushen Huoluo formula combined with Diane-35 to treat PCOS patients with kidney deficiency and blood stasis syndrome. The results showed that compared with oral Diane-35 alone, the curative effect was more prominent and lasting [21]. Hua Zhongshou and others gave Diane-35 combined with Tiaoqingcuyun pill to treat obese PCOS infertility patients. The research results showed that it could effectively reduce FSH, LH, T levels, promote endometrial hyperplasia, improve ovarian morphology and function, and improve ovulation rate and pregnancy rate [22]. chenyinxia et al. Treated PCOS with self-made Yishen Huatan Tiaoqing formula combined with Diane-35, decocted to 200ml, and warmed in the morning and evening. According to the result statistics, the total effective rate, sex hormone level and insulin index improvement were significantly better than those of Diane-35 alone [23]. caolianghua used Diane-35 combined with Yougui pills to treat PCOS, and made a statistical analysis of the levels of T, LH, FSH, insulin and blood lipids before and after treatment. The results showed that the levels of serum hormones, insulin and blood lipids were improved after treatment, and the effect of the combination was better than that of Diane-35 alone [24]. Xin Jun et al. Used Diane-35 combined with cangfu Daotan Decoction in the treatment of PCOS patients with phlegm dampness syndrome in traditional Chinese medicine, took it warm in the morning and evening, and stopped it during menstruation. The results showed that its clinical efficacy was significantly higher than that of patients who only took Diane-35 orally, and the improvement of hormone levels was also obvious [25]. yuanhuifang et al selected 80 patients with PCOS and randomly divided them into the control group and the treatment group. The control group was given Diane-35 oral treatment alone, while the treatment group was added Qilin Pill on the basis of the control group. The levels of LH, FSH, t, E2 and other levels before and after treatment in the two groups were observed. The results showed that the clinical efficacy of the treatment group was significantly better than that of the control group [26]. Zhang Meiling et al. Used self-made prescription for ovulation induction (Rhizoma Cyperi, Poria cocos, Cuscuta chinensis, parasitic mulberry, Paeonia alba, raspberry, Salvia miltiorrhiza, Cistanche deserticola, Dipsacus, epimedium, Purple River cart, Angelica sinensis) and Diane-35 in combination for 3 consecutive cycles in PCOS patients. The results showed that the total effective rate was as high as 90% [27]. Wu Mingzhu randomly selected 74 patients with PCOS. The reference group was treated with Diane-35 alone, while the observation group was treated with Kunling pill after menstruation was completely clean. The results showed that the luteinizing hormone, testosterone and ovarian size of the observation group were lower than those of the reference group, while the follicle stimulating hormone was higher than that of the reference group, and the total effective rate of clinical efficacy was higher than that of the reference group [28]. Wang Chunhuan randomly divided 87 patients

with PCOS of liver and kidney yin deficiency type into two groups. The control group was given Diane-35, and the observation group was treated with Zigui Decoction on the basis of the control group. The statistical results showed that the total effective rate of the observation group was higher than that of the control group [29]. Qian Zujuan selected 60 patients with PCOS and enrolled them. The control group was given Diane-35 orally, while the treatment group was given Diane-35 combined with Kuntai capsules. According to the research results and comparison, the successful ovulation rate, normal menstrual period rate and pregnancy rate of the treatment group were significantly higher than those of the control group [30].

5. Conclusion and Outlook

Oral ethinylestradiol and cyproterone tablets are currently the first choice drugs for the treatment of polycystic ovary syndrome, but due to its long-term use will cause certain adverse reactions, and the recurrence rate is relatively high after drug withdrawal, which will bring greater psychological pressure to patients. In recent years, the research on the combined application of traditional Chinese medicine and Diane-35 has observed the role of traditional Chinese medicine in improving the clinical symptoms and prolonging the curative effect of patients with polycystic ovary syndrome. At the same time, it has its unique effect in improving the quality of life of patients and relieving mental stress, and has less toxic and side effects. The traditional Chinese medicine treatment has a long history, is simple and convenient, and is based on the principle of "seeking the root cause of disease" from the concept of diagnosis and treatment, so Chinese medicine plays an irreplaceable role in the treatment of polycystic ovary syndrome. At present, most doctors still use Diane-35 alone or combined with metformin in the treatment of PCOS. There is still a lack of unified treatment norms in the treatment of PCOS by traditional Chinese medicine, and the sample size of most studies is small. It is expected that in the future, the treatment of polycystic ovary syndrome can be combined with the basic theory of traditional Chinese medicine while giving the patient Diane-35 treatment, and the appropriate dialectical treatment can be carried out to give the patient the whole course of traditional Chinese medicine treatment.

References

- [1] Ding Xiaonan, An Mingxia, Zhao Fanqin. *Diagnosis and treatment of phlegm dampness type polycystic ovary syndrome from the perspective of "eliminating phlegm and resolving fat"* [J] *Journal of practical internal medicine of traditional Chinese medicine*, 2023, 37 (07): 15-17.
- [2] Chen Jintang, Zhuang Liangwu, Lin Youguo. *Observation of the follicle effective rate of integrated traditional Chinese and Western medicine in the treatment of early polycystic ovary syndrome of kidney deficiency and phlegm dampness type* [J]. *Clinical research of traditional Chinese medicine*, 2020, 12 (20): 107-109.
- [3] Zhao Junli. *Research progress in the etiology and diagnosis of polycystic ovary syndrome* [J]. *World clinical medicine*, 2020, 41 (08): 587-593.
- [4] Guo Xiulian. *Clinical observation of modified Yishi guntan pill combined with Diane-35 in the treatment of polycystic ovary syndrome infertility* [J]. *Guangming traditional Chinese medicine*, 2018, 33 (18): 2741-2743.
- [5] Xie Deling, Jin Xun, Yao Lichan. *Clinical effect of integrated traditional Chinese and Western medicine in the treatment of phlegm dampness obesity polycystic ovary syndrome* [J] *World Journal of traditional Chinese medicine*, 2019, 14 (09): 2305-2308.
- [6] Mei Juli, Wang Jianxia. *Clinical observation of Bushen Huoxue Decoction Combined with Diane-35 in the treatment of polycystic ovary syndrome of kidney deficiency and blood stasis type* [J]. *Sichuan Traditional Chinese medicine*, 2015, 33 (12): 94-95.
- [7] Li Xiao, Zhang Yuhang, Zhou Yanyan. *The protective effect of invigorating the spleen, removing dampness and tonifying the kidney on ovarian function in patients with non-obese polycystic ovary syndrome* [J]. *Journal of traditional Chinese medicine*, 2019, 34 (09): 1977-1981.
- [8] Zhang Hongmei, Lei Lei. *Observation on the effect of siwuhefang combined with Diane-35 in improving endometrial receptivity of polycystic ovary syndrome* [J]. *Hunan Journal of traditional Chinese medicine*, 2020, 36 (05): 64-66.
- [9] Chen Caiyan, Xue Shanle. *Danggui Shaoyao Powder Combined with Diane-35 in the treatment of polycystic ovary syndrome* [J]. *Clinical Journal of traditional Chinese medicine*, 2018, 30 (08): 1511-1513.
- [10] He Wenjie, Zhao Rui. *Efficacy of Guizhi Fuling combined with Diane-35 in the treatment of polycystic ovary syndrome infertility and its effect on serum visfatin and high-sensitivity C-reactive*

- protein levels [J]. *Guangxi Medical Journal*, 2017, 39 (2): 165-168.
- [11] Xing Xingting, Xie Bo, Chen Xiaoping, et al. Clinical observation of Liqi Huatan Decoction in the treatment of hyperandrogenemia in polycystic ovary syndrome of phlegm and blood stasis type [J]. *Journal of Guangzhou University of traditional Chinese medicine*, 2023, 40 (6): 1388-1393.
- [12] Lu Lingyun, Shen Xiaoheng, Yuan Min. Clinical efficacy analysis of cangchai Tiaozhong decoction combined with Diane-35 in the treatment of phlegm dampness block polycystic ovary syndrome [J]. *World Journal of integrated traditional Chinese and Western medicine*, 2019, 14 (10): 1460-1463.
- [13] Cai Limei, Yu Rufen, Ding Xiangcui. Clinical observation of Zixian Zhuyun decoction combined with Diane-35 in the treatment of polycystic ovary syndrome infertility [J]. *Chinese Journal of Traditional Medical Science and Technology*, 2017, 24 (2): 203-205.
- [14] Liu Min, Cao Qi, Qian Qiaohong, et al. Clinical observation of effects of Baogui Capsules combined western medicine on anti-mullerian hormone level in patients with polycystic ovarian syndrome [J]. *Shanghai Journal of traditional Chinese medicine*, 2018, 52 (6): 40-43.
- [15] Yang Fan, Yang Lei, Yang Jianbing, et al Effect of cangfu Shenqu decoction combined with Diane-35 and Shenque point salt partitioned moxibustion on polycystic ovary syndrome infertility [J]. *Liaoning Journal of traditional Chinese medicine*, 2022, 49 (11): 127-130.
- [16] Yao Xin. Effect of daying-35 combined with Yishen Qutan Decoction on sex hormone levels and TCM syndrome scores in adolescent patients with polycystic ovary syndrome [J]. *e-journal of practical gynecological endocrinology*, 2022, 9 (05): 89-92.
- [17] Chen Xiaomei, Zou Yujun, Jiang Yan. Observation on the curative effect of traditional Chinese medicine Xiaofa combined with Diane-35 in the treatment of polycystic ovary syndrome [J]. *Journal of modern integrated traditional Chinese and Western medicine*, 2016, 25 (05): 501-503.
- [18] Liu Chunni, Liao Xinbo, Zhou Liyun. Clinical study on the treatment of polycystic ovary syndrome with four phase therapy of traditional Chinese medicine and Diane-35 [J]. *Guangming traditional Chinese medicine*, 2017, 32 (09): 1335-1338.
- [19] Li Yuchang, Zeng Lei, Li Yonghong, et al. Modified Dingjing decoction combined with Diane-35 in the treatment of polycystic ovary syndrome [J]. *Journal of traditional Chinese medicine*, 2018, 33 (11): 2235-2238.
- [20] Huang Ximei. Clinical observation of ovulation decoction combined with Diane-35 in the treatment of polycystic ovary syndrome [J]. *Chinese folk therapy*, 2018, 26 (12): 63-64.
- [21] Teng Jing, Yu Jun, Liao Hongyu. Clinical effect of Bushen Huoluo decoction combined with Diane-35 in the treatment of polycystic ovary syndrome with kidney deficiency and blood stasis syndrome [J]. *World Journal of traditional Chinese medicine*, 2017, 12 (12): 2942-2945.
- [22] Hua Zhongshou, Hou Zhiyan, Wang Hong, et al Clinical study of Tiaojingcuyun pill combined with Diane-35 in the treatment of obesity type polycystic ovary syndrome infertility [J]. *China pharmaceutical*, 2019, 28 (18): 38-40.
- [23] Chen Yingxia, Jin Hai'e, Li Xiuni. Yishen Huatan Tiaojing decoction combined with Diane-35 in the treatment of 60 cases of polycystic ovary syndrome [J]. *China Science and technology of traditional Chinese medicine*, 2019, 26 (03): 463-465.
- [24] Cao Lianghua. Effect evaluation of Diane-35 combined with Yougui Pill in the treatment of polycystic ovary syndrome [J]. *Journal of practical Gynecological Endocrinology (Electronic Edition)*, 2018, 5 (13): 95-96.
- [25] Xin Jun, Guo Huimei, Gao Xihuan, et al. Cangfu Daotan decoction combined with Diane-35 in the treatment of polycystic ovary syndrome [J]. *Journal of modern integrated traditional Chinese and Western medicine*, 2017, 26 (02): 197-199.
- [26] Yuan Huiyang, Hu Yajun. Clinical observation of Qilin pill combined with Diane-35 in the treatment of patients with polycystic ovary syndrome [J]. *Journal of Hubei University for nationalities (Medical Edition)*, 2018, 35 (03): 37-40.
- [27] Zhang Meiling, Yu Cibi, Luo Xinmei. Study on the curative effect of ovulation promoting self-made formula and Diane-35 on polycystic ovary syndrome [J]. *Clinical practice of integrated traditional Chinese and Western medicine*, 2019, 19 (09): 83-85.
- [28] Wu Mingzhu. Effect analysis of Diane-35 combined with Kunling pill in the treatment of polycystic ovary syndrome [J]. *Zhongwai medical*, 2021, 40 (28): 78-81.
- [29] Wang Chunhuan. Effect of modified Zigui decoction combined with Diane-35 on patients with polycystic ovary syndrome of liver kidney yin deficiency type [J]. *China Minkang medicine*, 2020, 32 (24): 100-102.
- [30] Qian Zujuan. Efficacy of Diane-35 combined with Kuntai Capsule in the treatment of polycystic ovary syndrome [J]. *E-journal of practical gynecological endocrinology*, 2022, 9 (30): 85-88.