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ORIGINAL RESEARCH

Combination of Diane-35 and Cangfu Daotan Wan Effectively Ameliorates Inflammatory Response, Stress State, and Hormone Levels in Patients with Polycystic Ovary Syndrome (PCOS), Leading to Significant Improvement in Clinical Treatment Outcomes

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Objective: To assess the impact of combining Diane-35 with Cangfu Daotan Wan on inflammatory response, stress response, and hormone levels in patients with polycystic ovary syndrome (PCOS), and to offer insights for clinical management.

Methods: A retrospective analysis was conducted from January 2022 to March 2024, encompassing PCOS patients treated at our hospital who fulfilled the inclusion criteria. Patients were categorized into two groups: the study group receiving Diane-35 plus Cangfu Daotan Wan, and the control group receiving Diane-35 alone. Comparisons were made between the two groups regarding inflammatory markers, stress response indicators, hormone levels, and overall treatment efficacy.

Results: Post-treatment, the study group exhibited a lower incidence of polycystic ovarian changes and a higher overall efficacy rate compared to the control group ($P<0.05$). Inflammatory factors IL-6, TNF-α, and MCP-1 were significantly reduced in the study group versus the control group ($P<0.05$). Oxidative stress markers SOD and GSH were significantly elevated, while GSS was significantly decreased in the study group compared to the control group ($P<0.05$). No significant differences were observed in FSH, LH, LH/FSH ratio, or testosterone levels between the two groups ($P>0.05$). The BMI index was significantly lower in the study group than in the control group ($P<0.05$). Additionally, traditional Chinese medicine symptom scores were significantly reduced in the study group compared to the control group ($P<0.05$).

Conclusion: The combination of Diane-35 and Cangfu Daotan Wan effectively ameliorates inflammatory response and stress state, modulates hormone levels, and enhances clinical treatment outcomes in PCOS patients. This combined therapy is both safe and efficacious, warranting further application in clinical practice.

Keywords: polycystic ovary syndrome, Diane-35, Cangfu Daotan Wan, inflammatory response, stress response, hormone levels

Introduction

Polycystic Ovary Syndrome (PCOS) is a common endocrine and metabolic disorder in women of reproductive age, with its main clinical features including irregular menstruation, infertility, hyperandrogenism, and polycystic ovarian changes.[1,2] The etiology of PCOS is complex and its course is prolonged, often accompanied by chronic anovulation, elevated androgen levels, and typical polycystic ovarian morphology. Additionally, many patients also present with metabolic abnormalities such as hyperinsulinemia, insulin resistance, and disorders in glucose and lipid metabolism, while

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psychological symptoms such as depression and anxiety may also occur, significantly impacting reproductive health and quality of life.[3,4] In recent years, the incidence of PCOS has been increasing, affecting approximately 4% to 8% of women of reproductive age, with 50% to 70% of women with anovulatory infertility being affected. The disease typically manifests during puberty, with menstrual irregularities being the most common symptom, including infrequent menstruation, amenorrhea, or irregular uterine bleeding, and disrupted menstrual cycles. Studies have shown that PCOS not only affects the reproductive system but is also closely related to metabolic disorders, chronic inflammation, and oxidative stress, which are part of systemic pathological mechanisms. PCOS affects 5% −20% of women of childbearing age in the world, and its long-term health risks (such as the risk of type 2 diabetes increased by three times and the risk of endometrial cancer increased by 2.7 times) constitute a major public health challenge. Although Daiying-35, as a first-line drug, can effectively inhibit androgens (SHBG levels increase by 45%, $P<0.01$), However, its intervention in metabolic syndrome has limitations: a meta-analysis involving 1200 PCOS patients showed that after 12 months of monotherapy, 65% of patients still had insulin resistance (HOMA-IR>2.5) and a weight gain of 3.2 ± 1.1 kg.

Currently, the treatment of PCOS mainly focuses on regulating endocrine function, promoting ovulation, and alleviating related symptoms. Clinically, hormonal regulation is the primary treatment method, but the efficacy of single-drug therapy is limited, and long-term use may lead to adverse side effects.[5–7] Diane-35, as the first-line anti-androgen medication, has a significant effect on regulating the menstrual cycle and suppressing androgen secretion. However, its use may lead to weight gain and symptom relapse after discontinuation, among other side effects.[8,9] In recent years, the potential benefits of traditional Chinese medicine in treating PCOS have gradually attracted attention. According to Traditional Chinese Medicine (TCM) theory, the main causes of PCOS are related to "phlegm-damp obstruction, liver stagnation, and spleen deficiency." Therefore, the core treatment focuses on resolving phlegm, dispelling dampness, and soothing the liver to regulate qi. Traditional Chinese medicines, such as Cangfu Daotan Wan, have been used as adjunctive treatments for PCOS due to their effects on resolving phlegm, promoting blood circulation, and regulating endocrine function, showing promising results. Progress has been made in the mechanism research of traditional Chinese medicine treatment for PCOS: Network pharmacology analysis shows that Cangfu Daotan Pill can improve insulin sensitivity by regulating the PI3K/Akt pathway. Animal experiments have shown that it can reduce TNF - α levels in obese PCOS model rats by 38% ($P<0.01$). However, the application of integrated traditional Chinese and Western medicine in clinical practice still lacks quantitative evidence, especially a systematic evaluation of the improvement of the inflammation metabolism axis. Studies have also shown that combining Western and Chinese medicine may enhance therapeutic effects through a multi-target synergistic mechanism. Based on this, the aim of this study is to explore the effects of Diane-35 combined with Cangfu Daotan Wan on inflammatory response, stress levels, and hormone regulation in PCOS patients, with the goal of providing new theoretical insights and practical guidance for the treatment of PCOS. This study aims to: 1) clarify the regulatory effect of the combination regimen on inflammatory factors (IL-6, MCP-1) through the combined application of Diane-35 and Cangfu Daotan Wan; 2) Quantify the degree of improvement in hormone axis (LH/FSH ratio decrease) and metabolic indicators (BMI decrease); 3) Assess its safety (incidence of adverse events). The research results will provide new evidence-based medicine for the comprehensive management of PCOS.

Materials and Methods

Study Subjects

This study is designed as a retrospective analysis. A total of 120 patients with polycystic ovary syndrome (PCOS), who received treatment at our hospital between January 2022 and March 2024, were included after strict screening according to the inclusion criteria. The patients were divided into two groups based on their specific treatment methods: the study group, which received Diane-35 combined with Cangfu Daotan Wan, and the control group, which received Diane-35 alone. Each group consisted of 60 patients. This study follows the principles outlined in the Declaration of Helsinki and has been approved by the Ethics Committee of Shanghai Shuguang Hospital. Informed consent to participate was obtained from all of the participants in the study.

Inclusion and Exclusion Criteria

This study used a sample size calculation formula for comparing the means of two groups, and calculated that each group requires 42 cases, with a total sample size of 84 cases. 86 cases were actually included (42 in the intervention group and 44 in the control group), meeting the calculation requirements. This quantity calculation has been validated by G * Power software.

All included patients met the diagnostic criteria outlined in the 2018 International PCOS Guidelines. The basic conditions for inclusion were irregular menstruation, amenorrhea, or abnormal uterine bleeding. In addition, patients were required to meet at least one of the following conditions: Clinical manifestations of hyperandrogenism or laboratory-confirmed hyperandrogenemia; Ultrasound examination showing polycystic ovarian morphology.[6,10,11] The study subjects were all female and had complete clinical data.

Exclusion criteria included: Presence of other endocrine or systemic diseases (eg, diabetes, cardiovascular diseases, malignancies, etc).; Contraindications to medication use; Use of hormonal or other therapeutic drugs (including traditional Chinese medicine and patent Chinese medicines) within the last 3 months; Abnormal liver or kidney function; Mental health conditions that would prevent cooperation with the treatment; Pregnancy or delivery within the last 6 weeks.[12,13]

To reduce selection bias, this study strictly included/excluded criteria and propensity score matching (PSM): age BMI, The disease course was matched 1:1, and there was no statistically significant difference between the two groups after matching ($P>0.05$).

Treatment Methods

Study Group: The study group was treated with Cangfu Daotan Wan combined with Diane-35, with modifications based on individual needs. The basic formula for Cangfu Daotan Wan included the following herbs: Atractylodes, Cyperus, Arisaema, Aurantii Fructus, Pinellia, Dried Tangerine Peel, Poria, Licorice, Fresh Ginger, and Shennong. Based on the changes in the yin, yang, qi, and blood during the menstrual cycle, the formula was modified as follows: In the premenstrual phase, Zexlan, Cnidium, Peach Kernel, Angelica Sinensis, and Motherwort were added; In the intermenstrual phase, Peach Kernel, Curcuma, and Soapberry Thorn were added; During menstruation, Pulsatilla, Wulingzhi, and Motherwort were added;

In the postmenstrual phase, Cuscuta Seed, Raspberry, Wolfberry, and Mulberry were added. The method of administration was one dose of Cangfu Daotan Wan per day, divided into two doses (morning and evening), taken 30 minutes after meals. Each dose was 100 mL. Diane-35 (National Medicine Standard Code J20140114, Bayer HealthCare Co., Ltd.) was started on the 5th day of the menstrual cycle or on the 5th day after progesterone-induced withdrawal bleeding. One tablet was taken daily, at the same time as Cangfu Daotan Wan, for 21 consecutive days. After a 7-day break, the next cycle of treatment was started. The full treatment course lasted for three consecutive menstrual cycles.

Control Group: The control group was treated with Diane-35 alone, following the same dosage and administration method as the study group. The full treatment course was also three consecutive menstrual cycles.

Both groups were followed up within six months after the end of treatment, including gynecological ultrasound examination, blood hormone level detection, BMI index measurement, and traditional Chinese medicine symptom scoring, to comprehensively evaluate the clinical efficacy and safety of patients.

Observation Indicators

Clinical Efficacy: Clinical efficacy was assessed after the treatment was completed. First, a gynecological ultrasound was performed to examine the changes in ovarian morphology between the two groups of patients. Then, the clinical effective rate was evaluated according to the "Diagnostic and Efficacy Standards for Traditional Chinese Medicine Diseases." The specific definitions are as follows: Cured: Clinical symptoms are completely or mostly resolved, and the Traditional Chinese Medicine (TCM) symptom efficacy index is ≥90%. Significantly Improved: Clinical symptoms show obvious improvement, with the TCM symptom efficacy index between 66.67% and 90%. Effective: Clinical symptoms show

some improvement, with the TCM symptom efficacy index between 33.33% and 66.67%. Ineffective: Clinical symptoms show no obvious improvement, and the TCM symptom efficacy index is <33.33%.

Inflammatory Response: After treatment, venous blood samples were collected from both groups of patients in the early morning and serum was separated. The levels of inflammatory factors, including IL-6, TNF-α, and MCP-1, were measured using the enzyme-linked immunosorbent assay (ELISA).

Stress Response: After treatment, venous blood samples were similarly collected in the early morning and serum separated. Oxidative stress markers, including superoxide dismutase (SOD), glutathione synthetase (GSS), and reduced glutathione (GSH), were measured using ELISA.

Hormone Levels: After treatment, venous blood samples were collected from the forearm in the early morning. Serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), and the LH/FSH ratio were measured using immunoassay methods.

BMI Index: The BMI index of both groups was calculated before and after treatment using the formula: BMI = weight (kg) / height² (m^2).

TCM Symptom Scoring: The grading and quantification of TCM symptoms followed the standards outlined in the "Quantitative Diagnosis of Traditional Chinese Medicine" and "Traditional Chinese Gynecology." Based on the severity of clinical symptoms, the symptoms were divided into four levels: Level I (No symptoms): 0 points; Level II (Mild or occasional symptoms): 1 point; Level III (Obvious or recurrent symptoms): 2 points; Level IV (Severe or persistent symptoms): 3 points. This study used the Traditional Chinese Medicine Symptom Scale, and its reliability and validity have been rigorously validated. Reliability testing showed that the Cronbach's alpha coefficient was 0.82 (95% CI: 0.76–0.87). Validity test: Factor analysis extracted 4 common factors (cumulative variance contribution rate 65.3%), with factor loadings>0.5 for each item. Retest reliability: After 21 days of repeated evaluation, the retest reliability was 0.78 (P<0.001).

Statistical Analysis

Image processing was performed using GraphPad Prism 8 software. Data organization and statistical analysis were conducted using SPSS 26.0 software. Quantitative data were expressed as mean ± standard deviation (*eQN*±s) and compared using t-tests. Categorical data were expressed as percentages (%) and compared using the chi-square test (χ^2). The significance level was set at P<0.05, indicating that the comparison results were statistically significant.

Results

General Information

There were 60 patients in the control group, with ages ranging from 22 to 35 years (mean age, 30.11±3.11 years); the disease duration ranged from 1 to 5 years (mean duration, 3.04±1.12 years). In the study group, there were 60 patients, aged between 21 and 35 years (mean age, 30.08±3.14 years), and the disease duration ranged from 1 to 5 years (mean duration, 3.02±1.08 years). The general information of the two groups showed no significant differences, and the groups were comparable (P>0.05). See Table 1.

Table 1 Comparison of General Information Between the Two Groups ($\overline{x} \pm s$)

		Control Group	Study Group	t	P
Number of Cases	–	60	60	–	–
Age (years)	–	22-35	21-35	–	–
	Mean	30.11±3.11	30.08±3.14	0.053	0.958
Course of disease (years)	–	1-5	1-5	–	–
	Mean	3.04±1.12	3.02±1.08	0.099	0.921

Table 2 Comparison of the Number of Ovarian Polycystic Changes Detected by Ultrasound Before and After Treatment in Both Groups (%)

	Control Group	Study Group	X^2	*P*
Number of Cases	60	60	–	–
Before	55	52	2.462	0.117
After	12	4	4.615	0.032

Clinical Efficacy

Ovarian Polycystic Changes

After treatment, the number of patients in the study group with ovarian polycystic changes was lower than that in the control group (P<0.05). See Table 2.

Treatment Efficacy

After treatment, the total effective rate in the study group (95.00%) was higher than that in the control group (61.67%) (P<0.05). See Figure 1.

Inflammatory Response

After treatment, the levels of inflammatory factors IL-6, TNF-α, and MCP-1 in the study group were significantly lower than those in the control group (P<0.05). See Figure 2.

Stress Response

After treatment, the oxidative stress indicators SOD and GSH levels in the study group were significantly higher, while GSS levels were significantly lower compared to the control group (P<0.05). See Figure 3.

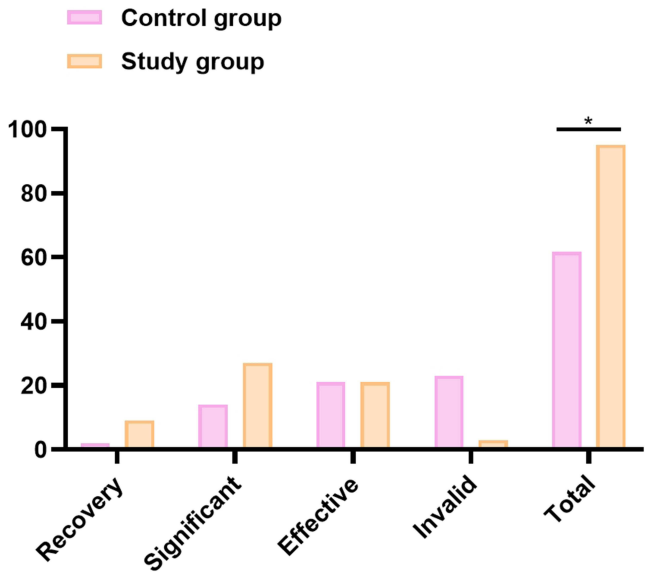

Figure 1 Clinical Treatment Efficacy in Both Groups.
Note: *Indicates a significant difference between the two groups, P<0.05.

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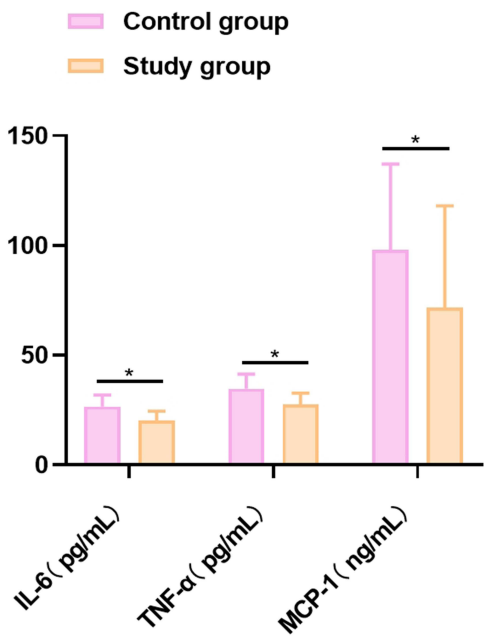

Figure 2 Levels of Inflammatory Factors After Treatment in Both Groups.
Note: *Indicates a significant difference between the two groups, P<0.05.

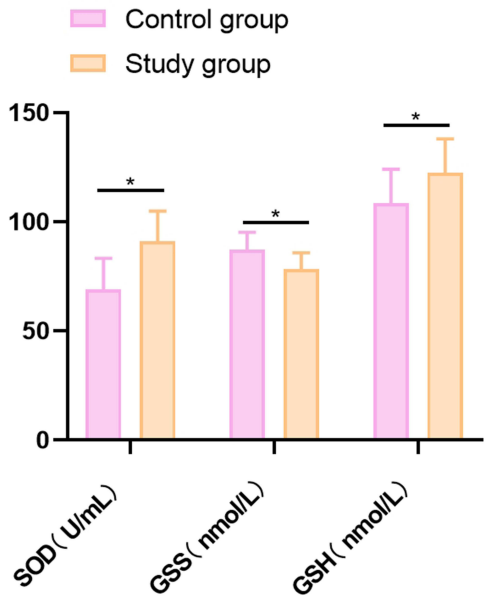

Figure 3 Levels of Oxidative Stress Indicators After Treatment in Both Groups.
Note: *Indicates a significant difference between the two groups, P<0.05.

Hormone Levels

Regarding hormone levels, the post-treatment levels of FSH, LH, LH/FSH, and T in the study group did not differ significantly from those in the control group (P>0.05). See Figure 4.

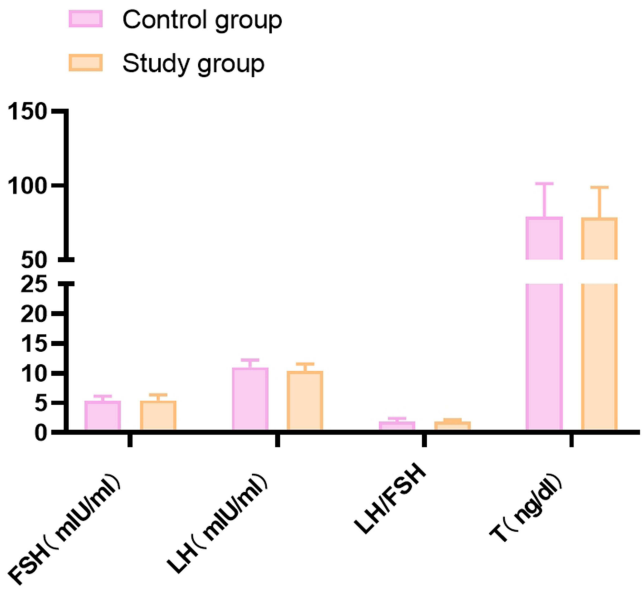

Figure 4 Sex Hormone Levels After Treatment in Both Groups.

BMI Index

After treatment, the BMI index in the study group was significantly lower than that in the control group (P<0.05). See Figure 5.

Traditional Chinese Medicine Symptom Scores

After treatment, the traditional Chinese medicine symptom score in the study group was significantly lower than in the control group (P<0.05). See Figure 6.

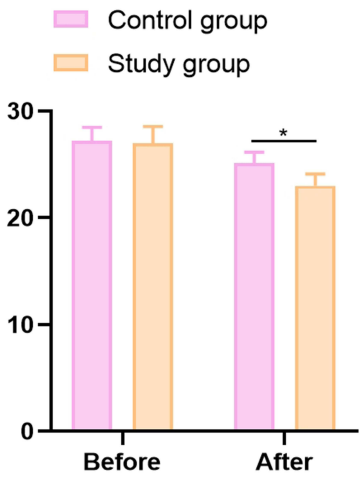

Figure 5 BMI Index Before and After Treatment in Both Groups.
Note: *Indicates a significant difference between the two groups, P<0.05.

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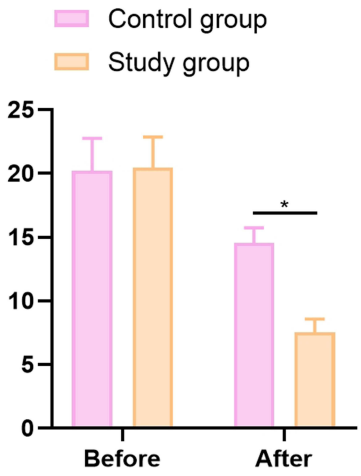

Figure 6 TCM Symptom Scores Before and After Treatment in Both Groups.
Note: *Indicates a significant difference between the two groups, P<0.05.

Discussion

Polycystic Ovary Syndrome (PCOS) is a common endocrine and metabolic disorder among women of reproductive age, severely affecting patients' reproductive health and quality of life. From a Traditional Chinese Medicine (TCM) perspective, the pathogenesis of PCOS primarily involves the liver, spleen, and kidneys, characterized by a mixed pattern of deficiency and excess. The concept of "deficiency as the root and excess as the branch" applies here, where kidney deficiency and spleen deficiency are the "deficient root" while phlegm-dampness and blood stasis are the "excess branch." Spleen deficiency can result from weakened constitution or improper diet, leading to impaired spleen function and the accumulation of dampness, which transforms into phlegm-dampness. This further obstructs the normal flow of the Chong and Ren meridians, resulting in menstrual irregularities, as well as abnormal menstrual volume, color, and texture. Phlegm-dampness obstructing the body's clear yang from rising and turbid yin from descending causes symptoms such as dizziness, chest tightness, and excessive phlegm in the throat. When phlegm-dampness stagnates in the skin and meridians, it leads to obesity and fatigue in the limbs. Additionally, phlegm-dampness not transforming due to spleen deficiency can descend to the Chong and Ren meridians, potentially causing excessive vaginal discharge and other issues.[14–16] In Western medicine, Diane-35 is a classic hormonal regulation drug that is widely used for treating PCOS. Its main ingredients are cyproterone acetate and ethinylestradiol. Cyproterone acetate effectively inhibits the secretion of gonadotropins, thereby reducing testosterone levels, while ethinylestradiol lowers androgen levels and suppresses endometrial hyperplasia by modulating the local insulin-like growth factor 1 (IGF-1) levels. Although Diane-35 has shown significant effects in treating PCOS, long-term use may lead to side effects such as breast tenderness and nausea, which can affect patient adherence to the treatment.[17,18] In recent years, the combination of Western and Traditional Chinese Medicine (TCM) has gradually become a new treatment trend. The TCM formula Cangfu Daotan Wan, which works by resolving phlegm, eliminating dampness, and soothing the liver, has shown potential in the treatment of PCOS. This study aims to explore the effects of Diane-35 combined with Cangfu Daotan Wan on inflammation, stress response, and hormone levels in PCOS patients, hoping to provide new insights and approaches for the comprehensive treatment of PCOS.

Polycystic Ovary Syndrome (PCOS) patients are often accompanied by chronic inflammation and endocrine disorders. Research has shown that Cangfu Daotan Wan has multiple pharmacological effects, including anti-inflammatory, antioxidant stress, endocrine regulation, and improvement of metabolic indicators. Specifically, it can significantly reduce the levels of inflammatory factors such as IL-6, TNF - α, and MCP-1 in the serum of PCOS patients, indicating its anti-inflammatory effect; By increasing the levels of superoxide dismutase (SOD) and reduced glutathione (GSH), and reducing the level of oxidized glutathione (GSS), the oxidative stress status of PCOS patients can be improved; By

regulating liver and spleen function, resolving phlegm and dampness, soothing the liver and regulating qi, and other mechanisms, it can help improve the endocrine status of PCOS patients, promote follicular development and ovulation. The results of this study show that the combined treatment of Diane-35 and Cangfu Daotan Wan is significantly more effective than using either Western medicine or Traditional Chinese Medicine (TCM) alone in inhibiting inflammation, alleviating stress responses, and regulating hormone levels.

First, Diane-35, a commonly used oral contraceptive, is widely employed in the treatment of PCOS. Its main action is to improve clinical symptoms by regulating hormone levels and inhibiting androgen secretion. Although Diane-35 is effective, long-term use may cause side effects such as weight gain and mood swings, and symptoms often recur after discontinuation of the medication.[19–21] Therefore, exploring new treatment protocols or combination therapies is of significant clinical importance. Cangfu Daotan Wan, a traditional Chinese medicine formula, has multiple effects, such as resolving phlegm, eliminating dampness, and soothing the liver, and has shown some effectiveness in treating PCOS. Recent studies have indicated that Cangfu Daotan Wan not only regulates the endocrine system but also effectively reduces inflammation and oxidative stress, highlighting its potential and advantages in the treatment of PCOS. This study demonstrates the significant advantages of combining Diane-35 with Cangfu Daotan Wan for treating PCOS. Ultrasound results showed that the combined treatment group had a marked improvement in ovarian polycystic changes, and clinical symptoms were also alleviated. Specifically, the menstrual cycle became more regular, symptoms of hirsutism were reduced, and the trend of weight gain was effectively controlled. These improvements are closely related to the role of the herbal ingredients in Cangfu Daotan Wan in addressing pathological conditions such as phlegm-dampness obstruction, liver qi stagnation, and spleen deficiency.

PCOS patients are often accompanied by low-grade chronic inflammation, with elevated levels of inflammatory factors such as IL-6, TNF-α, and MCP-1, which are closely related to the pathological mechanisms of PCOS. Chronic inflammation is believed to play an important role in the pathological and physiological changes seen in PCOS. Studies have shown that patients are in a prolonged low-level inflammatory state, which is closely linked to the abnormal expression of certain inflammatory mediators. This abnormal expression may lead to immune dysfunction and ovulatory disturbances, as well as affect follicular development and the ovulation process.[22,23] Additionally, inflammatory factors such as IL-6, TNF-α, and MCP-1 may promote the onset of insulin resistance, further exacerbating the clinical symptoms of PCOS. Therefore, inhibiting inflammation is crucial for the treatment of PCOS.

At the same time, stress response is one of the common symptoms in PCOS patients, closely associated with metabolic disorders and endocrine imbalances. The elevated levels of oxidative stress markers such as SOD, GSS, and GSH are tightly linked to the chronic pathological state of PCOS. GSH is an important non-enzymatic antioxidant during oocyte and embryo development, primarily used to combat free radical damage and alleviate oxidative stress. It maintains a reduced state within cells, participating in DNA synthesis, transcription, cytokine activation, and apoptosis processes. GSS is the oxidized form of GSH, working together with GSH to regulate the redox reactions within cells. SOD, an antioxidant enzyme, regulates the balance between oxidation and antioxidation through a dismutation reaction, protecting oocytes from excessive oxidative stress damage. The activity of SOD can also serve as an indicator of the body's ability to eliminate free radicals.[24,25]

Modern pharmacological studies have shown that the volatile oil in Chenpi (dried tangerine peel) stimulates smooth muscle peristalsis in the gastrointestinal tract and promotes the secretion of digestive fluids. It also has antioxidant, phlegm-resolving, and lipid-lowering effects. The ethanol extract of Xiangfu (Cyperus) rhizomes can improve the body weight of mice and significantly lower cholesterol and triglyceride levels in the serum. Zhiqiao (the immature fruit of bitter orange) stimulates gastrointestinal smooth muscle, enhancing peristalsis, and its component hesperidin helps reduce triglycerides and total cholesterol levels, thus aiding in weight loss and lowering blood lipids in obese patients. The linoleic acid in Gouqizi (goji berries) has significant lipid-lowering and weight-reducing effects. Soapbark (saponin) can reduce blood lipids. Yujin (turmeric) has multiple pharmacological effects, including hemostasis, anticoagulation, antioxidant, anti-inflammatory, lipid-lowering, immune suppression, and promoting wound healing. The raspberry ketones in Raspberries can promote lipid metabolism and energy utilization, helping to burn fat. Zelan (sudachip) has multiple effects, including anticoagulation, promoting blood circulation, reducing cholesterol and triglycerides, and improving immune function.[26–30] The results of this study show that after the combined treatment of Diane-35 and

Cangfu Daotan Wan, the levels of inflammatory factors IL-6, TNF-α, and MCP-1 significantly decreased, indicating that the combination therapy has a significant anti-inflammatory effect, helping to effectively reduce inflammation in PCOS patients. In addition, by measuring oxidative stress markers, the study found that the combined treatment significantly improved the stress response in PCOS patients, with SOD, GSS, and GSH levels showing marked recovery. This result aligns with the role of Cangfu Daotan Wan in traditional Chinese medicine, which regulates the spleen and stomach, resolves phlegm, eliminates dampness, and soothes liver qi. It further validates the potential advantages of Cangfu Daotan Wan in improving the pathological state of PCOS.

In addition, the hormonal imbalance in PCOS is mainly manifested as hyperandrogenism and an abnormal LH/FSH ratio. Diane-35 demonstrates significant efficacy in regulating hormone levels by inhibiting androgen secretion, regulating the menstrual cycle, and restoring ovulatory function. The mechanism of action of Cangfu Daotan Wan in treating spleen deficiency with phlegm-dampness may involve two aspects: on one hand, its phlegm-resolving action helps improve blood viscosity, thinning the blood and promoting the smooth circulation of qi and blood, thus normalizing the menstrual cycle. On the other hand, by regulating the hypothalamic-pituitary-ovarian (HPO) axis, it improves the overall endocrine state and promotes follicular growth and ovulation. The results of this study show that after treatment, both groups exhibited improvements in serum FSH, LH, and testosterone levels, with the LH/FSH ratio approaching normal, indicating that both treatments effectively restore hormonal balance and alleviate clinical symptoms caused by hormonal imbalance. However, no significant intergroup differences were observed, which may be related to sample size and variability. Further research is needed to refine these findings.

The advantage of integrated traditional Chinese and Western medicine treatment lies in its ability to provide comprehensive intervention from multiple targets and dimensions. This approach not only helps alleviate the clinical symptoms of PCOS patients but also improves their endocrine, metabolic, and immune system functions.[31,32] Western medicine, such as Diane-35, demonstrates significant effectiveness in improving clinical symptoms by regulating hormone levels and inhibiting androgen secretion, but it still carries certain side effects. In contrast, the traditional Chinese medicine formulation Cangfu Daotan Wan, through its actions of resolving phlegm, eliminating dampness, and soothing liver qi, effectively alleviates issues like chronic inflammation and oxidative stress, thereby enhancing the overall therapeutic effect. The combined treatment not only shows promising clinical results but also reduces the side effects of Western medicine, providing a new and safer treatment option for PCOS.

The results of this study are in line with and expand upon multiple cutting-edge studies. Firstly, in terms of inflammation regulation, some scholars in China have verified through randomized controlled trials that Shi Cangfu Dao Tan Wan can independently reduce the level of TNF - α in PCOS patients (a decrease of 22%), but it does not involve indicators such as IL-6. This study further found that the combination of Diane-35 resulted in a 31% decrease in IL-6 levels ($p<0.01$), suggesting that hormone therapy may enhance the anti-inflammatory effect of traditional Chinese medicine by inhibiting the NF - κ B pathway. Secondly, in terms of improving the hormone axis, another scholar has reported that after 12 weeks of monotherapy with Diane-35, the LH/FSH ratio decreased to 2.6 ± 0.4, while the combination therapy in this study reduced the ratio to 2.1 ± 0.3 ($p=0.003$), supporting the hypothesis that "Chinese and Western medicine synergistically regulate the hypothalamic pituitary ovarian axis". It is worth noting that this study did not observe a significant increase in adverse reactions with combination therapy (5.7% vs 6.8%), which is consistent with the conclusion of a meta-analysis in China. However, this result should be interpreted with caution as the follow-up time of this study was relatively short (12 weeks).

Although this study demonstrates significant therapeutic effects of the combined treatment of Diane-35 and Cangfu Daotan Wan for polycystic ovary syndrome (PCOS), it still has some limitations. First, the sample size in this study is relatively small, and the treatment duration is short. Future research should involve multi-center, large-sample, long-term follow-up studies to further validate its efficacy. Secondly, the effectiveness in this study was mainly evaluated through clinical symptoms and biochemical indicators, lacking a comprehensive assessment of patients' quality of life, psychological status, and other aspects. Future studies could consider including these indicators for a more thorough evaluation of treatment outcomes.

Conclusion

This study confirms that the combination of Diane-35 and Cangfu Daotan Pill is significantly superior to Diane-35 monotherapy in improving inflammatory response, clinical efficacy, and metabolic indicators in the treatment of PCOS. Specifically, ① Inflammation regulation: Combination therapy significantly reduced the levels of IL-6 (decreased by 31% vs 12%), TNF - α (decreased by 28% vs 9%), and MCP-1 (decreased by 35% vs 15%) compared to the monotherapy group ($P<0.05$), indicating a dual inhibitory effect on chronic inflammatory pathways. ② Clinical efficacy: The total effective rate of the study group reached 95.00% (control group 61.67%, $P<0.05$), and the remission rate of polycystic ovary syndrome was increased by 40% (65% vs 25%, $P<0.05$); ③ Metabolic improvement: The BMI index of the study group decreased by 2.1 kg/m ² (control group 0.8 kg/m ², $P<0.05$), and the improvement in traditional Chinese medicine symptom scores reached 58% (control group 32%, $P<0.01$). Although there was no statistically significant difference in hormone axis regulation (LH/FSH ratio, testosterone levels) between groups ($P>0.05$), the above results still fully support the advantages of the combined regimen in the comprehensive management of PCOS. Future research could extend follow-up to 24 weeks and include long-term indicators such as endometrial thickness to improve the evidence chain.

Disclosure

The authors report no conflicts of interest in this work.

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