Original Article
Application of Guijiaosan Shenque acupoint paste can improve the scores of obesity, endocrine and TCM symptoms in treating obese polycystic ovary syndrome

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Abstract: Objective: To explore the effect of Guijiaosan Shenque acupoint paste on the obesity, endocrine, and TCM symptom scores of obese polycystic ovary syndrome (PCOS) patients with phlegm-dampness block. Methods: From January 2020 to December 2020, 80 PCOS patients with phlegm-dampness block were recruited as the study cohort and randomly divided into a research group (RG) or a control group (CG), with 40 cases in each group. The CG was treated with herbal decoctions according to syndrome differentiation, while the RG was administered Guijiaosan paste at the Shenque acupoint in addition to the treatment administered to the CG. The body weight indexes, endocrine function, insulin resistance indexes, TCM syndrome scores, and safety index changes were compared between the two groups before and after the treatment. Results: Compared with the CG, the body weight indexes, endocrine function, insulin resistance indexes, and TCM syndrome scores in the RG were significantly improved (P<0.05), and there was no significant difference in the safety indexes between the two groups before the treatment (P>0.05). Conclusion: The application of Guijiaosan paste at the Shenque acupoint can effectively improve the obesity and endocrine functions of obese patients with PCOS and improve their clinical symptoms, so it is worthy of clinical promotion.

Keywords: Guijiaosan Shenque acupoint paste, obesity, polycystic ovary syndrome, endocrine functions, TCM symptom scores

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of childbearing age, and it is characterized by hirsutism, hyperandrogenism, anovulation, and polycystic ovaries. It is usually accompanied by insulin resistance and obesity and may develop into cardiovascular disease and metabolic syndrome. The development of PCOS is related to the patients' lifestyles, and treatment is usually administered to improve the patients' clinical symptoms [1-3]. Obesity is a common symptom in PCOS patients, and it affects the patients' psychology and quality of life. Weight control is also important in PCOS treatment [4]. Therefore, it is of great significance to seek an effective treatment for obese PCOS patients to improve their obesity and clinical symptoms.

PCOS has a complex pathogenesis, and it is difficult to treat obese PCOS due to insulin resistance and abnormal blood lipid metabolism [5-7]. Obesity can worsen PCOS, so weight control is usually the initial clinical treatment strategy. Moreover, some patients experience spontaneous ovulation, regular menstruation, and an improvement in their insulin resistance and blood lipid metabolism [8, 9]. At present, the routine treatment for PCOS is to reduce patients' insulin resistance and hyperandrogenism by improving their lifestyles and by administering drug treatment, in order to induce ovulation [10]. Surgery and assisted reproductive technology are used as a second-line treatment to assist patients with pregnancy needs [11]. In recent years, some studies have found that Chinese medicine has certain advantages in regulating female endocrine function, hormone

levels, and menstruation [12, 13]. Animal studies have shown that Liuwei Dihuang pills can significantly improve the pathogenesis of polycystic ovary in PCOS rats, restore follicular development, and reduce insulin resistance [14]. Clinical research shows that [15] Shouwu combined with acupuncture treatment can alleviate the clinical symptoms and improve the insulin resistance of PCOS patients with phlegm-dampness block. All the above studies show the excellent efficacy of Chinese medicine in the treatment of PCOS. However, there are no published studies on Guijiaosan paste in the treatment of PCOS with phlegm-dampness block, so the clinical efficacy of Guijiaosan is unclear.

Therefore, we used Guijiaosan Shenque acupoint paste to treat obese PCOS patients and studied its effects on obesity, endocrine function, and clinical symptoms, in order to provide information for clinical treatment.

Materials and methods

Clinical data

From January 2020 to December 2020, 80 patients with PCOS of the phlegm-dampness blocking type were recruited from the gynecological outpatient department of the South District of Guang'anmen Hospital. A random sequence was established using a random number table, and the established random sequence was concealed using an opaque envelope. Each patient who met the inclusion criteria was randomly assigned to the research group (RG) or the control group (CG) according to the established sequence, with 40 patients in each group. The CG was treated with herbal decoction based on syndrome differentiation, while the RG was treated with Guijiaosan Shenque point in addition to the treatment administered to the CG. This study was approved by the ethics committee of our hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) Women 18-50 years old. (2) This research met the diagnostic criteria of suspected PCOS issued by the Chinese health sector: ① Oligomenorrhea or amenorrhea or irregular uterine bleeding. ② Clinical manifestations of hyperandrogenism (acne, hirsutism) or hyperandrogenism. ③ PCOS was found by ultrasonography. If the patient has ① and meets ② or ③, she can be treated for suspected PCOS. (3) This research met the diagnostic criteria of the 2003 Rotterdam Conference [16]: ① Oligo-ovulation or anovulation. ② Clinical manifestations of hyperandrogenism. ③ PCOS was determined by ultrasonography. PCOS can be confirmed when the patients met two of the above three conditions. (4) This research met the criteria of phlegm-dampness blocking syndrome in *Guiding Principles for Clinical Research of New Traditional Chinese Medicine* (Trial) and *Gynecology of Traditional Chinese Medicine*. ① The main symptoms included late menstruation, hypomenorrhea, or even amenorrhea, infertility, obesity, hirsutism, acne, or oily skin. ② The secondary symptoms included fatigue, spontaneous perspiration, dizziness, chills, cold limbs, lumbosacral aching, tinnitus or deafness, abdominal distension, chest discomfort with shortness of breath, and excessive morbid leucorrhea and viscosity. ③ Tongue picture: The tongue is fat, tender, light or dark, with white greasy or slippery fur. ④ Pulse condition: Slippery or thin or weak. (5) Body mass index (BMI) ≥ 24 kg/m² and/or body fat rate (BFR) $\geq 28\%$. (6) No treatment drugs for PCOS were used in the previous month. (7) The patients voluntarily participated in this study and signed the informed consent form.

Exclusion criteria: (1) Women younger than 18 years old or older than 50 years old. (2) Patients with other diseases causing hyperandrogenism or with hyperandrogenism symptoms. (3) Patients with other diseases causing ovulation disorders. (4) Patients with gynecological malignant tumors. (5) Patients with severe heart, lung, liver, kidney, or nervous system diseases. (6) Patients with other severe cognitive impairments, aphasia, or mental disorders. Individuals with mental or legal disabilities or individuals unable to care for themselves. (7) Patients who are participating in the clinical trials of other drugs. (8) Patients without complete clinical data. (9) Patients who cannot persist taking the medication for 3 months or who cannot cooperate with the follow-up to complete the whole process of the clinical research.

Treatment plan

Both groups were treated with oral Chinese medicine based on syndrome differentiation,

and the Chinese medicine was made into granules by our hospital's granule pharmacy. The medicine was applied one dose per day in the morning and evening. In the RG, Guijiaosan paste was applied at the Shenque point, and the ingredients were *Cinnamomum cassia* (Kangmei Pharmaceutical Co., Ltd., item number: 99400822672) and *Pericarpium zanthoxyli* (Kangmei Pharmaceutical Co., Ltd., item number: 180300281), which were divided equally, ground into powder (5 g each time), and then placed in a filterable non-woven bag and fixed at the Shenque point of the navel with adhesive tape. The paste was applied before bedtime at 22 o'clock every night, removed at 6 o'clock every morning, placed for 8 hours every day, and stopped during menstruation. The treatment was performed for 3 months.

Outcome measures

The main outcome measures: the changes in the body weight indexes before and after the treatment were observed, including the BMI and BFR levels and the waist-hip ratios (WHR). The changes in endocrine function, including the human luteinizing hormone (LH), follicle stimulating hormone (FSH) and free testosterone (T) levels, were observed before and after the treatment. The changes in the TCM syndrome scores before and after the treatment in the two groups, including the main symptom scores and the secondary symptom scores, were tested. The sub-symptoms include menstrual cycles, menstrual periods, menstrual volumes, BMI, body fat, waist-hip ratio, acne, seborrheic skin and hirsutism, with 0 to 6 points for each item (mild: 0-16 points, moderate: 17-32 points, severe: ≥33 points). The secondary symptoms include heavy body fatigue, sliminess in the mouth and excessive phlegm, drowsiness, chest tightness and fullness, abdominal distention, excessive morbid leucorrhea, and loose or sticky stools, with 0-3 points for each item (mild: 0-7 points, moderate: 8-16 points, severe: ≥17 points).

Secondary outcome measures: The changes in the insulin resistance indexes before and after the treatment, including the fasting plasma glucose (FPG) levels, the fasting insulin (FINS), and the homeostasis model assessment of insulin resistance (Homa1-IR) were observed. The changes in the safety indexes, including the alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN) and serum creatinine (Scr) levels were observed before and after the treatment.

Statistical analysis

SPSS 23.0 was applied to statistically analyze the collected data, and GraphPad Prism 8 was used to plot the figures. The counting data were represented as the rate (%) and analyzed using chi-square tests, and were expressed as χ^2. The measurement data were represented as the (means ± SD), as were all the measurement data that conformed to a normal distribution. Independent sample t tests were used for the pair-wise comparisons, and paired t tests were used for the intra-group comparisons, all of which were expressed by t. P<0.05 was considered statistically significant.

Results

Baseline patient data

By comparing the baseline data, it was found that there were no significant differences in terms of age, BMI, BFR, smoking history, drinking history, residence, course of the disease, TCM syndrome scores, or the various laboratory indicators between the two groups (P>0.05), which were comparable, as shown in **Table 1**.

Changes in the body weight indexes

The body weight index changes before and after the treatment were measured. The results showed that there were no significant differences in the BMI, BFR, or WHR levels between the two groups before the treatment (P>0.05), but the BMI levels of the two groups after the treatment were significantly lower than the levels before the treatment (P<0.05), and the BMI of the RG was significantly lower than the BMI of the CG (P<0.05). There was no significant difference in the WHR levels between the two groups after the treatment (P>0.05). The BFR levels of the patients in the RG after the treatment were significantly lower than they were before the treatment, and significantly lower than the levels in the CG (P<0.05), as shown in **Table 2**.

Changes of endocrine function

The endocrine function was evaluated by measuring the LH, FSH, and T values. The results

Table 1. Baseline data

Factor	CG (n=40)	RG (n=40)	t/χ^2 value	P value
Age (years)	28.73±4.36	29.58±4.15	0.893	0.375
BMI (kg/m^2)	28.83±1.92	29.43±1.84	1.427	0.158
BFR (%)	34.67±3.24	34.19±3.41	0.645	0.521
History of smoking				
Yes	14 (35.00)	22 (55.00)	3.232	0.072
No	26 (65.00)	18 (45.00)		
History of drinking				
Yes	23 (57.50)	28 (70.00)	1.352	0.245
No	17 (42.50)	12 (30.00)		
Residence				
Urban	19 (47.50)	24 (60.00)	1.257	0.262
Rural	21 (52.50)	16 (40.00)		
Course of the disease	5.97±4.85	6.05±5.12	0.071	0.943
LH (mIU/mL)	13.64±5.47	13.23±5.61	0.331	0.742
FSH (mIU/mL)	6.06±1.88	6.12±1.79	0.146	0.884
T (ng/mL)	0.83±0.31	0.84±0.34	0.138	0.891
FPG (mmol/L)	5.40±1.86	5.44±1.64	0.102	0.919
FINS (uIU/mL)	7.42±4.13	7.36±3.97	0.066	0.947
Main symptom score	27.55±5.84	26.50±5.17	0.851	0.397
Sub-symptom score	9.03±3.21	9.13±3.68	0.130	0.897

showed that there were no significant differences between the two groups before the treatment (P>0.05). After the treatment, the LH, FSH, and T levels in the RG were significantly lower than they were before the treatment (P<0.05) and significantly lower than the corresponding levels in the CG (P<0.05), as shown in **Figure 1**.

Changes in the insulin resistance indexes

After the treatment, the FPG, FINS, and HOM-A1-IR values of patients in the CG were not significantly different from the values before the treatment (P>0.05). After the treatment, the values in the CG were not significantly different compared with the values before the treatment (P>0.05), but the values in the RG were significantly lower than they were before the treatment (P<0.05), and the insulin resistance index levels of the two groups after the treatment were significantly different compared with their levels before the treatment (P<0.05), as shown in **Figure 2**.

Comparison of TCM syndrome scores

The clinical symptoms of the two groups were evaluated using their TCM syndrome scores.

The results showed that there was no significant difference between the two groups before the treatment (P>0.05), but the main symptom scores and the sub-symptom scores of the two groups after the treatment were significantly lower than they were before the treatment (P<0.05), and the scores in the RG were significantly lower than the scores in the CG (P<0.05), as shown in **Table 3**.

Changes in the safety indexes

By evaluating the liver and kidney function indexes between the two groups, it was found that there were no significant differences between the two groups before the treatment (P>0.05). After the treatment, the ALT in the RG was significantly lower than it was before the treatment (P<0.05), but there was no significant difference in the CG (P>0.05). There were no significant differences in the AST, BUN, or Scr levels between the two groups compared with their levels before the treatment (P>0.05), and no serious adverse events were observed in the two groups, as shown in **Table 4**.

Discussion

PCOS is a highly prevalent disease that affects women of reproductive age all over the world [17]. It is a heterogeneous disease characterized by excessive androgen, ovarian dysfunction, and metabolic dysfunction, and it seriously affects women's quality of life, so individualized treatment is needed [18]. Oral contraceptives should be used as long-term first-line treatment for patients without reproductive requirements, and ovulation therapy is effective for patients with reproductive requirements [19]. Studies have shown that metformin can improve vascular endothelial function and endothelial dysfunction in women with PCOS [20], but the single application of metformin should not be used as the first-line therapy for patients with anovulation [21]. Hormone therapy is not suitable for infertile women, and insulin sensitizers have limited reproductive efficacy. However, current research shows that com-

Table 2. Changes in the body weight indexes

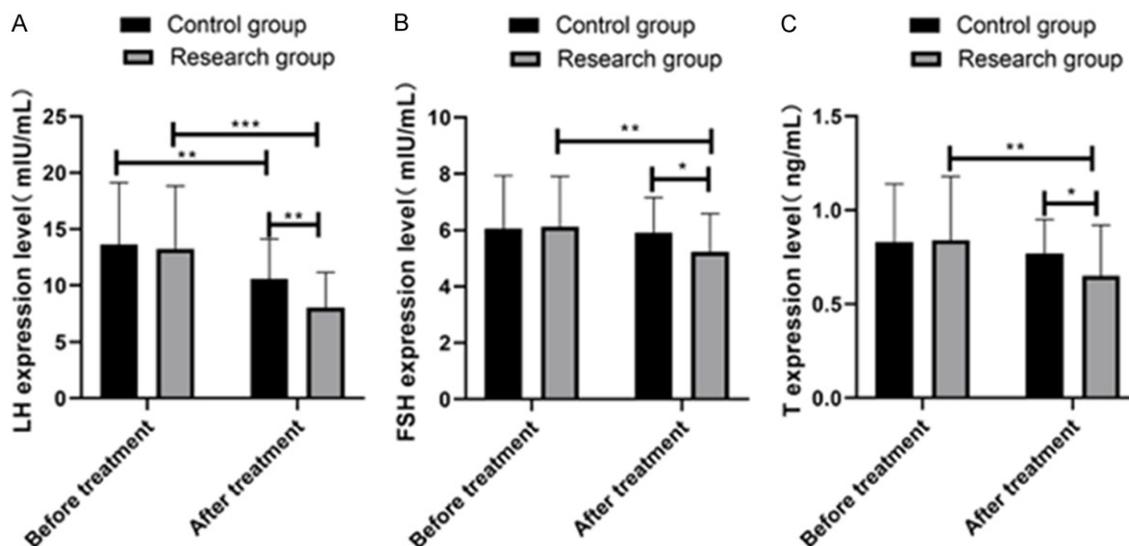| Group	BMI		BFR		WHR	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
CG (n=40)	29.41±2.26	28.45±1.94*	34.67±3.24	34.08±4.21	0.87±0.08	0.88±0.09
RG (n=40)	29.43±2.21	27.48±1.87*	34.19±3.41	31.12±5.34*	0.85±0.07	0.83±0.05
t value	0.040	2.277	0.645	2.753	1.190	3.071
P value	0.968	0.026	0.521	0.007	0.238	0.003

*means compared with before the treatment, $P<0.05$.

Figure 1. The endocrine function changes in the two groups before and after the treatment. A. There was no significant difference in the LH values between the two groups before the treatment, but after the treatment, the LH values of the RG were significantly lower than the LH values in the CG. B. There was no significant difference in the FSH values between the two groups before the treatment. After the treatment, the FSH of the RG was significantly lower than the FSH of the CG, and the FSH level was lower compared with its level before the treatment. C. There was no significant difference in the t values between the two groups before the treatment. After the treatment, the t values in the RG were significantly lower than the t values in the CG, and the t values were lower compared with before the treatment. * indicates $P<0.05$, ** indicates $P<0.01$, *** indicates $P<0.001$.

pounds isolated from Chinese herbal medicines have beneficial effects on PCOS [22]. Therefore, exploring Chinese medicine may have a curative effect on obese women with PCOS.

According to the theory of TCM, most of the patients are confirmed to have late menstruation, metrorrhagia, gynecologic abdominal lumps, amenorrhea, and infertility according to the different clinical symptoms. The main pathological basis of obese PCOS patients is excessive phlegm and dampness, which leads to irregular menstruation or infertility and affects the endocrine and metabolic systems. Guijiaosan is made from *Cinnamomum cassia*

and pericarpium zanthoxyli. Studies have shown that *Cinnamomum cassia* can improve the blood sugar and blood lipid levels to a certain extent [23], and pericarpium zanthoxyli has the effects of warming the middle-warmer and relieving pain, removing dampness and dispelling cold, and plays an important role in the clinical treatment of Chinese medicine. Considering these effects, Guijiaosan may have a good effect at treating obese PCOS patients. In order to explore the therapeutic value of Guijiaosan on PCOS, this study first evaluated the body weight indexes of the two groups before and after their treatment and found that the improvement of the BMI and BFR levels in the RG was more significant than
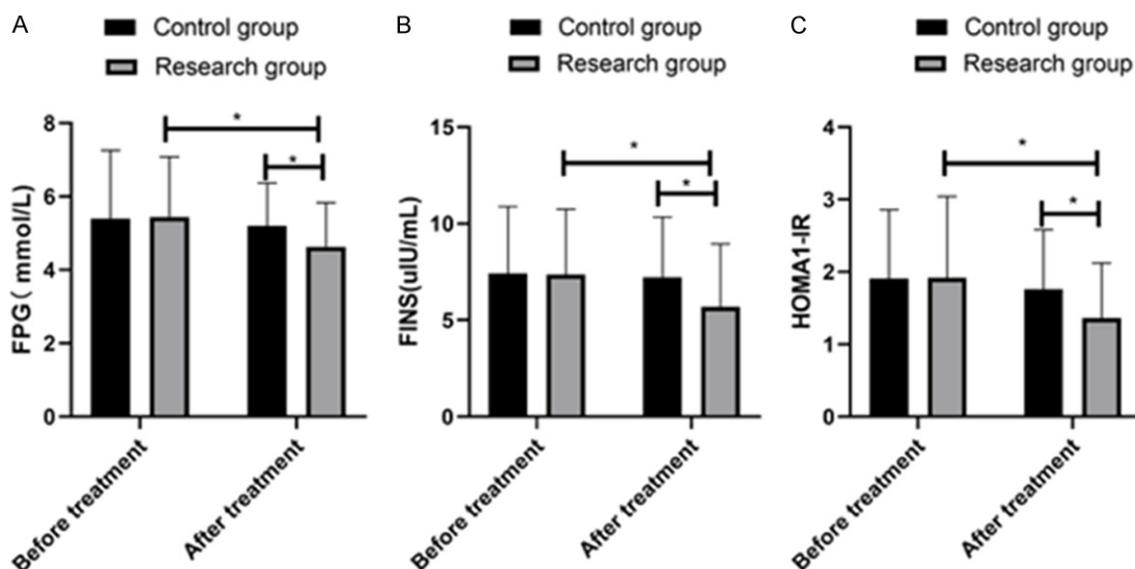
Figure 2. Changes in the insulin resistance indexes. A-C. There was no significant difference in the FPG/FINS/HOMA1-IR values between the two groups before the treatment. After the treatment, the FPG/FINS/HOMA1-IR values in the CG were not significantly different from their levels before the treatment, while the values in the RG were significantly lower than they were before the treatment. There was a significant difference between the two groups after the treatment. * indicates P<0.05, ** indicates P<0.01.

Table 3. Comparison of the TCM syndrome scores

Group	Main symptom score		Sub-symptom score	
	Before treatment	After treatment	Before treatment	After treatment
CG (n=40)	27.55±5.84	22.50±4.15	9.03±3.21	5.85±1.17
RG (n=40)	26.50±5.17	17.53±4.07	9.13±3.68	3.38±1.18
T value	0.851	5.408	0.130	9.401
P value	0.397	<0.001	0.897	<0.001

Table 4. Comparison of the safety indicators

Group	ALT (IU/L)		AST (IU/L)		BUN (mmol/L)		Scr (mmol/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
CG (n=40)	39.82±11.67	41.23±12.68	35.77±9.57	31.72±9.46	4.67±1.14	4.61±0.97	49.18±13.84	52.75±14.21
RG (n=40)	36.41±10.58	34.82±10.76	36.39±10.71	29.62±7.93	4.58±1.08	4.45±0.89	51.76±14.28	56.47±13.27
t value	1.369	2.438	0.273	1.076	0.363	0.769	0.821	1.210
P value	0.175	0.017	0.786	0.285	0.718	0.444	0.414	0.230

it was in the CG, which indicated that Guijiaosan can effectively reduce patients' body weight and BFR. Studies by Borzoei et al. [24, 25] showed that *Cinnamomum cassia* can improve the metabolic levels of PCOS patients, reduce their blood lipid levels, help to actively deal with complications and reduce the risk factors of PCOS. This is similar to the results of our research. Body weight is closely related to the prevalence and severity of PCOS. Once obese

PCOS patients become pregnant, the risk of pregnancy-related complications increases, complications such as gestational diabetes, hypertension, and premature birth. Guijiaosan can effectively reduce PCOS patients' weight, which is of great significance for avoiding these risks. We speculate that the mechanism may be that the components in cinnamon can effectively improve the glucose and lipid metabolism levels in PCOS and regulate the important fat

metabolism factor levels, thus achieving weight loss.

Endocrine disorders and insulin resistance are the core causes of PCOS, and they are closely related to each other and play important roles in the pathogenesis of PCOS [26]. Therefore, we compared the reproductive hormone levels between the two groups and found that the LH, FSH, and T values in the RG after the treatment were significantly lower than they were before the treatment and were significantly lower than they were in the CG. This indicates that Guijiaosan has a significant effect on improving patients' endocrine functions. By evaluating the changes in the insulin resistance indexes before and after the treatment, it was found that the FPG, FINS, and HOMA1-IR values of the patients in the RG were significantly lower than they were before the treatment, and there were significant differences compared with the values in the CG. This showed that Guijiaosan can improve insulin resistance, improve blood sugar levels, and maintain the blood sugar balance. *Cinnamomum cassia* has been proved to have anti-PCOS and anti-diabetes properties. Oral cinnamon extract can reduce the fasting blood glucose and blood lipid levels in patients with type 2 diabetes and can improve the insulin sensitivity in women with PCOS [27-29]. Dou et al. [30] found that cinnamon can improve insulin resistance and may be a potential therapeutic agent for PCOS. Pericarpium zanthoxyli has the efficacy of warming middle-warmer, dispelling cold, dehumidifying pain, and the combined treatment of pericarpium zanthoxyli and cinnamon is more effective. Then we evaluated the TCM syndrome scores of the two groups and found that after the treatment, the main symptom scores and sub- symptom scores of the two groups were significantly lower than they were before the treatment, and the scores of the RG were significantly lower than of the scores in the CG. This showed that Guijiaosan can effectively improve patients' clinical symptoms of patients. The Shenque point is located in the navel and is connected with the meridians. Because of its sensitivity, permeability and absorbability, it plays an important role in TCM [31]. Studies have shown [32] that the herbal-cake-partitioned moxibustion of "Shenque" (CV8-HCPM) can effectively improve endocrine disorders in dysmenorrheic rats.

Zhang et al. [33] showed that Shenque acupoint treatment has a more significant effect on weight loss than oral garlic oil. Therefore, we believe that Guijiaosan Shenque acupoint application has a better curative effect on obese PCOS. At the end of the study, we tested the liver and kidney function indexes of the two groups, and the results showed that there were no abnormalities and no serious adverse events in the two groups. This showed that Guijiaosan is highly safe for treating obese PCOS.

This research revealed that Guijiaosan Shenque acupoint paste has a therapeutic value for treating obese PCOS patients, but there are still some limitations to the study. First, due to the limited time period, this research failed to follow up on the patients for a long time, and the patients' recurrence and pregnancy rates were not determined. Second, we hope to add animal experiments in future studies to prove the validity of this study's results.

To sum up, Guijiaosan Shenque acupoint paste can effectively improve the obesity and endocrine function of obese PCOS patients, improve their clinical symptoms, and is highly safe, so it is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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