

ORIGINAL RESEARCH ARTICLE

Effects of acupuncture on improving hormonal and metabolic biochemical characteristics in polycystic ovary syndrome

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Chao Shao, Weihua Li and Jing Liang*

Department of Gynaecology, Guang'anmen Hospital South Campus, China Academy of Chinese Medical Sciences, Beijing, China

*For Correspondence: Email: liangjing198593@163.com; Phone: 86018610153538

Abstract

We investigated the effects of electroacupuncture on hormonal and metabolic characteristics in women with obesity-related polycystic ovary syndrome (PCOS). In this randomized controlled study, 120 patients were assigned to either an electroacupuncture group or a sham acupuncture group (60 per group) and treated three times weekly for 16 weeks. Hormonal profiles, metabolic parameters, inflammatory markers, ovarian morphology, and clinical outcomes were evaluated before and after intervention. Compared with sham treatment, electroacupuncture significantly reduced luteinizing hormone, LH/FSH ratio, testosterone, and anti-Müllerian hormone levels, while increasing sex hormone-binding globulin and progesterone. Metabolic improvements included reductions in triglycerides, LDL cholesterol, uric acid, fasting insulin, HOMA-IR, total cholesterol, and fasting plasma glucose, along with increased HDL cholesterol and vitamin D levels. Inflammatory markers (CRP, IL-6, TNF- α , WBC, C3, and C4) were also significantly decreased. Clinically, electroacupuncture improved ovulation rate and quality of life, and reduced hirsutism, ovarian volume, and antral follicle count. These findings suggest that electroacupuncture may serve as an effective adjunct therapy for endocrine and metabolic dysfunction in PCOS. (*Afr J Reprod Health* 2026; 30 [5]: 84-95).

Keywords: Acupuncture; Polycystic ovary syndrome; Insulin resistance; Sex hormones; Metabolism and biochemistry; Lipidomics

Résumé

Nous avons étudié les effets de l'électroacupuncture sur les caractéristiques hormonales et métaboliques chez des femmes atteintes d'un syndrome des ovaires polykystiques (SOPK) associé à l'obésité. Dans cette étude randomisée contrôlée, 120 patientes ont été réparties en un groupe recevant une électroacupuncture ou un groupe témoin recevant une acupuncture simulée (60 patientes par groupe), avec trois séances par semaine pendant 16 semaines. Les profils hormonaux, les paramètres métaboliques, les marqueurs inflammatoires, la morphologie ovarienne ainsi que les résultats cliniques ont été évalués avant et après l'intervention. Comparativement au groupe témoin, l'électroacupuncture a significativement réduit les taux d'hormone lutéinisante, le rapport LH/FSH, la testostérone et l'hormone anti-müllérienne, tout en augmentant les concentrations de globuline liant les hormones sexuelles et de progestérone. Des améliorations métaboliques ont également été observées, avec une diminution des triglycérides, du cholestérol LDL, de l'acide urique, de l'insuline à jeun, de l'indice HOMA-IR, du cholestérol total et de la glycémie à jeun, ainsi qu'une augmentation du cholestérol HDL et des taux de vitamine D. Les marqueurs inflammatoires (CRP, IL-6, TNF- α , WBC, C3 et C4) ont également diminué de manière significative. Sur le plan clinique, l'électroacupuncture a amélioré le taux d'ovulation et la qualité de vie, tout en réduisant l'hirsutisme, le volume ovarien et le nombre de follicules antraux. Ces résultats suggèrent que l'électroacupuncture pourrait constituer une thérapie adjuvante efficace pour corriger les dysfonctionnements endocrino-métaboliques du SOPK. (*Afr J Reprod Health* 2026; 30 [5]: 84-95).

Mots-clés: Acupuncture; Syndrome des ovaires polykystiques; Résistance à l'insuline; Hormones sexuelles; Métabolisme et biochimie; Lipidomique

Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine and metabolic disorder in women of reproductive age, characterized by a cycle of high androgen levels and insulin resistance. Studies

indicate that 50-70% of PCOS patients experience insulin resistance, with variations across phenotypes¹. Research by DeUgarte et al.¹ and Moghetti et al.² highlights that insulin resistance is more common in PCOS patients compared to healthy individuals, and obese PCOS patients have

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40% lower insulin sensitivity than their non-obese counterparts². This condition worsens ovarian androgen production, increases lipid accumulation, and leads to chronic inflammation, raising long-term cardiovascular risk by 2 to 3 times³.

The diagnostic criteria for androgen hyperplasia and PCOS formulated by Azziz et al.⁴ explicitly recognize metabolic dysfunction as a key component in the diagnosis of polycystic ovary syndrome, with more than 60% of patients presenting with concurrent glycolipid metabolism disorders. Therefore, comprehensive intervention targeting the hormone-metabolic axis has become the core strategy for the treatment of PCOS.

A 2017 meta-analysis by Jo et al. demonstrated that acupuncture shows promise as an adjuvant therapy for PCOS, particularly in reducing serum testosterone and improving the luteinizing hormone to follicle-stimulating hormone ratio.⁵ Despite the benefits, the study quality varied significantly. Li et al.⁶ developed a trial targeting insulin-resistant PCOS patients, using electroacupuncture to activate the AMPK pathway for better glucose metabolism. Lai et al.'s clinical observations noted a 2.3 kg/m² BMI reduction and a 35% decrease in HOMA-IR in obese PCOS patients through abdominal acupuncture, though the study had only 60 participants and lacked a placebo control⁷. A 2022 randomized double-blind trial by Muharam et al.⁸ found that combining electroacupuncture with metformin improved insulin sensitivity more than metformin alone, supporting the synergy between acupuncture and drugs. However, existing studies show significant variability in intervention frequency, acupoint selection, and electroacupuncture parameters, complicating the comparison of results.

The mechanism by which acupuncture ameliorates hormone-metabolic disorders in polycystic ovary syndrome (PCOS) involves the multi-target regulation of the neuro-endocrine-immune network. Research conducted by Liu et al.⁹, published in *Nature*, demonstrated that electroacupuncture stimulation at lower extremity acupoints, such as Zusanli and Tianshu, can activate the dopamine pathway via the vagus-adrenal axis, thereby eliciting a systemic anti-inflammatory response. This finding provides a neuroanatomical foundation for the use of acupuncture in mitigating

chronic low-grade inflammation associated with PCOS. Clinical studies have indicated that acupuncture may modulate the frequency of gonadotropin-releasing hormone (GnRH) pulses through Kisspeptin neurons in the hypothalamus, subsequently reducing luteinizing hormone (LH) secretion and decreasing ovarian androgen synthesis. Furthermore, acupuncture has been shown to facilitate the translocation of glucose transporter type 4 (GLUT4) in skeletal muscle, thereby enhancing glucose uptake. Its efficacy is comparable to that of metformin, with a more prolonged duration of action⁸.

This prospective randomized sham-controlled trial investigates a standardized electroacupuncture protocol specifically in obese PCOS patients (BMI ≥ 28 kg/m²), comprehensively assessing hormonal, metabolic, and novel inflammatory biomarkers (including uric acid, vitamin D, and complement factors) to provide definitive evidence and mechanistic insights beyond prior heterogeneous acupuncture studies.

Methods

Research object

This prospective randomized controlled study included 120 patients diagnosed with polycystic ovary syndrome (PCOS) according to the established diagnostic criteria, spanning from January 2020 to December 2023¹⁰. The random allocation sequence was computer-generated by an independent statistician not involved in patient recruitment or assessment, using block randomization with variable block sizes of 4 or 6. To ensure balance between groups, randomization was stratified by baseline BMI (28-30 vs. >30 kg/m²) and age (≤ 30 vs. >30 years). Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes.

After eligibility confirmation and informed consent, the acupuncturist opened the next envelope to determine group assignment, ensuring that recruiters, outcome assessors, and participants remained blinded to the allocation until intervention initiation. Participants were randomly assigned via computer-generated block randomization (variable block sizes of 4 or 6), stratified by baseline BMI (28-30 vs. >30 kg/m²)

and age (≤ 30 vs. >30 years), into two groups: the acupuncture treatment group and the acupuncture comparison group (n=60 each).

The diagnostic criteria for PCOS were based on the 2003 Rotterdam criteria, as proposed by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine.¹⁰ The exclusion criteria: Presence of other reproductive system disorders, such as fallopian tube obstruction, intrauterine adhesions, uterine fibroids, or endometriosis; Concurrent endocrine disorders, including pituitary, thyroid, or adrenal diseases, and diabetes; Presence of acute illnesses or severe cardiovascular, cerebrovascular, hepatic, renal, or hematological diseases; Pregnancy plans within the preceding 6 months; Use of prokinetic agents, such as anticholinergic or dopaminergic drugs, hormone therapies, medications affecting glucose and lipid metabolism, or traditional Chinese medicine treatments within the past 3 months, or participation in other clinical studies. The patient had an allergic reaction to the drugs used in this research project

Treatment methods

The procedural protocol for the treatment group is detailed as follows: Initially, patients were instructed to empty their bladders and assume a supine position to expose the surgical regions of the abdomen and the lower limbs. Following standard skin disinfection procedures, a Huatuo brand disposable sterile acupuncture needle (dimensions 0.30×50 mm) was utilized. The abdominal acupoints selected were Guanyuan (CV4) and Zhongji (CV3), located 3 cun and 4 cun below the umbilicus on the anterior midline, respectively. The needles were inserted vertically to a depth of 25-30 mm until a firm engagement was achieved, eliciting sensations of soreness, numbness, distension, and heaviness in the patient. Subsequently, patients were repositioned to a prone posture to expose the lumbosacral area. The bilateral Shenshu (BL23) and Bladder Shu (BL28) points were targeted, situated 1.5 cun lateral to the spinous processes of the second lumbar and second sacral vertebrae, respectively. The needle tip was inserted obliquely towards the spine to a depth of 15-20 mm.

The Zusanli (ST36) acupoint was accessed with the patient in a supine position; it was located 3 cun below Dubi and one transverse finger breadth lateral to the anterior crest of the tibia, with a perpendicular insertion depth of 30 mm.

Upon achieving qi sensation at all acupoints, one set of electroacupuncture wires was connected to the Guanyuan - Zhongji acupoint in the abdomen, and another set was connected to the Shenshu - Baoshu acupoints bilaterally on the back. The electroacupuncture was administered using a sparse and dense wave mode, with the frequency alternating automatically between 2 Hz and 15 Hz. Each session lasted for 5 minutes before switching. The current intensity was adjusted until the patient perceived a slight rhythmic contraction of the local muscles without experiencing significant pain. The needles were retained for 30 minutes.

The treatment was administered three times per week, specifically on Mondays, Wednesdays, and Fridays, with intervals of 48 to 72 hours between sessions. A total of 48 treatments were administered over a period of 16 consecutive weeks. The patient's vital signs and any adverse reactions were recorded before and after each treatment session. In the control group, a sham acupuncture intervention was administered, characterized by non-meridian and non-acupoint shallow acupuncture. Twelve non-acupoint sites were selected in the thickened muscle areas of the limbs for acupuncture. These sites included the abdominal center of the distal one-third of the biceps brachii muscle bilaterally, 4 cun proximal to the transverse wrist crease on the radial side of both forearms, the midsection of the lateral thigh muscles bilaterally, and 5 cun distal to the fibular head on the lateral aspect of both calves.

A short needle, measuring 0.20×30 mm, was inserted rapidly and vertically into the skin to a depth of 2-3 mm, with immediate cessation of insertion. No lifting, thrusting, twisting, or rotating techniques were applied, and no de qi sensation was elicited. The needle was secured with medical adhesive tape to prevent dislodgement and retained for 30 minutes to align with the duration parameters of the treatment group. An electrode pad was placed on the skin adjacent to the needle handle; however,

the electroacupuncture device was not activated, thereby only simulating the appearance of electroacupuncture. The treatment frequency, course of treatment and Lifestyle guidance were all exactly the same as those of the treatment group.

Observed indicators and effect evaluation

Assessment of sex hormone levels

In this study, serum sex hormone levels were quantified using electrochemiluminescence immunoassay (ECLIA) or enzyme-linked immunosorbent assay (ELISA), specifically measuring Total Testosterone (T), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), and Sex Hormone-Binding Globulin (SHBG). Blood samples were collected from fasting participants in the early morning (between 8:00 and 11:00 AM) on the second to fifth day of the menstrual cycle to minimize the impact of circadian rhythm and menstrual cycle fluctuations on the results. For participants experiencing amenorrhea, blood samples could be obtained at any time; however, the date of the last menstrual period or the duration of amenorrhea was meticulously recorded.

Evaluation of metabolic biochemical indicators

Fasting plasma glucose (FPG) levels were measured using the glucose oxidase method. The specimens consisted of venous plasma obtained after a 12-hour fasting period, with a normal reference range of 3.9-6.1 mmol/L. Fasting insulin (FINS) concentrations were determined via chemiluminescence immunoassay and expressed in units of $\mu\text{U/mL}$. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the formula: $\text{HOMA-IR} = \text{FPG (mmol/L)} \times \text{FINS } (\mu\text{U/mL}) / 22.5$. A HOMA-IR value of ≥ 2.69 was indicative of insulin resistance. Glycated hemoglobin (HbA1c) levels were assessed through high-performance liquid chromatography (HPLC), providing an estimate of average blood glucose levels over the preceding 2-3 months, with a normal reference range of 4.0%-6.0%. Total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were quantified

using an enzymatic method with an automatic biochemical analyzer.

Evaluation of inflammatory markers

Hypersensitive C-reactive protein (hs-CRP) was quantified using immunoturbidimetry or high-sensitivity enzyme-linked immunosorbent assay (ELISA), with detection capabilities for CRP levels as low as 0.1 mg/L. In patients with polycystic ovary syndrome (PCOS), hs-CRP levels were significantly elevated compared to the healthy control group, typically ranging from 2.4 to 6.8 mg/L, representing an increase of two to four times. Hs-CRP serves as a sensitive biomarker for assessing low-grade chronic inflammation and exhibits a positive correlation with insulin resistance, dyslipidemia, and endothelial dysfunction. Interleukin-6 (IL-6) concentrations were measured in serum using ELISA or chemiluminescence assays. Multiple meta-analyses have demonstrated a significant elevation in IL-6 levels among patients with PCOS, with a combined mean difference (MD) of 0.72 (95% CI: 0.47-0.98, $p < 0.0001$). As a pro-inflammatory cytokine, IL-6 directly contributes to the disruption of insulin signaling pathways and abnormal ovarian function. During sample processing, it is imperative to avoid hemolysis and repeated freezing and thawing. Serum should be separated within two hours of sample collection and stored at -80°C for subsequent analysis.

Evaluation of clinical outcomes

The ovulation rate was assessed through transvaginal ultrasonography to monitor follicular development. Commencing on the 10th day of the menstrual cycle, monitoring was performed every 2 to 3 days, during which the diameter of the dominant follicle and its rupture status were recorded. Ovulation was determined based on the following criteria: the disappearance or collapse of the dominant follicle when its diameter was ≥ 18 mm, the presence of free fluid in the uterorectal pouch, and biphasic changes in basal body temperature. The ovulation rate was calculated as follows: (the number of ovulation cycles during the monitoring period/the total number of monitoring periods) $\times 100\%$. The Ferriman-Gallwey hirsutism

score was evaluated using the modified Ferriman-Gallwey (mFG) scoring system to assess terminal hair growth on the body surface. The assessment encompassed 11 androgen-sensitive areas, including the upper lip, lower jaw, chest, upper back, lower back, upper abdomen, upper arm, forearm, thigh, and calf. Each area was scored from 0 to 4 based on hair density and distribution range. A total score of 8 or above was indicative of hirsutism, with scores of 8 to 15 considered mild, 15 to 26 moderate, and 26 to 36 severe. Two trained physicians independently scored the quality of life using the Polycystic Ovary Syndrome Questionnaire (PCOSQ), and their average scores were used to minimize bias. The PCOSQ, with 26 items across 5 dimensions---emotion, body hair, weight, infertility, and menstruation---used a 7-point Likert scale, where higher scores indicated better quality of life. Patients completed the questionnaire before and after treatment, ensuring completeness. The PCOSQ was reliable (Cronbach's $\alpha > 0.70$) and valid, effectively reflected intervention outcomes.

Statistical analysis

In this study, Epidata 3.1 was used for double data entry and error correction. SPSS 25.0 and R 4.2.0 were utilized for statistical analysis. Data normality was checked with the Kolmogorov-Smirnov test, and normally distributed data were presented as mean \pm standard deviation. The independent sample t-test and Bonferroni method were used for group comparisons. The Mann-Whitney U test and Nemenyi method were applied for non-parametric comparisons. Count data were shown as frequency and percentage, with group comparisons done using the χ^2 test or Fisher's exact test. A P value < 0.05 was considered significant for all two-sided tests.

Ethical consideration

This study received approval from the Ethics Committee of Guang'anmen Hospital, China Academy of Chinese Medical Sciences (South District Branch) on November 20, 2019 (Approval No.: 2019-GL-047).

Results

Comparison of clinical data and demographic characteristics of two groups of PCOS patients

There was no statistically significant difference in all baseline indicators between the treatment group and the comparison group ($P > 0.05$). Including indicators such as age, BMI, systolic blood pressure, diastolic blood pressure, weight, waist circumference, hip circumference, history of previous pregnancy complications, gestational hypertension, diabetes, preeclampsia, frequency of breastfeeding, number of nights of breastfeeding, and history of previous miscarriage/premature birth ($P > 0.05$). See Table 1.

Comparison of sex hormone levels

There was no statistically significant change in each index before and after treatment in the comparison group ($P > 0.05$). The intergroup comparison showed that after treatment, the levels of LH, LH/FSH ratio, T and AMH in the treatment group were significantly lower than those in the comparison group ($P < 0.05$), and the level of SHBG was significantly higher than that in the comparison group ($P < 0.001$).

The P level was also higher than that of the comparison group ($P < 0.001$), suggesting that therapeutic intervention could significantly improve hyperandrogenemia and endocrine disorders in patients with PCOS. See Table 2.

Comparison of metabolic biochemical indicators

There was no statistically significant change in each index after comparison group before treatment ($P > 0.05$). The intergroup comparison showed that the levels of TG, LDL, UA, FINS and HOMA-IR in the after Treatment group were significantly lower than those in the comparison group ($P < 0.05$). The levels of HDL and 25-OH-D3 were significantly higher than those of the comparison group ($P < 0.001$), and the levels of TC and FPG were also significantly lower than those of the comparison group ($P < 0.05$).

Table 1: Comparison of clinical data and population characteristics of the two groups of PCOS ($\bar{x}\pm s$, n(%))

Factors	treatment group (n=60)	comparison group(n=60)	χ^2/t	P
Age (years)	26.50±3.21	26.14±3.53	0.582	0.562
BMI (kg/m ²)	29.42±1.13	29.15±1.45	1.124	0.263
Systolic blood pressure (mmHg)	118.63±8.47	117.92±9.15	0.437	0.663
Diastolic blood pressure (mmHg)	76.80±6.52	75.95±7.18	0.673	0.502
Weight (kg)	73.25±8.36	72.18±9.04	0.672	0.503
Waist circumference (cm)	92.35±5.82	91.68±6.41	0.603	0.548
Hip circumference (cm)	105.72±4.93	104.86±5.27	0.924	0.357
Previous history of pregnancy complications (n(%))	18(30.0)	16(26.7)	0.186	0.666
Gestational hypertension (n(%))	8(13.3)	6(10.0)	0.379	0.538
Diabetes (n(%))	4(6.7)	3(5.0)	0.152	0.697
Preeclampsia (n(%))	6(10.0)	7(11.7)	0.100	0.752
Frequency of breastfeeding (times/day)	6.23±1.45	6.41±1.38	0.686	0.494
Number of Suckling at night (times)	2.35±0.68	2.42±0.71	0.549	0.584
History of abortion/premature (n(%))	21(35.0)	19(31.7)	0.169	0.681

Table 2: Comparison of sex hormone Levels between the two groups patients ($\bar{x}\pm s$)

	treatment group (n=60)		comparison group(n=60)		t	P
	before treatment	after treatment	before treatment	after treatment		
FSH(mIU/ml)	5.50±1.28	5.62±1.35	5.55±1.98	5.48±1.87	0.592	0.555
LH(mIU/ml)	10.24±2.87	7.83±2.15	9.68±3.14	9.42±2.76	3.210	0.002
LH/FSH	1.86±0.48	1.42±0.38	1.74±0.55	1.71±0.49	3.524	0.001
P(mmol/L)	0.82±0.38	1.15±0.42	0.79±0.41	0.85±0.39	3.850	<0.001
T(ng/mL)	0.74±0.28	0.51±0.19	0.71±0.31	0.68±0.27	3.762	<0.001
SHBG(IU/ml)	44.28±8.35	58.64±9.72	46.13±9.08	47.95±8.86	6.148	<0.001
AMH(ng/mL)	7.79±3.02	6.35±2.58	7.56±3.18	7.42±3.05	2.042	0.043

It is suggested that therapeutic intervention can significantly improve lipid metabolism disorders, hyperuricemia, insulin resistance and vitamin D deficiency in patients with PCOS. See Table 3.

Comparison of inflammatory markers

The comparison of inflammatory markers between the two groups of patients before treatment showed that there were no statistically significant differences in hs-CRP, IL-6, TNF- α , WBC, complement C3 and complement C4 ($P>0.05$), and the baselines were comparable. after treatment, the treatment group hs-CRP decreased from (8.42±2.15) mg/L to (3.15±1.08) mg/L ($t=16.824$, $P<0.001$). IL - 6 by pg/mL (12.57 + 3.24) to (6.84 + 2.15) pg/mL ($t = 11.362$, $P < 0.001$), the TNF

alpha by pg/mL (15.68 + 4.32) to (9.46 + 3.08) pg/mL ($t = 9.185$, $P < 0.001$).

The WBC by (7.85 + 1.46) $\times 10^9 / L$ fell to (6.12 + 1.15) $\times 10^9 / L$ ($t = 7.284$, $P < 0.001$), the C3 by g/L (1.35 + 0.28) fell to 1.08 + / - 0.19 g/L ($t = 6.842$, $P < 0.001$). Complement C4 decreased from (0.28±0.08) g/L to (0.22±0.06) g/L ($t=4.862$, $P<0.001$), and the differences were statistically significant. See Table 4.

Clinical outcomes

There was no statistically significant change in each index after comparison group before treatment ($P > 0.05$). The intergroup comparison showed that the ovulation rate and quality of life score of the after Treatment group were significantly higher than those of the comparison group ($P < 0.001$).

Table 3: Comparison of metabolic biochemical indicators between two groups of PCOS patients ($\bar{x}\pm s$)

	Treatment group (n=60)		Comparison group (n=60)		t	P
	Before treatment	After treatment	Before treatment	After treatment		
TC(mmol/L)	4.80±1.34	4.21±1.18	4.75±1.29	4.68±1.25	2.248	0.026
TG(mmol/L)	2.01±1.52	1.35±0.86	1.95±1.44	1.88±1.31	2.542	0.012
HDL(mmol/L)	1.34±0.27	1.76±0.48	1.36±0.31	1.38±0.35	4.872	<0.001
LDL(mmol/L)	2.79±0.74	2.23±0.51	2.82±0.71	2.75±0.68	4.785	<0.001
UA(μ mol/L)	371.32±75.44	298.45±58.63	368.50±72.18	362.75±70.52	5.243	<0.001
25-OH-D3(ng/ml)	58.96±14.81	71.24±16.52	57.83±15.20	59.41±15.87	4.165	<0.001
FPG(mmol/L)	4.95±0.55	4.72±0.42	5.02±0.61	4.98±0.58	3.267	0.001
FINS(μ IU/mL)	56.50±30.41	28.36±18.52	54.80±28.75	52.15±26.93	5.136	<0.001
HOMA-IR	2.11±0.79	1.63±0.45	2.08±0.82	1.98±0.75	2.942	0.004

Table 4: Comparison of inflammatory markers between the two groups of patients ($\bar{x}\pm s$)

	Treatment group (n=60)		Comparison group (n=60)		t	P
	Before treatment	After treatment	Before treatment	After treatment		
hs-CRP(mg/L)	8.42±2.15	3.15±1.08	8.26±2.24	7.98±2.13	13.862	<0.001
IL-6(pg/mL)	12.57±3.24	6.84±2.15	12.73±3.18	12.45±3.06	10.542	<0.001
TNF- α (pg/mL)	15.68±4.32	9.46±3.08	15.92±4.15	15.73±4.28	8.936	<0.001
WBC($\times 10^9$ /L)	7.85±1.46	6.12±1.15	7.78±1.52	7.65±1.48	5.842	<0.001
Complement C3(g/L)	1.35±0.28	1.08±0.19	1.33±0.31	1.29±0.28	4.526	<0.001
Complement C4(g/L)	0.28±0.08	0.22±0.06	0.27±0.09	0.26±0.08	2.985	0.003

Table 5: Comparison of clinical outcomes between the two groups of patients ($\bar{x}\pm s$)

	Treatment group (n=60)		Comparison group (n=60)		t	P
	Before treatment	After treatment	Before treatment	After treatment		
Ovulation rate (n(%))	12(20.0)	47(78.3)	10(16.7)	18(30.0)	25.846	<0.001
Ferriman-Gallwey score	16.45±4.28	9.32±3.15	15.87±4.15	14.26±4.03	7.254	<0.001
PCOSQ	58.62±8.47	78.85±9.36	57.93±9.12	61.24±9.58	10.847	<0.001
Volume of the left ovary (V/mL)	12.15±2.73	8.42±2.15	12.37±2.86	11.85±2.64	7.862	<0.001
Volume of the right ovary (V/mL)	13.21±2.94	8.95±2.38	13.15±2.79	12.68±2.71	8.125	<0.001
Number of antral follicles (in number)	15.71±3.75	9.43±2.62	15.64±3.64	14.58±3.47	8.936	<0.001

The Ferriman-Gallwey hirsutism score, volume of the left ovary, volume of the right ovary and the number of antral follicles were all significantly lower than those of the comparison group ($P < 0.001$), suggesting that therapeutic intervention can significantly improve ovulation function, clinical manifestations of hyperandrogenism, ovarian morphology and quality of life in patients with PCOS. See Table 5.

Discussion

This study systematically assessed the integrated regulatory effects of the Yumu acupoint electroacupuncture protocol on the hormone-metabolism-inflammation network in patients with polycystic ovary syndrome (PCOS). The findings confirmed that acupuncture significantly ameliorated hyperandrogenemia, insulin resistance,

lipid metabolism disorders, and chronic low-grade inflammation, thereby increasing the ovulation rate to 78.3%. This multi-dimensional intervention for PCOS provides robust clinical evidence. The study results indicate that post-treatment levels of luteinizing hormone (LH), the LH/follicle-stimulating hormone (FSH) ratio, total testosterone, and anti-Müllerian hormone (AMH) in the acupuncture group were significantly lower than those in the sham acupuncture comparison group, while sex hormone-binding globulin (SHBG) and progesterone levels were significantly elevated. The comprehensive improvement of these sex hormones represents the core manifestation of acupuncture's regulatory effect on the hypothalamic-pituitary-ovarian (HPO) axis function. The observed reduction in the LH/FSH ratio aligns with findings from previous research. The meta-analysis conducted by Jo et al.⁵ demonstrated that acupuncture significantly decreased the weighted mean difference of LH, while exerting no significant effect on FSH levels. This aligns with the present study's findings, which also indicate a lack of statistical significance in FSH changes. This selective modulation may be attributed to acupuncture's activation of hypothalamic GnRH neurons via κ -opioid receptors, which reduces pulse frequency and corrects the characteristic high-frequency LH secretion pattern observed in patients with PCOS². Notably, the absolute reduction in LH and the LH/FSH ratio in this study exceeded the effect sizes reported by Jo et al. This discrepancy may be due to the use of 2-15 Hz dense-wave electroacupuncture in the current study, as opposed to the 2-100 Hz variable-frequency stimulation employed in previous studies. The continuous application of low-frequency components (2 Hz) may more effectively engage the vagal-adrenal axis anti-inflammatory pathway, thereby indirectly enhancing insulin sensitivity in the hypothalamus and restoring the sensitivity of GnRH neurons to negative feedback⁹. The selection of acupoints for Yu Mu follows the principles of anterior and posterior acupoint matching and corresponding to internal organs. It may produce a stronger segmental regulatory effect through somal-sympathetic nerve-visceral reflexes, directly acting on the T12-L2 spinal cord segment. This segment

simultaneously controls the uterus, ovaries, and adrenal glands, achieving an integrated effect within the same segment¹¹. All the people included in this study were obese PCOS with a BMI of ≥ 28.0 kg/m². However, the studies included by Jo et al.⁵ had higher heterogeneity and no phenotype limitation. Central insulin resistance was more severe in obese patients and they might be more sensitive to acupuncture regulation³.

The reduction in total testosterone observed in this study was significantly greater than the effect previously reported for acupuncture monotherapy⁶, yet it was comparable to the outcomes of the study by Muharam et al.⁸, which combined electroacupuncture with metformin. The efficacy of this combined treatment approach may be intricately linked to the specific selection of acupoints utilized in this study. The Guanyuan acupoint is strategically located along the ilioventral nerve and the reproductive femoral nerve. Its stimulation is capable of activating the L1-L2 segments of the spinal cord and inhibiting the activity of CYP17A1, a crucial enzyme involved in androgen synthesis within ovarian membrane cells, via sympathetic nerve fibers⁷. Additionally, the Zusanli acupoint, known for being a convergence point of multiple meridians, can enhance the expression of SHBG mRNA in the liver, thereby increasing testosterone-binding capacity and reducing the free androgen index (FAI)¹². In this study, SHBG levels increased by 32.5%, which significantly exceeds the average increase of 12-18% reported in previous acupuncture studies.

The underlying mechanism may be associated with the enhancement of phosphorylation in the AMPK signaling pathway and the promotion of transcriptional activity of peroxisome proliferator-activated receptor γ (PPAR γ) in hepatocytes due to electroacupuncture stimulation¹³. Although the observed reduction in anti-Müllerian hormone (AMH) levels was statistically significant ($P < 0.05$), the effect size was relatively modest, akin to the approximately 15-20% reduction in AMH reported by Legro et al.¹⁴ with the use of thiazolidinedione drugs, yet lower than the 30-40% reduction achieved through laparoscopic ovarian drilling (LOD). This suggests that acupuncture primarily inhibits the excessive recruitment of preantral and small antral follicles

rather than directly disrupting the ovarian stroma, resulting in a comparatively mild decrease in AMH levels. The comparison group's AMH levels exhibited an unexpected slight decline, which, although not statistically significant, may indicate the presence of a placebo effect or natural fluctuations during the observation period. This phenomenon was also noted in the randomized controlled trials conducted by Stener-Victorin et al.¹⁵, underscoring the importance of incorporating placebo controls in such studies.

The comprehensive enhancement of metabolic indicators observed in this study represents a pivotal finding. Notably, the reduction in HOMA-IR and fasting insulin levels surpasses those reported in studies focusing solely on acupuncture or in combination studies, such as that by Muharam⁷. This marked improvement may be attributed to the low-frequency stimulation at 2 Hz, which can trigger the release of β -endorphin, enhance tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1) in skeletal muscle, and facilitate GLUT4 translocation¹⁶. Additionally, the 15 Hz high-frequency component appears to improve hepatic insulin sensitivity by upregulating adiponectin and downregulating leptin resistance¹⁷. The study exclusively included participants with a BMI of ≥ 28 kg/m². In obese patients with polycystic ovary syndrome (PCOS), peripheral insulin resistance predominantly occurs in skeletal muscle and adipose tissue, which are precisely the primary targets of acupuncture. The study reported a 32.8% reduction in triglycerides (TG), a 20.1% decrease in low-density lipoprotein (LDL), a 31.3% increase in high-density lipoprotein (HDL), and a modest reduction in total cholesterol (TC). This lipid-lowering pattern, as opposed to cholesterol-lowering, aligns with the findings of a network meta-analysis of 12 acupuncture lipid-lowering randomized controlled trials (RCTs) conducted by Yang et al.¹⁸. The study demonstrated that acupuncture was more effective in reducing triglyceride (TG) levels compared to total cholesterol (TC) levels. Mechanistically, stimulation of the Zusanli acupoint appears to activate the AMPK-ACC-CPT1 pathway, thereby promoting the β -oxidation of fatty acids. Furthermore, stimulation of the Guanyuan acupoint is transmitted via the vagus nerve to the nucleus

solitarius (NTS), leading to the inhibition of the excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis and a subsequent reduction in cortisol-driven lipolysis. Notably, this study observed a 19.6% decrease in uric acid levels, an effect that has been largely overlooked in previous acupuncture studies on polycystic ovary syndrome (PCOS). Given the reciprocal relationship between hyperuricemia and insulin resistance, acupuncture may regulate uric acid levels by enhancing the function of the renal URAT1 transporter and modulating intestinal uric acid metabolic flora.

This finding suggests a novel target for metabolic intervention in PCOS¹⁹.

The observed 20.8% increase in 25-hydroxyvitamin D3 (25-OH-D3) in this study was an unanticipated outcome. Vitamin D deficiency is prevalent in 67-85% of individuals with polycystic ovary syndrome (PCOS) and is independently correlated with insulin resistance and hyperandrogenemia²⁰. Conventionally, acupuncture is not considered to directly augment vitamin D levels. Nonetheless, electroacupuncture stimulation may enhance the metabolic efficiency of vitamin D by upregulating the activity of CYP27B1 hydroxylase in the kidneys, thereby facilitating the conversion of 25(OH)D3 to its active form, 1,25-dihydroxyvitamin D3 (1,25(OH)2D3)²¹. The randomized controlled trial conducted by Thys-Jacobs et al.²² demonstrated that the reduction in the homeostasis model assessment of insulin resistance (HOMA-IR) achieved through the combined intervention of vitamin D3 supplementation and acupuncture (38%) was significantly greater than that achieved with vitamin D alone (22%), indicating a synergistic effect. A notable finding of this study is the substantial reduction in inflammatory markers. High-sensitivity C-reactive protein (hs-CRP) levels decreased from 8.42 to 3.15 mg/L, interleukin-6 (IL-6) levels decreased by 45.6%, and tumor necrosis factor-alpha (TNF- α) levels decreased by 39.6%. The effect sizes for these reductions were all greater than 0.8, indicating a large effect. In contrast, metformin treatment over a period of six months resulted in only an approximate 25% reduction in hs-CRP levels. While thiazolidinedione drugs exhibit potent anti-inflammatory effects, their use is associated with adverse effects such as weight gain and edema. In

this study, levels of Complement C3 and C4 decreased by 20.0% and 21.4%, respectively, representing the first systematic report within the context of polycystic ovary syndrome (PCOS) acupuncture research. Activation of the complement system is a critical aspect of chronic low-grade inflammation in PCOS, with C3a and C4a directly affecting ovarian granulosa cells by inhibiting aromatase activity and impeding the conversion of androgens to estrogens. The observed reduction in complement levels corresponded with a decrease in testosterone and an increase in progesterone. The benefits of acupuncture for ovulation induction include its non-invasive nature, high repeatability, and concurrent improvements in metabolism and inflammation, which collectively reduce the risk of miscarriage following conception. Additionally, the reduction in ovarian volume and the decrease in the number of antral follicles indicate that acupuncture may reverse the morphological changes associated with polycystic ovaries. The substantial enhancement in quality of life encompasses five dimensions: mood, body hair, weight, infertility, and menstruation. Psychological stress aggravates PCOS symptoms by activating the HPA axis, while acupuncture reduces cortisol levels, upregulates 5-HT and β -endorphins, and directly improves emotional states.

This study employed a prospective randomized, sham-controlled trial design. Despite the establishment of concurrent sham controls, potential biases were minimized through rigorous randomization and allocation concealment procedures. However, as with all clinical trials, the possibility of unmeasured confounders cannot be entirely excluded. Although the baseline comparability analysis indicated no statistically significant differences, the single-center nature and specific inclusion criteria may limit generalizability to other PCOS phenotypes. Furthermore, while fixed parameters were utilized in this study, individual variations in pain threshold, skin impedance, and subcutaneous fat thickness among patients could have resulted in inconsistent levels of effective stimulation.

Study strengths and limitations

This study's primary strengths lie in its rigorous prospective randomized sham-controlled design with computer-generated stratified randomization and allocation concealment, which substantially reduces selection and performance bias. Our use of a standardized electroacupuncture protocol—encompassing fixed acupoint selection, consistent stimulation parameters (2-15Hz), and clearly defined sham procedures—addresses a critical limitation of prior acupuncture research that suffered from significant heterogeneity. By exclusively enrolling obese PCOS patients, we created a phenotypically homogeneous cohort, enhancing internal validity and allowing more precise evaluation of treatment effects in this metabolically vulnerable subgroup. The comprehensive biomarker panel, including novel assessments of uric acid metabolism, vitamin D status, and complement C3/C4, provides mechanistic insights beyond conventional endpoints. Nevertheless, several limitations warrant consideration. First, the single-center design and modest sample size limit generalizability to diverse ethnic populations and healthcare systems. Second, the 16-week intervention duration, while sufficient for detecting biochemical improvements, precludes assessment of long-term reproductive outcomes such as pregnancy and live birth rates. Third, our fixed acupuncture parameters, though enhancing reproducibility, may not represent optimal individualized treatment. Fourth, although we implemented a sham control, nonspecific physiologic effects cannot be entirely excluded. Finally, the absence of long-term follow-up and cost-effectiveness analysis restricts understanding of sustained benefits and implementation feasibility.

Conclusion

This study substantiates that the electroacupuncture regimen targeting Shu Mupei acupoints systematically ameliorates hormonal imbalances, metabolic disorders, chronic inflammation, and clinical outcomes in patients

with obesity-related polycystic ovary syndrome (PCOS). The magnitude of its effects surpasses those reported in most prior studies concerning

metabolic and inflammatory markers, potentially due to the synergistic effects of Shu Mupei acupoints, the careful selection of obesity phenotypes, and the implementation of an adequately prolonged treatment course.

Conflict of interests

The authors declared no conflict of interest

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