Effects of electroacupuncture and Chinese kidney-nourishing medicine on polycystic ovary syndrome in obese patients

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Abstract

OBJECTIVE: To explore the effect of electroacupuncture and Chinese kidney-nourishing medicine on insulin (INS), adiponectin (APN), leptin (LEP), and glucolipid metabolism of obese patients with polycystic ovary syndrome (PCOS).

METHODS: Sixty-seven obese PCOS patients were randomly divided into two groups. Thirty-three patients in the acupuncture-medicine group were treated three times a week with electroacupuncture at the Tianshu (ST 25), Zhongwan (CV 12), Qihai (CV 6), Sanyinjiao (SP 6), Geshu (BL 17), and Ciliao (BL 32) acupoints. They also took the Chinese drug, Tiankui capsule, for 3 months as a course of treatment. Point-taking and treatment in the electroacupuncture group of 34 patients was the same as those in the acupuncture-medicine group. We observed and compared the changes in the obesity-related indexes of body weight (BW), body mass index (BMI), and waist-hip ratio (WHR), as well as fasting plasma glucose (FPG), fasting insulin (FINS), APN, and LEP.

RESULTS: BW, BMI, WHR, and FINS decreased and insulin sensitivity index (ISI) and APN were higher in the acupuncture-medicine group than in the electroacupuncture group (P<0.01). There was no obvious difference in LEP between the two groups (P>0.05).

CONCLUSION: Acupuncture combined with medicine is better than just electroacupuncture for obese PCOS patients by improving obesity-related indexes, insulin sensitivity, and APN level. This indicates that acupuncture-medicine therapy is worth clinical popularization.

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Key words: Electroacupuncture; Reinforcing kidney; Polycystic ovary syndrome; Obesity; Insulin; Adiponectin; Leptin

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common gynecological disease with reproductive dysfunction, endocrine disorder, and abnormal glucolipid metabolism. It...
is characterized by complex causes of disease and diversified clinical manifestations. PCOS, the main cause for menstrual disorder and infertility in women of childbearing age, is manifests clinically as oligomenorrhea or amenorrhea, infertility, obesity, hirsutism, acne, or psychosis. Obesity, the most common complication of PCOS, is the driving force and cause of other metabolic diseases. More than 50% of PCOS patients are overweight or obese and most suffer from central (abdominal) obesity. Patients with abdominal obesity easily contract glucolipid metabolic disorder and cardiovascular-diseases. Moreover, the endocrine function of female patients is more easily affected. Obesity can promote PCOS and eventually disrupt endocrine and metabolic function. Appropriately reducing the body weight of obese PCOS patients can improve endocrine disorder to restore ovulatory function. Therefore, the key to treatment of obese PCOS patients lies in finding a way to reduce obesity, and improve lipid metabolism and endocrine disorder.

Based on the curative effects of Chinese medicine and acupuncture on obesity and PCOS in previous research, we compared electroacupuncture combined with Chinese kidney-nourishing medicine (Tiankui capsule) with normal electroacupuncture. We observed their effects on obese indexes, insulin sensitivity, adiponectin, leptin, and other lipid metabolism measures in obese PCOS patients and explored the mechanism.

METHODS

General data
Sixty-seven patients at a PCOS clinic in the Shanghai Institute of Acupuncture, Moxibustion and Meridians from July 2010 to December 2011 were randomly divided into two groups. The age of the 33 patients in the acupuncture-medicine group was 17-39 years and (25±6) years on average. Their illness course was 1-20 years and (7±4) years on average. Their body weight was 60-95 kg and (76±9) kg on average. The age of the 34 patients in the electroacupuncture group was 17-37 years and (25±5) years on average. Their illness course was 1-20 years and (7±4) years on average. Their body weight was 64-99 kg and (77±9) kg on average. There was no statistical difference in general data between the two groups (P>0.05).

Diagnostic standards
Diagnostic standards in Western Medicine: PCOS was diagnosed according to the Rotterdam criteria issued by the European Human Reproduction and Embryology Research Center and the American Society for Reproductive Medicine in January 2003. Patients conforming to two of the following indexes were diagnosed as suffering from PCOS: (a) oligoovulation or no ovulation, (b) clinical manifestations of hyperandrogenemia and (or) hyperandrogenism (such as hirsutism and acne), and (c) ≥12 small follicles, 2-9 mm in diameter, in both ovaries, and (or) ovarian volume ≥10 mL. Patients with congenital adrenal hyperplasia, thyroid disease, androgen secreting tumors, or Cushing’s syndrome were excluded.

Obesity was diagnosed according to the Asian adult obese index of Body Mass Index (BMI) ≥25 stipulated by WHO in 2000. BMI=body weight (kg)/height (m)². Standards for inclusion: (a) Patients conforming to PCOS diagnostic criteria in Western Medicine and syndrome differentiation in TCM. (b) Patients with no secondary PCOS, namely, no other systemic diseases. (c) Female patients 14-45 years old. (d) Patients accepting no other treatments 3 months before treatment and during treatment. (e) Patients voluntarily participating in the study and signing a participation release agreement passed by the ethical evaluation of Yueyang Hospital of TCM Combined with Western Medicine affiliated to Shanghai University of TCM.

Therapies
Acupuncture-medicine group:
Treatment with electroacupuncture: there were two groups of main acupoints. Group I, included bilateral acupoints Sanyinjiao (SP 6), Xuehai (SP 10), Zusani (ST 36), Tianshu (ST 25), Daheng (SP 15), Daimai (GB 26), Dahe (KI 12), Zigong (EX-CA 1), Taixi (KI 3), Zhongwan (CV 12), Qihai (CV 6), and Guanyuan (CV 4). Group II, included bilateral acupoints Sanyinjiao (SP 6), Taixi (KI 3), Yinlingquan (SP 9), Ganshu (BL 18), Geshu (BL 17), Shen shu (BL 23), Pishu (BL 20), and Ciliao (BL 32). The bilateral acupoints Hegu (LI 4), Gongsun (SP 4), Fenglong (ST 40) and Diji (SP 8) were added for
phlegm blockage and blood stasis. Bilateral acupoints Zhigou (TE 6), Quchi (LI 11), Taiyong (LR 3), and Yanglingquan (GB 34) were added for damp-heat accumulation.

For treatment with electroacupuncture, needles, 0.28-0.32 mm in diameter and 40-75 mm in length, were inserted into acupoints with the uniform reinforcing-reducing method. After needle sensation, needles at the bilateral acupoints Tianzhu (ST 25), Sanyinjiao (SP 6), Zhongwan (CV 12), and Qihai (CV 6), or bilateral acupoints Pishu (BL 20), Shenshu (BL 23), Ciliao (BL 32), and Sanyinjiao (SP 6) were connected to a G6805II electric stimulator with continuous wave, 2 Hz frequency and an electrical current tolerable to patients. The needle was retained for 40 min. The rest of the acupoints were manipulated once every 10 min. Acupuncture was performed 3 times a week for a menstrual cycle or a month as a course of treatment. After three courses of treatment, the therapeutic effect was observed.

Treatment with Chinese medicine: Tiankui capsule, developed by Obstetric and Gynecological Hospital affiliated to Fudan University, consists of Dihuang (Radix Rehmanniae), Zhihu (Rhizoma Anemarrhenae), Xianlingpi (Herba Epimedium), Huzhang (Polygonum Cauplidatum), Mabiancao (Verbenae), Danggui (Radix Angelicae Sinensis), Taoren (Semem Paeoniae), Huangjing (Rhizoma Polygonati), Shichangpu (Herba Epimedium), Guiban (Carapax et Plastrum Testudinis), and Buguzhi (Fructus Polonaceae). Tiankui Capsule was orally taken, six capsules a time, in the morning and evening, for three months.

Electroacupuncture group: Acupoint selection, manipulation, and treatment course were the same as in the acupuncture-medicine group.

Indexes and methods for observation
The indexes of Body Weight (BW), Body Mass Index (BMI), and Waist Hip Rate (WHR) were observed before and after treatment in the two groups. BMI=weight (kg)/height (m)². WHR=WC/HC. WC is waist circumference (cm) at the navel when the patient is upright. HC is hip circumference (cm) around the hip femoral trochanter.

Fasting insulin (FINS) and fasting plasma glucose (FPG) in the serum were observed before and after treatment in the two groups. FINS was determined with a radioimmunooassay kit from Beijing North Biotechnology Institute. FPG was determined with a glucose assay kit from Shanghai Rongsheng Biotechnology Co., Ltd. (Shanghai, China).

Adiponectin (APN) level in the serum was observed before and after treatment in the acupuncture-medicine group. APN was determined with a human adiponectin ELISA kit from American RD Company American R&D Systems Inc. (Minneapolis, MN, USA).

Statistical analysis
SPSS 15.0 statistical software (SPSS Inc., Wacker Drive, Chicago, IL, USA) was used. Measurement data conforming to a normal distribution are expressed with mean ± standard deviation (x±s). Measurement data not conforming to a normal distribution are expressed with the median (Q1-Q3). Group t-test was used for the difference between the two groups. Paired t-test was used for the difference before and after treatment in the same group. A non-parameter test was used for data not in a normal distribution. There was a statistical difference while P<0.05.

RESULTS
Patient withdrawal
During observation, two patients withdrew from the electroacupuncture group and were ultimately excluded from statistics. No patients withdrew from the acupuncture-medicine group.

Comparison of BW, BMI, and WHR before and after treatment
Table 1 shows that there was a statistical difference (P<0.01) in BW, BMI, and WHR before and after treatment in the acupuncture-medicine group and in BW and BMI in the electroacupuncture group (P<0.05). The BW, BMI, and WHR in the acupuncture-medicine group were lower than those in the electroacupuncture group (P<0.01, P<0.01, and P<0.05, respectively).

Comparison of FPG, FINS, and ISI before and after treatment
Table 2 shows that there was a statistical difference (P<0.01) in FPG, FINS, and ISI before and after treatment in the acupuncture-medicine group. There was no statistical difference (P>0.05) in FINS and ISI before and after treatment in the electroacupuncture group. FINS, and ISI improved more in the acupuncture-medicine than the electroacupuncture group (P<0.01). No statistical difference was found in FPG between the two groups (P>0.05).

Comparison of APN and LEP before and after treatment
There was a much higher APN after treatment in the acupuncture-medicine (P<0.01) and electroacupuncture groups (P<0.05) (Table 3). There was no obvious difference (P>0.05) in LEP before and after treatment in the two groups.
**DISCUSSION**

Obese PCOS is clinically characterized by reproductive dysfunction, endocrine disorder, and abnormal glucose-lipid metabolism. In recent years, lifestyle changes and stress have raised its incidence to 7%-8% in women of childbearing age. The complex pathogenesis of PCOS and lack of precise theoretical basis for its pathogenic hypotheses make effective therapy difficult to develop. Clinical and experimental research have discovered that PCOS affects women’s fertility and is closely related to type II diabetes, hyperlipemia, hypertension, cardiovascular disease and metabolic syndrome, and possibly increases the risk of contracting endometrial carcinoma and breast cancer. Of PCOS patients, 50%-70% are overweight or obese making obesity the most common symptom. Most patients exhibit abdominal obesity. PCOS patients with abdominal obesity often have glucose-lipid metabolism disorders, which lead to reproductive problems and aggravate the ovaries to promote the development of PCOS. Therefore, obese PCOS patients are more likely to have relevant clinical symptoms than those who are not obese. Western treatment of PCOS can promote ovulation, normalize endocrine metabolism, and improve clinical symptoms. However, drug dependence or relapse after disuse of drugs and toxic side effects of oral medication greatly limit the clinical use of Western Medicine. TCM including acupuncture can have certain curative effects on PCOS. However, it takes longer for Chinese medicine or acupuncture to take effect than Western Medicine in the treatment of PCOS. Therefore, it is difficult for patients to persist on treatment because of its slow effect and potential for relapse. Nevertheless, acupuncture combined with Chinese medicine has advantages over each alone. The Handbook of Prescription for Emergencies states that, “Those who apply acupuncture without moxibustion or moxibustion without acupuncture are not good doctors. Those who know both medicine and acupuncture are good doctors.” Therefore, exploring whether acupuncture plus medicine takes effect more quickly with fewer side effects than each alone is important in directing the clinical treatment of obese PCOS.

According to its clinical manifestations, PCOS can be attributed to "amenorrhea," "infertility," "masses in the abdomen," or "obesity" in TCM. Obese PCOS patients often have kidney deficiency and phlegm-dampness constitutions. A deficiency of kidney essence

### Table 1 Comparison of BW, BMI, and WHR before and after treatment (x ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>BW (kg)</th>
<th>BMI</th>
<th>WHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture combined with chinese herb therapy group</td>
<td>33</td>
<td>Before treatment</td>
<td>75.6±8.8</td>
<td>29.0±3.5</td>
<td>0.9±0.7</td>
</tr>
<tr>
<td>Pure electroacupuncture</td>
<td>32</td>
<td>Before treatment</td>
<td>77.2±9.4</td>
<td>29.5±3.5</td>
<td>0.9±0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>67.7±10.6b</td>
<td>25.9±3.9b</td>
<td>0.9±0.7b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>77.0±9.4c</td>
<td>29.4±3.6c</td>
<td>0.9±0.8c</td>
</tr>
</tbody>
</table>

Notes: BW: body weight; BMI: body mass index; WHR: waist-hip ratio; PCOS: polycystic ovary syndrome. "<0.05, compared with the datum before treatment in the same group; "<0.01, "<0.05, compared with the datum in the electroacupuncture group.

### Table 2 Comparison of FPG, FINS, and ISI before and after treatment (x ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>FPG (mmol/L)</th>
<th>FINS (mU/L)</th>
<th>ISI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture combined with chinese herb therapy group</td>
<td>22</td>
<td>Before treatment</td>
<td>4.5422±0.7867</td>
<td>31.5327±6.5822</td>
<td>0.0077±0.0029</td>
</tr>
<tr>
<td>Pure electroacupuncture</td>
<td>21</td>
<td>Before treatment</td>
<td>4.4429±0.9179</td>
<td>33.8438±11.1318</td>
<td>0.0076±0.0026</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>4.0263±0.7003</td>
<td>21.3341±4.5388</td>
<td>0.0129±0.0054</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>4.0563±0.7077</td>
<td>30.7257±6.6543</td>
<td>0.0086±0.0021</td>
</tr>
</tbody>
</table>

Notes: FPG: fasting plasma glucose; FINS: fasting insulin; ISI: insulin sensitivity index; PCOS: polycystic ovary syndrome. "<0.01, compared with the datum before treatment in the same group; "<0.01, compared with the datum in the electroacupuncture group.

### Table 3 Comparison of APN and LEP before and after treatment (x ±s)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>APN (µg/mL)</th>
<th>LEP (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture combined with chinese herb therapy group</td>
<td>22</td>
<td>Before treatment</td>
<td>5.1±2.7</td>
<td>5.4±2.2</td>
</tr>
<tr>
<td>Pure electroacupuncture</td>
<td>21</td>
<td>Before treatment</td>
<td>5.3±2.1</td>
<td>5.9±2.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>8.3±2.8a</td>
<td>6.0±1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>6.6±2.4c</td>
<td>6.8±1.8</td>
</tr>
</tbody>
</table>

Notes: PCOS: polycystic ovary syndrome; APN: adiponectin; LEP: leptin. "<0.01, "<0.05, compared with the datum before treatment in the same group; "<0.05, compared with the datum in the electroacupuncture group.
makes it difficult for the ovum to develop. A deficiency of kidney Yang cannot warm spleen Yang, causing an obstructed circulation of Qi and blood and making water accumulate into phlegm. A deficiency of kidney-Yin cannot nourish the uterus, causing fewer menses.9 Phlegm-dampness is not only the metabolic product of spleen deficiency and kidney deficiency, but also the cause of Qi stagnation. The stagnation of phlegm-dampness causes a rough flow of Qi and a disorder of Qi transformation in triple energizer. Prescription for Saving Lives says that a "Blockage of Qi in triple energizer and obstruction of vessels make water accumulate into phlegm, leading to various diseases." This situation further causes imbalance of Yin and Yang. Stagnation of Qi, blood, and phlegm-dampness in the Chong and conception vessels make it difficult for the ovum to be discharged, causing oligomenorrhea, amenorrhea, and infertility. Stagnation of phlegm-dampness causes rough circulation of Qi and blood, forming masses in the abdomen and polycystic ovaries. The pathogenesis for obese PCOS mainly lies in kidney deficiency and stagnation of phlegm-dampness in the uterus. Therefore, this disease should be treated mainly by nourishing kidney, strengthening spleen, dissolving phlegm, and removing dampness. In addition, treatment should soothe liver and promote blood circulation.10,12 Tiankui capsule can nourish kidney, strengthen spleen, remove dampness, dissolve phlegm, promote blood circulation, and eliminate blood stasis. The ingredients Xianlingpi (Herba Epime-dium), Huangjing (Rhizoma Polygonati), Buguzhi (Fructus Poriae), and Guiban (Carapax et Plastrum Testudinis) can warm and nourish kidney Yang, enrich kidney-Yin, and regulate the Chong and conception vessels. These ingredients have a similar effect as sex hormones and can promote gonadal (ovarian) function. The adjunct ingredients Danggui (Radix Angelicae Sinensis), Taoren (Semem Persicae), Dihuang (Radix Rehmanniae), Zhimu (Rhizoma Anemarrhenae), Huizhang (Polygonum Cuspidatum), Mabiancao (Verbena), and Shichangpu (Rhizoma Acori Graminei) can promote blood circulation, regulate menstruation, regulate Qi flow, generate blood, clear away heat, eliminate swelling, dissolve phlegm, remove blood stasis, lower blood glucose and lipids, and regulate uterine function. Tiankui capsule can promote microcirculation and endocrine function of the ovary and improve glucolipid metabolism of obese PCOS patients.13,15 Electro-acupuncture at Zhongwan (CV 12), Qihai (CV 6), and Guanyuan (CV 4) can regulate the Chong and conception vessels, warm kidney Yang, and generate blood. Electro-acupuncture at Taixi (KI 3) and Dahe (KI 12) can nourish kidney-essence to regulate menstruation. Electro-acupuncture at Sanyinjiao (SP 6) can dredge the channels of the kidney, liver, and spleen. Electro-acupuncture at Xuehai (SP 10), Daheng (SP 15) and Yinlingquan (SP 9) can invigorate spleen, remove dampness, and dissolve phlegm. Electro-acupuncture at Zusanli (ST 36) and Tianshu (ST 25) can regulate Qi flow, remove dampness, dissolve phlegm and reduce lipids. Electro-acupuncture at Daimai (GB 26) can regulate all channels. Electro-acupuncture at Zigong (EX-CA1) can enrich Qi and blood, promote ovulation, and regulate menstruation. Electro-acupuncture at Ganshu (BL 18), Geshu (BL 17), Shenshu (BL 23), Pishu (BL 20), and Ciliao (BL 32) can regulate functional activities of Qi in internal organs. In addition to the main acupoints, Hegu (LI 4), Gongsun (SP 4), Fenglong (ST 40), and Diji (SP 8) can be added for phlegm stagnation and blood stasis to further strengthen the effect of dissolving phlegm and removing blood stasis. Zhigou (TE 6), Quchi (LI 11), Taichong (LR 3), and Yanglingquan (GB 34) can be added for damp-heat accumulation to soothe liver and clear collateral vessels. All these acupoints used together can enrich kidney essence, regulate the Chong and conception vessels, and nourish the uterus. In this study, we found that Chinese medicine plus electroacupuncture can regulate Yin, Yang, Qi, and blood; normalize kidney function, the Chong and conception vessels, and the uterus; promote ovarian micro-circulation and endocrine function; improve glucolipid metabolism; and reduce the body weight of obese PCOS patients.

Obese PCOS patients often have insulin resistance (IR) and hyperinsulinemia (HI). Insulin resistance, particularly ovarian local IR, will cause hyperandrogenism and inhibit follicular maturation.14 HI inhibits the synthesis of liver sex hormones and globulin, promotes the biological activity of free testosterone and inhibits follicular maturation to cause infertility.15 IR is a very important link in the development of obese PCOS. APN is closely related to IR and has an important influence on IR pathogenesis of obese PCOS. APN is a new method to treat obese PCOS and probe its pathogenesis. APN, a plasma protein secreted by adipose tissue, can affect the metabolism of blood glucose and lipids, promote the transformation of preadipocytes into mature adipocytes, enhance insulin sensitivity, eliminate inflammation, resist atherosclerosis, and plays an important role in the occurrence and development of IR.18,19 APN has an antagonistic effect on IR.20 The normal concentration of APN in non-obese healthy patients is 5–30 μg/mL. An increase in lipids will cause a decrease in APN to increase body weight.21–23 Obesity24–27 and its related diseases (PCOS28–30 and type II diabetes31) reduce APN in the plasma. Therefore, the lower the APN level in obese PCOS patients, the more severe the IR and clinical symptoms.52 This study shows that BW, BMI, and WHR improvement is followed by a decrease in serum FINS level and a significant increase in ISI and APN levels, when treated with electroacupuncture plus medicine. However, the relationship between APN and IR in the pathogenesis of obese PCOS needs to be studied further. This study suggests that acupunc-
tecture plus medicine can increase APN level and reduce insulin resistance in obese PCOS patients to improve signs of abdominal obesity and abnormal glucolipid metabolism.

Leptin (LEP), a protein hormone secreted by fat cells, is encoded by the obese (OB) gene. In addition to regulating diet and metabolism, LEP may stimulate the secretion of growth hormone, prolactin, and other anterior pituitary hormones.\textsuperscript{3,36} This influences the synthesis and secretion of insulin and steroid hormones, leading to obesity, reproductive dysfunction, and metabolic disorder.\textsuperscript{35-37} However, there are different opinions on the relationship of LEP to obesity and PCOS. Once the sensitivity of visceral lipids to insulin declines, lipids are easily decomposed by LEP to create IR.\textsuperscript{38} However, others\textsuperscript{39-42} believe that an increase in LEP may not be closely related to PCOS and is just a factor that influences obesity. An increase in LEP levels in obese PCOS patients may result from obesity. The results of this study show that with an improvement in obesity-related indexes in obese PCOS patients, no obvious difference was observed in LEP levels before and after treatment. This indicates that there is no direct relation between LEP and the pathogenesis of PCOS. The exact relationship between LEP and obese PCOS is to be further confirmed.

This study showed that the improvement of obesity-related indexes, insulin resistance, and adiponectin level in the acupuncture-medicine group was better than that in the electroacupuncture group in the treatment of obese PCOS patients. Therefore, electroacupuncture plus Chinese medicine might originate from the same therapeutic principle. Both methods use TCM theories, methods, formulae and medicines (acupoints) to stimulate the self-regulatory function of human body and gradually normalize nerves, endocrine function, lipid metabolism, and visceral functions. The results of this study also suggest that acupuncture plus medicine can provide more benefits than electroacupuncture alone in the same course of treatment. Therefore, we provided clinical data and a theoretical basis for the treatment of obese PCOS with Chinese medicine and acupuncture.

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