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Complementary Therapy with Traditional Chinese Medicine for Polycystic Ovarian Syndrome

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Abstract

Polycystic ovarian syndrome (PCOS) is a common, heterogeneous, complex, endocrinopathic condition that causes menstrual dysfunction and infertility in women. Traditional Chinese medicine (TCM) has been widely used for PCOS in Far-East countries for thousands of years. There are significant advantages in treating PCOS with TCM. This chapter aims to investigate the current developments in TCM therapy for PCOS.

Keywords: complementary and alternative therapy, traditional Chinese medicine, polycystic ovarian syndrome, acupuncture, moxibustion

1. Introduction

1.1. Definition

Polycystic ovarian syndrome (PCOS) is characterized by endocrine and ovarian disorders that affect quality of life in women of reproductive age. In 1935, PCOS was first described by Stein and Leventhal with a description of seven women suffering from amenorrhea, hirsutism, and enlarged ovaries with multiple cysts [1, 2]. Some different criteria about the National Institute of Health (NIH), Rotterdam criteria, Androgen Excess Society and Polycystic Ovary Syndrome Society guidelines (AE-PCOS) are shown in **Table 1** [3–8].

1.2. Epidemiology

Globally, PCOS affects 5–20% of women of reproductive age [9]. One report summarized the incidence of PCOS as 6–13% in Hispanic women, 3–9% in African American women, and 2–9% in Asian women [10]. The prevalence of PCOS in different geographical regions ranges from

Title	NIH 1992	Rotterdam 2003	AE-PCOS 2006	NIH 2012 extension of Rotterdam 2003
Criteria	<ul style="list-style-type: none"> Clinical or biochemical androgen excess Rare ovulations 	<ul style="list-style-type: none"> Clinical or biochemical androgen excess Oligo- or anovulation Polycystic ovaries 	<ul style="list-style-type: none"> Clinical or biochemical androgen excess Ovarian dysfunction and/or polycystic ovaries 	<ul style="list-style-type: none"> Clinical or biochemical androgen excess Oligo- or anovulation Polycystic ovaries
Restriction	Need both criteria	Need two of three criteria	Need both criteria	<ul style="list-style-type: none"> Need two of three criteria Specifically identifying the four sub-phenotype: <ul style="list-style-type: none"> A. Androgen Excess + Ovulatory Dysfunction + Polycystic Ovaries B. Androgen Excess + Ovulatory Dysfunction C. Androgen Excess + Polycystic Ovaries D. Ovulatory Dysfunction + Polycystic Ovarian Morphology
Exclusion	Exclusion of other androgen excess and other similar etiology			

Table 1. Diagnostic criteria for PCOS.

5 to 10% according to the NIH 1990 criteria, from 10 to 15% according to the AE-PCOS 2006 criteria, and from 6 to 21% when the Rotterdam criteria are applied [7]. East Asian subjects (Korean, Chinese, and Thai) appear to have a lower prevalence of PCOS (about 5%) compared to Caucasian women (11–20%) [11].

One systematic review and meta-analysis showed the incidence of PCOS phenotypes using the 2012 NIH criteria was 50% for phenotype A, 13% for phenotype B, 14% for phenotype C, and 17% for phenotype D [12].

1.3. Comorbidities

Patients with PCOS often have comorbidities such as obesity, insulin resistance/type II diabetes mellitus (Type II DM), dyslipidemia, hypertension/cardiovascular disease, infertility/subfertility, or cancer. One systematic review and meta-analysis demonstrated that women with PCOS had a pooled prevalence of 61% for overweight [body mass index (BMI) > 25], 49% for obesity (BMI > 30), and 54% for central obesity [13]. Insulin resistance (IR) is present in 50–80% of these women, which is associated with obesity [14, 15]. Both lean (30%) and obese women (70%) with PCOS show decreased insulin sensitivity [16].

Around 27% of premenopausal women with PCOS have type II DM [17]. Dyslipidemia may be up to 70% in women with PCOS [18, 19]. In a large study of European and American women with PCOS, the total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels increased significantly, up to 29 and 16 mg/dl, respectively, in non-Hispanic white, obese women with PCOS compared to obese women without PCOS [19]. This study also noted that the total cholesterol and LDL-C levels were elevated significantly, up to 32 and 32 mg/dl, respectively, in nonobese women with PCOS compared to nonobese women without PCOS [19]. Another worldwide systematic review and meta-analysis demonstrated that triglycerides (TG) and LDL-C levels were 26 and 12 mg/dl higher, and high-density lipoprotein cholesterol (HDL-cholesterol) concentration was 6 mg/dl lower than that of controls [20].

One clinical study demonstrated that nearly 26% of women with PCOS have hypertension [21]. The metabolic imbalances in patients with PCOS cause chronic low-grade inflammation and cardiovascular disturbances, which increase the risk of cardiovascular disease [22]. One systematic review and meta-analysis showed a 2-fold increased risk of coronary heart disease (CHD) and stroke for women with PCOS compared to those without PCOS [23].

Women with PCOS account for around 80% of women with anovulatory infertility [24, 25]. A recently systematic review and meta-analysis showed that women of all ages with PCOS were at a significantly increased risk [odds ratio (OR) up to 2.79] for endometrial cancer [26]. Moreover, this study also revealed that when women over 54 years of age were excluded from the analysis, the risk for women with PCOS increased more (OR up to 4.05) for endometrial cancer and for ovarian cancer (OR up to 2.52), but stable for breast cancer [26].

2. Etiology

The etiology of PCOS is still not clear. A systematic review suggested that post-natal exposure to androgens results in reprogramming of the hypothalamic-pituitary-ovarian-axis [27]. Recently, some clinical studies have confirmed that human fetal androgen excess promotes PCOS development after birth by checking infant blood levels at term [28]. The circulating androgen levels of the human female fetus in the second trimester can increase into the male range and mid-gestational amniotic testosterone levels in female fetuses of PCOS mothers may be higher than those in normal mothers, which might influence fetal development [28]. Another review article mentioned that the fetal ovary is more likely to produce an excess of androgens in response to maternal human chorionic gonadotropin (hCG) in subjects genetically predisposed to PCOS [29]. Furthermore, some genetic variations are associated with PCOS. For example, DENND1A is found in the cytoplasm and nuclei of ovarian theca cells. Over expression of DENND1A variant 2 results in a PCOS-like phenotype, and knock-down of DENND1A variant 2 in PCOS theca cells reversed this phenotype [30]. In addition, a recent review showed that genome-wide association studies (GWAS) have identified some loci containing genes with clear roles in reproductive (LHCGR, FSHR, and FSHB) and metabolic (INSR and HMGA2) dysfunction in PCOS [31].

3. Diagnosis

There are several diagnostic criteria for PCOS such as NIH 1990/2012, ESHRE/ASRM 2003 (Rotterdam), or AE-PCOS 2006. Diagnosis of PCOS should take into consideration the history, clinical manifestations, ultrasound imaging results, and serum examination results.

3.1. History taking

Menstrual abnormality such as oligo-anovulation (OA) is usually noted [32]. According to the Rotterdam criteria, OA is defined as less than eight episodes of menses a year or cycle lengths of more than 35 days [5]. A stricter definition, such as less than eight menstruations and/or two cycles of less than 22 or more than 42 days per year, the prevalence of OA drops to 14% and OA becomes highly predictive of PCOS [33, 34]. Although 30% of women with PCOS will have normal menses [2, 35], 85–90% of women with OA have PCOS, while 30–40% of women with amenorrhea have PCOS [2, 36]. After the age of 40, women with PCOS often have more regular menstrual cycles while women over 30 who develop OA are less likely to have PCOS [32].

Weight gain and central obesity are common presentations in PCOS and usually come before the onset of anovulatory cycles [14]. In the United States, the prevalence of obesity in girls aged 12–19 years in 2007–2008 was 17%, compared with 50–80% among adolescent girls with PCOS [13, 37–40].

3.2. Clinical manifestations

Clinical manifestations are acne, hirsutism, and androgenic alopecia. Some patients appear with only one or two manifestations, while a few patients have all the three [2]. Sixty percent of patients with PCOS have hirsutism and 15–25% patients have acne [6].

3.3. Other diagnostic methods

The BMI, blood pressure, waist circumference (WC), and hip circumference should be measured at the initial visit. Fasting lipid profile, sugar and glycohemoglobin, or a 2-hour oral glucose tolerance test (OGTT) should be performed if PCOS is suspected at the initial visit. Trans-vaginal ultrasound is indicated rather than trans-abdominal ultrasound if the patient has one of either irregular menstruation or HA. The Rotterdam PCOM criteria, considered to have sufficient specificity and sensitivity to define PCOM, requires the presence of ≥ 12 follicles measuring 2–9 mm in diameter and/or increased ovarian volume ($>10 \text{ cm}^3$) in a single ovary or both ovaries [32, 41–42]. In 2014, the AE-PCOS guidelines suggested using follicle number per ovary (FNPO) ≥ 25 for the definition of PCOM when using newer technology that allows maximal resolution of ovarian follicles (such as a transducer frequency of more than 8 MHz) [41, 43].

Serum hormone examination, such as serum androgens, should be performed on women with clinical appearance of PCOS. In addition, anti-Müllerian hormone (AMH) in women is generated by granulosa cells, and preantral and antral follicles, and its major function seems to be limited to inhibit the development of the initial stage of follicular maturation [44]. Serum

AMH in women with PCOS is higher than in healthy women, which probably reflects the number of small follicles observed on the ultrasounds of polycystic ovaries [45]. Studies have reported that 97% of women with AMH >10 ng/mL had PCOS and this correlated positively with LH, total testosterone, and DHEA [45, 46]. Besides, serum AMH revealed high predictive ability for the presence of OA or amenorrhea [45, 46]. Recently, serum AMH is proving to be a better tool to understand ovarian function and follicular count; however, the clinical use of serum assays for AMH still poses some technical problems [33, 44].

4. Conventional management and limitations

Management of PCOS is limited to improve clinical manifestations, since the real etiology of the disorder is unclear [47]. While multiple cardiovascular risk factors such as obesity, dyslipidemia, hypertension, and DM are prevalent in PCOS, current therapeutic management of PCOS usually focuses firstly on the treatment of metabolic disturbances (anovulation, menstrual irregularity, and hirsutism) and secondly on the control of reproductive hormones or insulin levels [48]. Lifestyle modifications including increased exercise, dietary changes, and weight loss are appropriate first-line interventions for many women with PCOS [49]. Diet therapy for patients with PCOS includes the design of low-calorie diets to achieve weight loss or preserve a healthy weight, restrict the intake of simple sugars, and increase the consumption of foods with a low glycemic index and refined carbohydrates, a decrease in the consumption of trans and saturated fatty acids, and awareness of possible deficiencies such as omega-3, vitamin D, and chromium [50]. One systematic review and meta-analysis demonstrated that moderate physical activity mostly 12 or 24 weeks would improve ovulation, decreased IR (9–30%), and weight loss (4.5–10%) [51]. The AE-PCOS guidelines suggested a target of caloric, diet, and body weight control in PCOS women with more restrictions if dyslipidemia occurred [52–54]. The detailed information is listed in **Table 2** [52–54].

Nutrition recommendations	Methods
Limitation of calories	Decrease current diet 500–1000 kcal/day
Reduction of fat	Decrease total fat (less than 30% total caloric intake) and saturated fat (less than 10% total caloric intake)
Favor foods intake	Increase fiber, vegetables, fruit, cereals, wholegrain breads, monounsaturated and polyunsaturated fat intake
Suggestions if dyslipidemia	Expect reduction in LDL-C (%)
Reduce body weight by 7–10%	5–8%
Decrease saturated fat to 7% total energy	8–10%
Decrease dietary cholesterol to <200 mg daily	3–5%
Decrease transfat to 1% total energy	2%
Increase 2 g of plant stanols daily	6–0%
Add 5–10 g viscous fiber daily	3–5%

Table 2. Nutritional recommendations for PCOS women from the AE-PCOS society.

Medical agents	Indication and effect	Limitations
Clomiphene citrate	<ul style="list-style-type: none">*As an ovary-stimulating drug in subfertile /infertile women*Nonsteroidal synthetic hormone consisting of a racemic mixture of two stereoisomers (40% enclomiphene [EnC] and 60% zuclomiphene [ZuC]), with anti-estrogenic properties	<ul style="list-style-type: none">*Possible fetal malformations, mainly neural tube defects and hypospadias*Increased risk of endometrial cancer, especially at doses greater than 2000 mg and high (more than 7) number of cycles
Metformin	<ul style="list-style-type: none">*Usually used in young girls and adolescents with PCOS as first-line monotherapy or in combination with anti-androgen medications and OCPs*Improve hyperandrogenemia and symptoms of androgen excess*Recovery ovary function with normal menses*Assist in weight reduction*Reduce in metabolic parameters of insulin resistance	<ul style="list-style-type: none">*Promoting ovulation is still controversial*Maybe increase IR after a 2-year period of intervention
Oral conceptions	<ul style="list-style-type: none">*Contain estrogen (almost exclusively ethinylestradiol) and a progestin*Decrease androgens and block the effect of androgens by inhibiting of ovarian androgen production and by increasing SHBG*Advantageously combined with an anti-androgen to attain a better effect when treating hirsutism and alopecia	<ul style="list-style-type: none">*Progestins, such as chlormadinone and drospirenone, may increase venous thrombosis events and may be contraindicated in severe obesity patients.*Little effect in blocking mild to moderate hirsutism or alopecia with OCPs only
Anti-androgens	<ul style="list-style-type: none">*Competitive antagonism of the androgen receptor (spironolactone (SPA), cyproterone acetate, flutamide) or suppression of 5α-reductase (5αR, such as finasteride) to prevent the conversion of 5α-dihydrotestosterone into free testosterone*Suppress the effects of androgen in the hair follicle or in the pilosebaceous unit	<ul style="list-style-type: none">*SPA may induce hyperkalemia, breast discomfort, dry skin, gastritis, headaches and dizziness*Intermenstrual spotting may occur if the women taking SPA as monotherapy*SPA has the potential for teratogenicity
Steroids	<ul style="list-style-type: none">*Physiologic doses of prednisolone or dexamethasone can reduce androgen output directly	<ul style="list-style-type: none">*Less effective for the treatment of hirsutism
Statins	<ul style="list-style-type: none">*Lipid-lowering agents with multiple actions to improve dyslipidemia*Combined with an OCP can improve hirsutism	<ul style="list-style-type: none">*Statins alone do not improve hirsutism, menstruation, or BMI

Table 3. Current medical agents and limitations for PCOS.

Unfortunately, lifestyle interventions are associated with low adherence and sustainability, and engagement, compliance, and sustainability remain challenging [55]. Medical treatment of PCOS is indicated if lifestyle modifications are a failure or unsuitable. Medical treatments include clomiphene citrate, metformin, oral contraceptives (OCPs), anti-androgen, steroids, and statins. One-year randomized clinical trial (RCT) showed that combined oral contraceptives plus spironolactone can decrease hirsutism score, androgens, and DHEA levels with fewer menstrual dysfunction [56]. Another randomized, controlled crossover study demonstrated that both metformin and myoinositol significantly reduced the insulin response to OGTT and

improved insulin sensitivity [57]. Metformin could reduce body weight, improve menstrual pattern, and decrease LH, oestradiol levels, androgens, and AMH levels [57]. **Table 3** lists the medical treatment agents and limitations for PCOS [58–67].

Bariatric surgery is used for weight reduction in patients with morbid obesity. One systematic review showed that bariatric surgery can improve postoperative conception rates, hirsutism, menstrual irregularities, and hormonal abnormalities in women with PCOS [68]. Another systematic review and meta-analysis about bariatric surgery demonstrated that the incidence of PCOS preoperatively was 45.6%, which significantly decreased to 6.8 and 7.1% at the 1 year follow-up and study endpoint, respectively [69]. Moreover, it also demonstrated nearly a 50% improvement in menstrual irregularity and a 30% improvement in hirsutism [69]. There is still a lack of evidence for the improvement in fertility after bariatric surgery [68, 69]. One report revealed the tendency of increasing infant mortality in the bariatric group and bariatric surgery may have its own unique risk-benefit ratio with regards to pregnancy results [70].

5. Traditional Chinese medicine

Traditional Chinese medicine formulas and herbs have been used to manage the health problems of women for hundreds of years. Classically, Chinese medicine prescription is composed of many herbs to treat a specific disease. According to the principles of TCM syndrome patterns for PCOS, one study showed that Shen deficiency with blood-stasis syndrome was the most frequent pattern noted in these patients, followed by Pi-deficiency with phlegm-dampness syndrome, Pi-Shenyang-deficiency syndrome, and Shen-yin deficiency syndrome [71]. Another study demonstrated that TCM syndrome patterns presented in patients with PCOS were mostly amalgamative, of which Shen deficiency and Gan stagnancy are the basic syndromes [72]. One earlier study revealed that elevated levels of testosterone correlated more with the TCM syndrome pattern of Shen-Yi deficiency compared to other patterns [73]. Interestingly, there is one study that describes the correlation between TCM syndrome patterns of PCOS and ovulation induction effects [74]. The effects of clomiphene on patients with phlegm-dampness accumulation syndrome and Shen-yin deficiency syndrome were poorer than in patients with Shen-yang deficiency syndrome and Gan-stagnancy transformed heat syndrome, which suggested the degree of reproduction endocrine dysfunction or the metabolism disturbance of the former two syndrome patterns were more severe than the latter two syndrome patterns [74].

5.1. Chinese herbal formulas for PCOS

5.1.1. *Jia-Wei-Xiao-Yao-San*

Jia-Wei-Xiao-Yao-San, also called Dan-Zhi-Xiao-Yao-San, consists of Moutan Radicis Cortex, Radix Paeoniae Rubra, Bupleuri Radix, Angelicae Sinensis Radix, Poria, Glycyrrhizae Radix, Atractylodes Ovatae Rhizoma, Zingiberis Rhizoma Recens, and Menthae Herba. According

to the principles of TCM, Jia-Wei-Xiao-Yao-San disperses stagnated liver qi for relief of qi stagnation and suppresses heat and nourishes the blood. One study showed that a danzhi xiaoyao pill could improve ovulation rates and pregnancy rates in anovulation infertility patients with PCOS complicated by IR [75]. It was also reported as the most frequently prescribed formula for patients with PCOS in north Taiwan [76].

5.1.2. Wen-Jing-Tang

Wen-Jing-Tang consists of *Cinnamomi Ramulus*, *Evodiae Fructus*, *Ligustici Rhizoma*, *Angelicae sinensis Radix*, *Paeoniae Radix*, *Ginseng Radix*, *Glycyrrhizae Radix*, *Zingiberis Rhizoma Recens*, *Moutan Radicis Cortex*, *Ophiopogonis Tuber*, *Pinelliae Tuber*, and *Asini Corii Gelatinum*. According to the principles of TCM, Wen-Jing-Tang would promote blood circulation to dispel blood stasis, dispels cold by warming the meridians, benefits qi, and nourishes the blood. One study showed that Wen-Jing-Tang was effective in regulating endocrine conditions in the treatment of ovulation disorders in patients with PCOS [77]. It suggested that Wen-Jing-Tang is adequate for the clinical management of PCOS in women with various constitutions (as determined by the matching theory of eight-principle pattern identification) [77].

5.1.3. Cang-Fu-Dao-Tan-Wan

Cang-Fu-Dao-Tan-Wan consists of *Atractylodes Lanceae Rhizoma*, *Cyperi Rhizoma*, *Pinelliae Rhizoma*, *Citri Reticulata Pericarpium*, *Poria*, *Citrus aurantium L.*, *Glycyrrhiza Radix*, and *Arisaema heterophyllum Bl.* According to principles of TCM, Cang-Fu-Dao-Tan-Wan resolves phlegm and dissipates masses, eliminates dampness, and relieves depression. One study evaluated the efficacy of a modified Cangfu Daotan pill combined with clomiphene in patients with PCOS. The results showed that the modified Cangfu Daotan pill could improve symptoms, increase ovarian artery blood flow, and lower FSH and LH [78]. Another study evaluated a modified Cangfu Daotan Decoction (MCDD) on endometrial receptivity in infertility patients with PCOS [79]. MCDD could increase pregnancy rates with improving insulin resistance, endometrial blood flow, endometrial receptivity, and increasing the uncoupling protein (UCP2) expression [79]. UCP2 expression, negatively regulating the hypersensitivity of insulin, has been reported to be significantly higher in early stage follicles of ovary tissue in PCOS patients [80], but the mechanism and function in the endometrium remains unknown.

5.2. Single Chinese herbs for PCOS

5.2.1. Cyperi Rhizoma

Cyperi Rhizoma, also called Xiang Fu in Chinese, originates from dried roots of *Cyperus rotundus L.* According to the principles of TCM, it can disperse and rectify depressed liver-energy, regulating menstruation, and arresting pain. *Cyperi Rhizoma* was also reported as the most frequently prescribed single herb in north Taiwan for patients with PCOS [76]. It may have potential for PCOS treatment due to its pharmacological benefits resulting in anti-androgenic, anti-diabetic, anti-lipidemic, anti-obesity, and weight-control effects in obese patients according to the present research results [81, 82].

5.2.2. *Radix Salvia Miltiorrhiza*

Radix Salvia Miltiorrhiza, also called Dan Shen in Chinese, originates from dried roots of *Salvia miltiorrhiza* Bunge. According to the principles of TCM, Dan Shen can promote blood flow to regulate menstruation, cool blood, and dispel blood stasis. Tanshinone, the main ingredient of *Salvia miltiorrhiza* Bunge [83], may decrease the level of androgen and improve the index of lipid metabolism, such as lower total cholesterol and TG, and increase HDL levels, in patients with PCOS [84]. Some animal studies have shown that Cryptotanshinone can reverse reproductive disturbances by decreasing the levels of SHBG, testosterone, estradiol, and LH, as well as the LH/FSH ratio, and can improve metabolic disturbances, such as abnormal levels of LDL-C and FINS by dehydroepiandrosterone (DHEA)-induced PCOS [84, 85].

5.2.3. *Coptidis Rhizoma*

Coptidis Rhizoma, also called Huang Lian in Chinese, originates from dried roots of *Coptis deltoidea* C.y.Cheng et Hsiao. or *Coptis chinensis* Franch. or *Coptis teeta* Wall. According to the principles of TCM, *Coptidis Rhizoma* can clear heat, eliminate dampness, spill fire, and induce detoxification. The isoquinoline alkaloid and the major constituent, berberine, are derived from this herb [86]. A previous randomized study showed that berberine, compared with metformin, could decrease BMI, lipid parameters, and total FSH requirements, and increase the live birth rate with fewer gastrointestinal adverse events in patients with PCOS undergoing IVF treatment [87]. Another earlier randomized study demonstrated that berberine, compared with metformin, could reduce total cholesterol, TG, LDL-C, WC, and waist-to-hip ratio, as well as elevate HDL-C and SHBG in patients with PCOS [88]. *Coptidis Rhizoma* may have potential for the management of PCOS.

6. Acupuncture and moxibustion

As with TCM formulas and single Chinese herbal therapy, acupuncture and moxibustion have also been used to treat clinical manifestations of PCOS for hundreds of years. Traditionally, acupuncture and moxibustion were performed by inserting needles into or burning moxa sticks upon specific points (acupoints) on the meridians of the body surface. Acupuncture and moxibustion work by regulating energy flow, also called Qi in Chinese, over the meridians. Newer therapeutic methods include electro-acupuncture (EA), laser-acupuncture, burning moxa granules on the top of the needle, points pasting, and far-infrared moxibustion.

Clinical effects of acupuncture are mediated by activation of somatic afferent nerves innervating the skin and muscle, which, via modulation of the activity in the somatic and autonomic nervous system, may regulate metabolic and endocrine functions in patients with PCOS [89]. One analysis showed that the acupoints of Sanyinjiao (SP 6), Guanyuan (CV 4), Zigong (EX-CA 1), Zhongji (CV 3), and Qihai (CV 6) are most frequently used in the clinical management of acupuncture for patients with PCOS [90]. This report also demonstrated the meridians of the main acupoints are the conception vessel, stomach meridian of the foot-yangming, and the spleen meridian of

foot-taiyin. The main acupoints are distributed in the lower limbs, lower abdomen, and back [90]. In the special points, usage of front-mu points, five-shu points, and back-shu points are more frequently used and the prescription is usually an average of five to seven acupoints [90].

One prospective clinical study investigated responses to 5 weeks of EA in overweight-obese women with PCOS [91]. The results showed that HbA1c levels and circulating and adipose tissue androgens were significantly decreased, together with modulation of vagal activity and adipose tissue sympathetic activity [91]. A systematic review and meta-analysis demonstrated that manual acupuncture (MA) or EA can improve clinical pregnancy rates and ongoing pregnancy rates, and lower the risk of ovarian hyperstimulation syndrome (OHSS) in women with PCOS undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) [92]. Another RCT revealed that serum androgens decreased and menstrual frequency increased after 16 weeks of EA intervention, while the acne improved after the 16-week follow-up in the EA group compared to the exercise group [93]. The other RCT showed that serum levels of AMH were significantly decreased in the EA group compared with the change in the exercise group after 16 weeks of intervention, but there was no difference in the exercise group and the no intervention group at 32 weeks follow-up [94]. An earlier RCT found that abdominal acupuncture for obese patients with PCOS can reduce BMI and WHR and increase menstrual frequency more effectively, and with fewer adverse effects, than metformin after a 6-month trial [95].

True (EA group) and sham (Park sham device group) acupuncture (EA V.S. Park sham device) may have similar effects on mean ovulation rates and reproductive endocrine changes, but the true acupuncture group could show lower fasting insulin and free testosterone levels after 8 weeks of intervention [96]. Another RCT showed that the utilization of acupuncture with or without clomiphene, compared with control acupuncture and placebo, did not increase live births in patients with PCOS [97]. A recent systematic review and meta-analysis demonstrated that acupuncture may be more likely to improve ovulation rates and menstruation frequency than no acupuncture in patients with PCOS [98]. This report also noted that acupuncture could be as an adjunct to medication with regard to LH, LH/FSH ratio, testosterone, fasting insulin, and pregnancy rates [98]. Another study revealed that there were very few RCTs have been reported and there was deficient evidence to support the use of acupuncture for management of ovulation problems in patients with PCOS [99].

7. Conclusions

Traditional Chinese medicine formulas or single herbs have been shown to be effective in many clinical or animal studies to restore regular menstruation, relieve symptoms, and improve ovulation dysfunction in patients with PCOS. Acupuncture, both EA and MA, have the potential to change the local ovarian hyperandrogenic environment and improve reproductive and endocrine metabolic disorders in PCOS. Thus, better outcomes can be achieved through complementary therapy with TCM for PCOS, expediting and boosting treatment efficacy, and ultimately leading to decreased medical costs. However, more clear, effective, and safe evidence for the use of TCM management for PCOS is needed in the future.

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References

- [1] Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *American Journal of Obstetrics and Gynecol.* 1935;**29**:181-191
- [2] Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clinical Epidemiology.* 2013;**6**:1-13. DOI: 10.2147/CLEP.S37559
- [3] Szydlarska D, Machaj M, Jakimiuk A. History of discovery of polycystic ovary syndrome. *Advances in Clinical and Experimental Medicine.* 2017;**26**:555-558. DOI: 10.17219/acem/61987
- [4] Zawadski JK, Dunaif A. 1992 Diagnostic criteria for polycystic ovary syndrome: Towards a rational approach. In: Dunaif A, Givens JR, Haseltine FP, Merriam GR, eds. *Polycystic ovary syndrome*. Boston: Blackwell Scientific Publications; p. 377-384
- [5] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertility and Sterility.* 2004;**81**:19-25. DOI: 10.1016/j.fertnstert.2003.10.004
- [6] Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, Janssen OE, Legro RS, Norman RJ, Taylor AE, Witchel SF. Androgen Excess Society. Positions statement: Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An Androgen Excess Society guideline. *Journal of Clinical and Endocrinology Metabolism.* 2006;**91**:4237-4245. DOI: 10.1210/jc.2006-0178
- [7] Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. *Fertility and Sterility.* 2016;**106**:6-15. DOI: 10.1016/j.fertnstert.2016.05.003

- [8] National Institutes of Health. Evidence-based methodology workshop on polycystic ovary syndrome, December 3-5, 2012 [Internet]. Available from: <https://prevention.nih.gov/docs/programs/pcos/FinalReport.pdf> [Accessed 2017-6-25]
- [9] Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, Lizneva D, Natterson-Horowitz B, Teede HJ, Yildiz BO. Polycystic ovary syndrome. *Natural Reviews Disease Primers*. 2016;**2**:16057. DOI: 10.1038/nrdp.2016.57
- [10] Wang S, Alvero R. Racial and ethnic differences in physiology and clinical symptoms of polycystic ovary syndrome. *Seminars in Reproductive Medicine*. 2013;**31**:365-369. DOI: 10.1055/s-0033-1348895
- [11] Huang Z, Yong EL. Ethnic differences: Is there an Asian phenotype for polycystic ovarian syndrome? *Best Practices and Research Clinical Obstetrics and Gynaecology*. 2016;**37**:46-55. DOI: 10.1016/j.bpobgyn.2016.04.001
- [12] Lizneva D, Kirubakaran R, Mykhalchenko K, Suturina L, Chernukha G, Diamond MP, Azziz R. Phenotypes and body mass in women with polycystic ovary syndrome identified in referral versus unselected populations: Systematic review and meta-analysis. *Fertility and Sterility*. 2016;**106**:1510-1520.e2. DOI: 10.1016/j.fertnstert.2016.07.1121
- [13] Lim SS, Davies MJ, Norman RJ, Moran LJ. Overweight, obesity and central obesity in women with polycystic ovary syndrome: A systematic review and meta-analysis. *Human Reproduction Update*. 2012;**18**:618-637. DOI: 10.1093/humupd/dms030
- [14] Orio F, Muscogiuri G, Nese C, Palomba S, Savastano S, Tafuri D, Colarieti G, La Sala G, Colao A, Yildiz BO. Obesity, type 2 diabetes mellitus and cardiovascular disease risk: An update in the management of polycystic ovary syndrome. *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 2016;**207**:214-219. DOI: 10.1016/j.ejogrb.2016.08.026
- [15] Cascella T, Palomba S, De Sio I, Manguso F, Giallauria F, De Simone B, Tafuri D, Lombardi G, Colao A, Orio F. Visceral fat is associated with cardiovascular risk in women with polycystic ovary syndrome. *Human Reproduction*. 2008;**23**:153-159. DOI: 10.1093/humrep/dem356
- [16] Randeve HS, Tan BK, Weickert MO, Lois K, Nestler JE, Sattar N, Lehnert H. Cardiometabolic aspects of the polycystic ovary syndrome. *Endocrine Reviews*. 2012;**33**:812-841. DOI: 10.1210/er.2012-1003
- [17] Peppard HR, Marfori J, Iuorno MJ, Nestler JE. Prevalence of polycystic ovary syndrome among premenopausal women with Type 2 diabetes. *Diabetes Care*. 2001;**24**:1050-1052. PMID: 11375369
- [18] Kim JJ, Choi YM. Dyslipidemia in women with polycystic ovary syndrome. *Obstetrics and Gynecology Science*. 2013;**56**:137-142. DOI: 10.5468/ogs.2013.56.3.137
- [19] Legro RS, Kusanman AR, Dunaif A. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. *American Journal of Medicine*. 2001;**111**:607-613. PMID: 11755503

- [20] Wild RA, Rizzo M, Clifton S, Carmina E. Lipid levels in polycystic ovary syndrome: Systematic review and met analysis. *Fertility and Sterility*. 2011;**95**:1073-1079. DOI: 10.1016/j.fertnstert.2010.12.027
- [21] Orbetzova MM, Shigarminova RG, Genchev GG, Milcheva BA, Lozanov LB, Genov NS, Zacharieva SZ. Role of 24-hour monitoring in assessing blood pressure changes in polycystic ovary syndrome. *Folia Med (Plovdiv)*. 2003;**45**:21-25. PMID: 15366662
- [22] Baldani DP, Skrgatic L, Ougouag R. Polycystic ovary syndrome: Important underrecognised cardiometabolic risk factor in reproductive-age women. *International Journal of Endocrinology*. 2015;**2015**:786362. DOI: 10.1155/2015/786362
- [23] de Groot PC, Dekkers OM, Romijn JA, Dieben SW, Helmerhorst FM. PCOS, coronary heart disease, stroke and the influence of obesity: A systematic review and meta-analysis. *Human Reproduction Update*. 2011;**17**:495-500. DOI: 10.1093/humupd/dmr001
- [24] Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, Stener-Victorin E, Fauser BC, Norman RJ, Teede H. The management of anovulatory infertility in women with polycystic ovary syndrome: An analysis of the evidence to support the development of global WHO guidance. *Human Reproduction Update*. 2016;**22**:687-708. DOI: 10.1093/humupd/dmw025
- [25] Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Consensus on infertility treatment related to polycystic ovary syndrome. *Human Reproduction*. 2008;**23**:462-477. DOI: 10.1093/humrep/dem426
- [26] Barry JA, Azizia MM, Hardiman PJ. Risk of endometrial, ovarian and breast cancer in women with polycystic ovary syndrome: A systematic review and meta-analysis. *Human Reproduction Update*. 2014;**20**:748-758. DOI: 10.1093/humupd/dmu012
- [27] Paixão L, Ramos RB, Lavarda A, Morsh DM, Spritzer PM. Animal models of hyperandrogenism and ovarian morphology changes as features of polycystic ovary syndrome: A systematic review. *Reproductive Biology and Endocrinology*. 2017;**15**:12. DOI: 10.1186/s12958-017-0231-z
- [28] Dumesic DA, Goodarzi MO, Chazenbalk GD, Abbott DH. Intrauterine environment and polycystic ovary syndrome. *Seminars in Reproductive Medicine*. 2014;**32**:159-165. DOI: 10.1055/s-0034-1371087
- [29] De Leo V, Musacchio MC, Cappelli V, Massaro MG, Morgante G, Petraglia F. Genetic, hormonal and metabolic aspects of PCOS: An update. *Reproductive Biology and Endocrinology*. 2016;**14**:38. DOI: 10.1186/s12958-016-0173-x
- [30] Trofimova T, Lizneva D, Suturina L, Walker W, Chen YH, Azziz R, Layman LC. Genetic basis of eugonadal and hypogonadal female reproductive disorders. *Best Practices in Research and Clinical Obstetrics and Gynaecology*. 2017; pii: S1521-6934(17)30069-X. DOI: 10.1016/j.bpobgyn.2017.05.003

- [31] Jones MR, Goodarzi MO. Genetic determinants of polycystic ovary syndrome: Progress and future directions. *Fertility and Sterility*. 2016;**106**:25-32. DOI: 10.1016/j.fertnstert.2016.04.040
- [32] Barbieri RL, Ehrmann DA. [Internet]. 2017. Available from: https://www.uptodate.com/contents/diagnosis-of-polycystic-ovary-syndrome-in-adults?source=search_result&search=pcos%20diagnosis%20adult&selectedTitle=1~150 [Accessed: 2017-6-30]
- [33] Dewailly D. Diagnostic criteria for PCOS: Is there a need for a rethink? *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;**37**:5-11. DOI: 10.1016/j.bpobgyn.2016.03.009
- [34] van Hooff MH, Voorhorst FJ, Kaptein MB, Hirasing RA, Koppenaal C, Schoemaker J. Predictive value of menstrual cycle pattern, body mass index, hormone levels and polycystic ovaries at age 15 years for oligo-amenorrhoea at age 18 years. *Human Reproduction*. 2004;**19**:383-392. DOI: 10.1093/humrep/deh079
- [35] Balen A, Conway G, Kaltsas G. Polycystic ovary syndrome: The spectrum of the disorder in 1741 patients. *Human Reproduction*. 1995;**10**:2107-2111. PMID: 8567849
- [36] Hart R. Definitions, prevalence and symptoms of polycystic ovaries and the polycystic ovary syndrome. In: Allahbadia GN, Agrawal R, editors. *Polycystic Ovary Syndrome*. Kent, UK: Anshan, Ltd; 2007:15-26
- [37] Ogden C, Carroll M. Prevalence of Obesity among Children and Adolescents: United States, Trends 1963-1965 through 2007-2008. Hyattsville, MD: Centers for Disease Control and Prevention, National Center for Health Statistics; 2010
- [38] Glueck CJ, Aregawi D, Winiarska M, Agloria M, Luo G, Sieve L, Wang P. Metformin-diet ameliorates coronary heart disease risk factors and facilitates resumption of regular menses in adolescents with polycystic ovary syndrome. *Journal of Pediatric Endocrinology and Metabolism*. 2006;**19**:831-842. PMID: 16886591
- [39] Glueck CJ, Morrison JA, Friedman LA, Goldenberg N, Stroop DM, Wang P. Obesity, free testosterone, and cardiovascular risk factors in adolescents with polycystic ovary syndrome and regularly cycling adolescents. *Metabolism* 2006;**55**:508-514. DOI: 10.1016/j.metabol.2005.11.003
- [40] Glueck CJ, Morrison JA, Wang P. Insulin resistance, obesity, hypofibrinolysis, hyperandrogenism, and coronary heart disease risk factors in 25 pre-perimenarchal girls age < or =14 years, 13 with precocious puberty, 23 with a first-degree relative with polycystic ovary syndrome. *Journal of Pediatric Endocrinology and Metabolism*. 2008;**21**:973-984. PMID: 19209619
- [41] Zhu RY, Wong YC, Yong EL. Sonographic evaluation of polycystic ovaries. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;**37**:25-37. DOI: 10.1016/j.bpobgyn.2016.02.005
- [42] Balen AH, Laven JS, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary: International consensus definitions. *Human Reproduction Update*. 2003;**9**:505-514. PMID: 14714587

- [43] Dewailly D, Lujan ME, Carmina E, Cedars MI, Laven J, Norman RJ, Escobar-Morreale HF. Definition and significance of polycystic ovarian morphology: A task force report from the androgen excess and polycystic ovary syndrome society. *Human Reproduction Update*. 2014;**20**:334-352. DOI: 10.1093/humupd/dmt061
- [44] Ozzola G. Anti-Müllerian hormone: A brief review of the literature. *Clin Ter*. 2017;**168**: e14-e22. DOI: 10.7417/CT.2017.1976
- [45] Łebkowska A, Kowalska I. Anti-Müllerian hormone and polycystic ovary syndrome. *Endokrynologia Polska*. 2017;**68**:74-78. DOI: 10.5603/EP.a2016.0065
- [46] Tal R, Seifer DB, Khanimov M, Malter HE, Grazi RV, Leader B. Characterization of women with elevated antimüllerian hormone levels (AMH): Correlation of AMH with polycystic ovarian syndrome phenotypes and assisted reproductive technology outcomes. *American Journal of Obstetrics & Gynecology*. 2014;**211**:59.e1-8. DOI: 10.1016/j.ajog.2014.02.026
- [47] Andrade VH, Mata AM, Borges RS, Costa-Silva DR, Martins LM, Ferreira PM, Cunha-Nunes LC, Silva BB. Current aspects of polycystic ovary syndrome: A literature review. *Revista Da Associacao Medica Brasileira* (1992). 2016;**62**:867-871. DOI: 10.1590/1806-9282.62.09.867
- [48] Nayaker BS, Thomas S, Ramachandran S, Loganathan S, Sundari M, Mala K. Polycystic ovarian syndrome-associated cardiovascular complications: An overview of the association between the biochemical markers and potential strategies for their prevention and elimination. *Diabetes & Metabolic Syndrome*. 2017; pii: S1871-4021(17)30165-0. DOI: 10.1016/j.dsx.2017.07.004
- [49] Bates GW, Legro RS. Longterm management of Polycystic Ovarian Syndrome (PCOS). *Molecular Cell Endocrinology*. 2013;**373**:91-97. DOI: 10.1016/j.mce.2012.10.029
- [50] Faghfoori Z, Fazelian S, Shadnough M, Goodarzi R. Nutritional management in women with polycystic ovary syndrome: A review study. *Diabetes & Metabolic Syndrome*. 2017; pii: S1871-4021(17)30011-5. DOI: 10.1016/j.dsx.2017.03.030
- [51] Harrison CL, Lombard CB, Moran LJ, Teede HJ. Exercise therapy in polycystic ovary syndrome: A systematic review. *Human Reproduction Update*. 2011;**17**:171-183. DOI: 10.1093/humupd/dmq045
- [52] De Sousa SM Dr, Norman RJ Prof. Metabolic syndrome, diet and exercise. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;**37**:140-151. DOI: 10.1016/j.bpobgyn.2016.01.006
- [53] Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W, Lobo R, Norman RJ, Talbott E, Dumesic DA. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: A consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. *The Journal of Clinical Endocrinology & Metabolism*. 2010;**95**:2038-2049. DOI: 10.1210/jc.2009-2724

- [54] Rosenzweig JL, Ferrannini E, Grundy SM, Haffner SM, Heine RJ, Horton ES, Kawamori R. Endocrine Society. Primary prevention of cardiovascular disease and type 2 diabetes in patients at metabolic risk: An endocrine society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2008;**93**:3671-3689. DOI: 10.1210/jc.2008-0222
- [55] Naderpoor N, Shorakae S, de Courten B, Misso ML, Moran LJ, Teede HJ. Metformin and lifestyle modification in polycystic ovary syndrome: Systematic review and meta-analysis. *Human Reproduction Update*. 2015;**21**:560-574. DOI: 10.1093/humupd/dmv025
- [56] Alpañés M, Álvarez-Blasco F, Fernández-Durán E, Luque-Ramírez M, Escobar-Morreale HF. Combined oral contraceptives plus spironolactone compared with metformin in women with polycystic ovary syndrome: A one-year randomized clinical trial. *European Journal of Endocrinology*. 2017;**177**:399-408. DOI: 10.1530/EJE-17-0516
- [57] Tagliaferri V, Romualdi D, Immediata V, De Cicco S, Di Florio C, Lanzone A, Guido M. Metformin vs myoinositol: Which is better in obese polycystic ovary syndrome patients? A randomized controlled crossover study. *Clinical Endocrinology (Oxf)*. 2017;**86**:725-730. DOI: 10.1111/cen.13304. Epub 2017 Feb 10
- [58] Skalkidou A, Sergeantanis TN, Gialamas SP, Georgakis MK, Psaltopoulou T, Trivella M, Siristatidis CS, Evangelou E, Petridou E. Risk of endometrial cancer in women treated with ovary-stimulating drugs for subfertility. *Cochrane Database of Systematic Reviews*. 2017;**3**:CD010931. DOI: 10.1002/14651858.CD010931.pub2
- [59] Scaparrotta A, Chiarelli F, Verrotti A. Potential teratogenic effects of clomiphene citrate. *Drug Safety*. 2017;**40**:761-769. DOI: 10.1007/s40264-017-0546-x
- [60] Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists (AACE); American College of Endocrinology (ACE); Androgen Excess and PCOS Society (AES). American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society Disease State Clinical Review. Guide to the best practices in the evaluation and treatment of polycystic ovary syndrome—part 1. *Endocrine Practices*. 2015;**21**:1291-1300. DOI: 10.4158/EP15748.DSC
- [61] Hsia Y, Dawoud D, Sutcliffe AG, Viner RM, Kinra S, Wong IC. Unlicensed use of metformin in children and adolescents in the UK. *British Journal of Clinical Pharmacology*. 2012;**73**:135-139. DOI: 10.1111/j.1365-2125.2011.04063.x
- [62] Bednarska S, Siejka A. The pathogenesis and treatment of polycystic ovary syndrome: What's new? *Advances in Clinical and Experimental Medicine*. 2017;**26**:359-367. DOI: 10.17219/acem/59380
- [63] Tang T, Glanville J, Hayden CJ, White D, Barth JH, Balen AH. Combined lifestyle modification and metformin in obese patients with polycystic ovary syndrome. A randomized, placebo-controlled, double-blind multicentre study. *Human Reproduction*. 2006;**21**:80-89. DOI: 10.1093/humrep/dei311

- [64] Oppelt PG, Mueller A, Jentsch K, Kronawitter D, Reissmann C, Dittrich R, Beckmann MW, Cupisti S. The effect of metformin treatment for 2 years without caloric restriction on endocrine and metabolic parameters in women with polycystic ovary syndrome. *Experimental and Clinical Endocrinology & Diabetes*. 2010;**118**:633-637. DOI: 10.1055/s-0029-1237705
- [65] Lizneva D, Gavrilova-Jordan L, Walker W, Azziz R. Androgen excess: Investigations and management. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;**37**:98-118. DOI: 10.1016/j.bpobgyn.2016.05.003
- [66] Moreno LE, Bonnell A, Neher JO, Safranek S. Clinical Inquiry: What therapies alleviate symptoms of polycystic ovary syndrome? *Journal of Family Practices*. 2015;**64**:247-249. PMID: 25973451
- [67] Raval AD, Hunter T, Stuckey B, Hart RJ. Statins for women with polycystic ovary syndrome not actively trying to conceive. *Cochrane Database Systematic Reviews*. 2011;**10**:CD008565. DOI: 10.1002/14651858.CD008565.pub2
- [68] Butterworth J, Deguara J, Borg CM. Bariatric surgery, polycystic ovary syndrome, and infertility. *Journal of Obesity*. 2016;**2016**:1871594. DOI: 10.1155/2016/1871594
- [69] Skubleny D, Switzer NJ, Gill RS, Dykstra M, Shi X, Sagle MA, de Gara C, Birch DW, Karmali S. The impact of bariatric surgery on polycystic ovary syndrome: A systematic review and meta-analysis. *Obesity Surgery*. 2016;**26**:169-176. DOI: 10.1007/s11695-015-1902-5
- [70] Legro RS. Ovulation induction in polycystic ovary syndrome: Current options. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2016;**37**:152-159. DOI: 10.1016/j.bpobgyn.2016.08.001
- [71] Li XB, Lan XY, Ou AH. Distribution of Chinese medicine syndrome patterns and its laws in patients with polycystic ovarian syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2011;**31**:323-326. PMID: 21485070
- [72] Zhang XJ, Gui SQ, Qian QH. Preliminary exploration on Chinese medicine syndrome type distribution in patients with polycystic ovary syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2010;**30**:689-693. PMID: 20929122
- [73] Li XP, Zheng CS, Hong ZJ. Correlation between sex hormone and insulin and various TCM syndrome types in patients with polycystic ovarian syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2007;**27**:996-998. PMID: 18173145
- [74] Zhao H, Wang XE, Zhang T. Correlation between Chinese medicine syndrome types of polycystic ovary syndrome and ovulation induction effect. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2011;**31**:896-898. PMID: 21866657
- [75] Liu Y, Mao LH. Effect of danzhi xiaoyao pill on ovulation induction of polycystic ovarian syndrome patients of pathogenic fire derived from stagnation of gan-qi. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2013;**33**:1191-1195. PMID: 24273971

- [76] Chen HW, Chiang WJ, Chen CL, et al. Characteristics and Prescription Patterns of Traditional Chinese Medicine in Polycystic Ovary Syndrome. *Journal of Chengdu University of TCM*. 2015;**38**:120-123. DOI: 10.13593/j.cnki.51-1501/r.2015.04.120
- [77] Ushiroyama T, Hosotani T, Mori K, Yamashita Y, Ikeda A, Ueki M. Effects of switching to wen-jing-tang (unkei-to) from preceding herbal preparations selected by eight-principle pattern identification on endocrinological status and ovulatory induction in women with polycystic ovary syndrome. *American Journal of Chinese Medicine*. 2006;**34**:177-187. DOI: 10.1142/S0192415X06003746
- [78] Hong Y, Sun B. Curative Estimation of Using Modified Cangfu Daotan Pill and Clomiphene in the Treatment of Polycystic Ovarian Syndrome Complicated with Infertility. *Journal of Sichuan of Traditional Chinese Medicine*. 2016;**34**:90-93
- [79] Ding CF, Wang CY, Yang X, Zheng RH, Yan ZZ, Chen WQ. Effect of modified cangfu daotan decoction in improving endometrial receptivity in infertility patients with polycystic ovarian syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2014;**34**:1297-1301. PMID: 25566617
- [80] Liu Y, Jiang H, He LY, Huang WJ, He XY, Xing FQ. Abnormal expression of uncoupling protein-2 correlates with CYP11A1 expression in polycystic ovary syndrome. *Reproduction Fertility and Development*. 2011;**23**:520-526. DOI: 10.1071/RD10266
- [81] Pirzada AM, Ali HH, Naeem M, Latif M, Bukhari AH, Tanveer A. *Cyperus rotundus* L.: Traditional uses, phytochemistry, and pharmacological activities. *Journal of Ethnopharmacology*. 2015;**174**:540-560. DOI: 10.1016/j.jep.2015.08.012
- [82] Lemaure B, Touché A, Zbinden I, Moulin J, Courtois D, Macé K, Darimont C. Administration of *Cyperus rotundus* tubers extract prevents weight gain in obese Zucker rats. *Phytotherapy Research*. 2007;**21**:724-730. DOI: 10.1002/ptr.2147
- [83] Xia Y, Zhao P, Huang H, Xie Y, Lu R, Dong L. Cryptotanshinone reverses reproductive disturbances in rats with dehydroepiandrosterone-induced polycystic ovary syndrome. *American Journal of Translational Research*. 2017;**15**(9):2447-2456. PMID: 28559995. PMCID: PMC5446527
- [84] Zhang JY, Xue HY, Su J, Zuo YH, Fan XQ, Cheng YQ. Clinical effects of tanshinone on polycystic ovary syndrome patients with hyperandrogenism. *Guangxi Medical Journal*. 2015;**37**:767-769. DOI: 10.11675/j.issn.0253-4304.2015.06.11
- [85] Yu J, Zhai D, Hao L, Zhang D, Bai L, Cai Z, Yu C. Cryptotanshinone Reverses Reproductive and Metabolic Disturbances in PCOS Model Rats via Regulating the Expression of CYP17 and AR. *Evidence-Based Complementary and Alternative Medicine*. 2014;**2014**:670743. DOI: 10.1155/2014/670743
- [86] Ong M, Peng J, Jin X, Qu X. Chinese Herbal Medicine for the Optimal Management of Polycystic Ovary Syndrome. *American Journal of Chinese Medicine*. 2017;**45**:405-422. DOI: 10.1142/S0192415X17500252

- [87] An Y, Sun Z, Zhang Y, Liu B, Guan Y, Lu M. The use of berberine for women with polycystic ovary syndrome undergoing IVF treatment. *Clinical Endocrinology (Oxf)*. 2014;**80**:425-431. DOI: 10.1111/cen.12294
- [88] Wei W, Zhao H, Wang A, Sui M, Liang K, Deng H, Ma Y, Zhang Y, Zhang H, Guan Y. A clinical study on the short-term effect of berberine in comparison to metformin on the metabolic characteristics of women with polycystic ovary syndrome. *European Journal of Endocrinology*. 2012;**166**:99-105. DOI: 10.1530/EJE-11-0616
- [89] Raja-Khan N, Stener-Victorin E, Wu X, Legro RS. The physiological basis of complementary and alternative medicines for polycystic ovary syndrome. *American Journal of Physiology. Endocrinology and Metabolism*. 2011;**301**:E1-E10. DOI: 10.1152/ajpendo.00667.2010
- [90] Jin C, Pang R, Xu L, Wu Z, Zhao J. Clinical rules for acupoint selection and prescription composition in treatment of polycystic ovary syndrome with acupuncture. *Zhongguo Zhen Jiu*. 2015;**35**:625-630. DOI: 10.13703/j.0255-2930.2015.06.032
- [91] Stener-Victorin E, Maliqueo M, Soligo M, Protto V, Manni L, Jerlhag E, Kokosar M, Sazonova A, Behre CJ, Lind M, Ohlsson C, Højlund K, Benrick A. Changes in HbA1c and circulating and adipose tissue androgen levels in overweight-obese women with polycystic ovary syndrome in response to electroacupuncture. *Obesity Science and Practice*. 2016;**2**:426-435. DOI: 10.1002/osp4.78
- [92] Jo J, Lee YJ. Effectiveness of acupuncture in women with polycystic ovarian syndrome undergoing in vitro fertilisation or intracytoplasmic sperm injection: A systematic review and meta-analysis. *Acupuncture in Medicine*. 2017;**35**:162-170. DOI: 10.1136/acupmed-2016-011163
- [93] Jedel E, Labrie F, Odén A, Holm G, Nilsson L, Janson PO, Lind AK, Ohlsson C, Stener-Victorin E. Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: A randomized controlled trial. *American Journal of Physiology. Endocrinology and Metabolism*. 2011;**300**:E37-45. DOI: 10.1152/ajpendo.00495.2010
- [94] Leonhardt H, Hellström M, Gull B, Lind AK, Nilsson L, Janson PO, Stener-Victorin E. Serum anti-Müllerian hormone and ovarian morphology assessed by magnetic resonance imaging in response to acupuncture and exercise in women with polycystic ovary syndrome: secondary analyses of a randomized controlled trial. *Acta Obstet Gynecol Scand*. 2015;**94**:279-287. DOI: 10.1111/aogs.12571
- [95] Zheng YH1, Wang XH, Lai MH, Yao H, Liu H, Ma HX. Effectiveness of abdominal acupuncture for patients with obesity-type polycystic ovary syndrome: A randomized controlled trial. *Journal of Alternative Complementary Medicine*. 2013;**19**:740-745. DOI: 10.1089/acm.2012.0429
- [96] Pastore LM, Williams CD, Jenkins J, Patrie JT. True and sham acupuncture produced similar frequency of ovulation and improved LH to FSH ratios in women with polycystic ovary syndrome. *The Journal of Clinical Endocrinology & Metabolism*. 2011;**96**:3143-3150. DOI: 10.1210/jc.2011-1126

- [97] Wu XK, Stener-Victorin E, Kuang HY, Ma HL, Gao JS, Xie LZ, Hou LH, Hu ZX, Shao XG, Ge J, Zhang JF, Xue HY, Xu XF, Liang RN, Ma HX, Yang HW, Li WL, Huang DM, Sun Y, Hao CF, Du SM, Yang ZW, Wang X, Yan Y, Chen XH, Fu P, Ding CF, Gao YQ, Zhou ZM, Wang CC, Wu TX, Liu JP, Ng EHY, Legro RS, Zhang H; PCOSAct Study Group. Effect of acupuncture and clomiphene in chinese women with polycystic ovary syndrome: A randomized clinical trial. *JAMA*. 2017;**317**:2502-2514. DOI: 10.1001/jama.2017.7217
- [98] Jo J, Lee YJ, Lee H. Acupuncture for polycystic ovarian syndrome: A systematic review and meta-analysis. *Medicine (Baltimore)*. 2017;**96**:e7066. DOI: 10.1097/MD.00000000000007066
- [99] Lim CE, Ng RW, Xu K, Cheng NC, Xue CC, Liu JP, Chen N. Acupuncture for polycystic ovarian syndrome. *Cochrane Database Systematic Reviews*. 2016;**5**:CD007689. DOI: 10.1002/14651858.CD007689.pub3