

The efficacy of using acupuncture in managing PCOS

Hui Chen¹, Chi Eung Danforn Lim^{1,2,*}

1. *School of Life Sciences, Faculty of Science, University of Technology Sydney, Sydney Australia*

2. *NICM Health Research Institute, Western Sydney University, Sydney, Australia*

* Correspondence Author

Key points

- Acupuncture is a popular option for women with PCOS as an alternative treatment
- There are a limited number of RCTs on the efficacy of the effect acupuncture on symptom management/fertility treatment in PCOS
- Acupuncture shows some efficacy of managing PCOS, especially in conjunct with the pharmaceutical treatments
- More well-designed RCTs with a larger population are needed to further confirm the efficacy of acupuncture

Abstract

Purpose of review Polycystic ovarian syndrome (PCOS) is a common reproductive disorder, which significantly impairs the fertility of 3-10% of women at reproductive age. It is getting very popular for women with PCOS to seek alternative therapies to treat PCOS, e.g. acupuncture. This review examines the currently available evidence from the randomised controlled trial to guide future recommendation on using acupuncture to assist the treatment of PCOS.

Recent findings PCOS is manifested by oligo-amenorrhoea, infertility, and hirsutism. The standard treatment of PCOS includes oral pharmacological agents, lifestyle changes, and surgical modalities. Pharmacologically based therapies are only effective in 60% of the patients, which are also associated with different side effects. As such, acupuncture offered an alternative option. Acupuncture can affect beta-endorphin production, which may, in turn, affect gonadotropin-releasing hormone secretion and affecting ovulation and menstrual cycle. Therefore, it is postulated that acupuncture may induce ovulation and restore menstrual cycle via increasing beta-endorphin production.

Summary Although modern medical science has discovered the action mechanisms underlying how acupuncture may manage the symptoms of PCOS, majority of the trials are small in sample

size and lack of consistency in the choice of acupoints. Larger scale trials are needed to provide standardised protocols.

Keywords: complementary medicine, acupuncture, PCOS, menstrual cycle, fertility, RCT

Introduction

Polycystic ovarian syndrome (PCOS) is reported to affect 3-10% of women at reproductive age, whereas among women with menstrual disorders, the rate ranged from 37% to 90% (1, 2). However, it is also estimated that 75% of individuals with PCOD are not diagnosed (1). The current first-line pharmacological therapy for such patients is the oral selective estrogen receptor modulator such as clomiphene, which is ineffective in 40% of the patients diagnosed with PCOS with significant side effects, eg. headaches, bloating, mood swings, and breast tenderness. With the increasing popularity of Chinese medicine, as well as formal regulation by Medicine Boards in different countries, Chinese medicine starts to enter the mainstream medicare system outside China and Asian countries. As such, more women with PCOS choose to use acupuncture and herbal medicine to aid fertility and symptom management. This review will only discuss the potential efficacy of acupuncture using the evidence from currently available randomised controlled trial (RCT) in the literature.

Manifestation and diagnostic criteria of PCOS

Clinically, PCOS is one of the most common endocrine conditions causing chorionic anovulation and anovulatory infertility (3). There is no distinct difference in races and ethnicities preference when it comes to PCOS (1). It is mainly caused by an imbalanced sex hormone, manifested by hyperandrogenism (excessive production of androgen). This further leads to the symptoms of oligo-amenorrhoea (infrequent or very light menstruation), infertility (failure to conceive) and hirsutism (excessive hair growth). Infertility and metabolic disorders (eg. obesity, insulin resistance, and type 2 diabetes) are the major complaints (4). On the other hand, obesity appears to exacerbate the development of PCOS in a certain population with a genetic or familial predisposition (5). As such, POCS is proposed to be a multi-factorial disease, with the interactions between genetic and multiple environmental factors. This leads to the difficulties of treating this condition with a single method.

There are three different sets of diagnostic criteria, established by National Institutes of Health International Conference on PCOS in 1990, the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) in 2003

(referred to as the Rotterdam criteria), and the Androgen Excess Society and PCOS Society (AE-PCOS) in 2006 as reviewed by Wolf et al (1). There are slight differences between each guideline, but most include hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. Rotterdam criteria are most widely used by the clinicians in most countries. Although early diagnosis as early as puberty may have some benefit of preventing future infertility, it is very difficult to do so due to the common issue of anovulation in young girls during the normal progression of puberty.

Current treatment guidelines

Combined contraceptives, including oral contraceptive pills, are commonly prescribed for patients of all ages with PCOS to manage the clinical symptoms (eg. oligo-amenorrhoea) and associated hormonal disturbances (eg. hyperandrogenism) (6). Based on several RCTs, the efficacy of such treatment is even comparable to placebo in improving the hormonal disturbances, including total testosterone and free androgen index (6). As such, lifestyle modification and metformin are commonly prescribed in combination with the pharmacological therapy to manage the symptoms and metabolic disorders, such as obesity, insulin resistance, and hyperlipidemia due to the link between metabolic disorders and hyperandrogenism (6). Currently, the first-line pharmacological therapy for anovulatory infertility in women with PCOS is the administration of oral ovulation induction such as letrozole, clomiphene citrate, and metformin (6).

Letrozole is a non-steroidal aromatase inhibitor. In anovulatory women, aromatase inhibitors downregulate oestrogen biosynthesis and reduce negative feedback to the hypothalamus, which leads to stronger gonadotropin-releasing hormone release (7). Letrozole is the preferred prescription over clomiphene these days due to its significant efficacy advantage to clomiphene, despite low to moderate quality of evidence (7). Aromatase inhibitors do have the adverse effects associated with anti-oestrogenic effects in the endometrium and cervix.

On the other hand, clomiphene citrate is an oral selective oestrogen receptor modulator, which was the first line choice for decades. However, up to 40% of women with PCOS taking clomiphene medication showed little clinical improvement (8). However, there is a high risk of ovarian hyperstimulation syndrome and multiple pregnancies with clomiphene therapy which has been known for decades (9). Compared with clomiphene, the risk of multiple-pregnancy is lower with letrozole.

Metformin is an anti-diabetic agent which improves insulin sensitivities in glucose deposit organs, such as skeletal muscle and fat. This is based on the theory that increasing insulin sensitivity can reduce serum androgen levels thus improving fertility, therefore metformin has been widely prescribed for women with obesity and insulin resistance to aid pregnancy(10-12). Some evidence suggests that metformin seems to offer some than clomiphene therapy, whereas others also have shown similar effects of both therapies to induce pregnancy (13). However, for morbidly obese women, lifestyle modification to lose weight is still recommended prior to any of these two treatments, as weight loss can improve the sensitivity to such treatments (14, 15).

Nevertheless, exogenous gonadotrophin preparations are the next option for women who do not respond to resistant to the abovementioned therapies, in addition to surgical options, such as laparoscopic ovarian drilling.

Acupuncture as an alternative treatment option

Women with PCOS seek both fertility and symptom control, such as irregular menstrual cycles, amenorrhoea, insulin resistance, polycystic ovaries, androgen disturbance, hirsutism and/or acne. Current available pharmacological based therapies are associated with various side effects. It is getting very popular for women with PCOS to seek alternative therapy e.g., acupuncture in the treatment of PCOS among western countries. According to a review on 51 reports from 49 surveys conducted in 15 countries, there are remarkable stability in the rates of the population who are users of complementary and alternative medicine in Australia (49%, 52%, 52%; 1993, 2000, 2004) and USA (36%, 38%; 2002, 2007) (16). In Australia, it has been reported that 9.2% of the Australian population have used acupuncture according to a national population-based survey performed in 2005 (17). In the US, about 4.1% of the respondents of a national cross-sectional survey reported lifetime use and 1.1% (2.13 million) reported recent use of acupuncture (16).

Body acupuncture and ear acupuncture have been used as treatments for women with PCOS that have oligo/anovulation. Different sized sterile needles are used for body acupuncture by the stimulation of body acupuncture points through body needling. Ear acupuncture adopts either needles or pellets to stimulate the acupuncture points on the external ears. Electroacupuncture (also known as electrostimulation) is using electrical impulses of

acupuncture needles to stimulate acupuncture points. In RCTs of acupuncture, sham acupuncture/placebo acupuncture are used, which is to stimulate random place that is not the actual acupuncture point. However, how sham acupuncture should be performed still remains controversial and can be different from study to study. Some practitioners believe that even random point stimulation can have therapeutic effects, which yet to be proved by properly designed clinical studies.

Acupuncture is known to be a safe treatment. There are still some rare transient adverse effects, such as skin erythema, bruising, bleeding, and pain. Report of a significant complication is exceedingly rare. One observational study including more than 200,000 participants who received acupuncture for pain found an adverse event rate of 8.6% (18); while another similar study estimated that the serious adverse event rate is between 0 and 1.1 per 10,000 treatments (19).

Evidence of efficacy of acupuncture

The choices by the patients to use acupuncture are mostly by recommendation or traditional beliefs. There is uncertainty in the medical community regarding the efficacy of acupuncture for oligo/anovulatory women with PCOS. This is largely due to the absence of high-quality RCTs. Most of the research on the efficacy of acupuncture has been carried out in China, where the control/sham treatment have not been properly controlled in most trials (20). Such studies were also published in Chinese journals, making it difficult to access by non-Chinese speaking clinicians. In addition, most of such studies employed the combination of acupuncture, herbal decoction/pill, and moxibustion, without adopting proper sham control for these approaches, which makes it difficult to interpret the outcome and separate the individual effects.

Several reviews including our own Cochrane review make it easy to have an overview of the currently available evidence. From a clinical point of view, the management of PCOS has been an evolving area where current paradigms were continuously challenged with novel modalities. This reviews addressed both women with PCOS who seek fertility and those that seek symptom control, which can provide an objective basis for healthcare practitioners to recommend acupuncture treatment for women with PCOS.

There is a limited number of clinical studies on acupuncture using RCT design to study its efficacy on oligo/anovulation in women with PCOS. A recent Cochran review published by our

group systemically examined 8 RCTs with 1546 women (2). The diagnostic criteria of PCOS in this Cochran review were based on the ESHRE and ASRM consensus in Rotterdam in 2003, which is any woman with two of the three listed criteria as having PCOS, namely oligo or anovulation, hyperandrogenemia or polycystic ovaries. In those RCTs, acupuncture (or electroacupuncture) was compared to no treatment, sham acupuncture, lifestyle intervention (relaxation, physical exercise), and conventional treatment of PCOS (e.g. clomiphene, Diane-35). Although various bias has been identified in different studies, overall, acupuncture along seems have only a marginal improvement in achieving pregnancy and birth than sham acupuncture. However, intermenstrual days were significantly improved by acupuncture compared with the sham acupuncture, suggesting some physiological impacts of the needling. The outcome of using acupuncture in conjunction with any other interventions is inconclusive though, mainly due to the low power of the RCTs available for this review. Therefore, more quality RCTs using high power design are needed in future research.

However, our Cochran review excluded any study using Chinese herbals or moxibustion. There have also been a few systemic review and meta-analysis of the RCTs on acupuncture, which also take into consideration the combination of acupuncture and herbal medicine and/or moxibustion, with or without the use of conventional pharmaceutical treatment. Several meta-analyses papers suggest that the best effect occurs when acupuncture was combined with Chinese herbal medicines, moxibustion treatment, or conventional pharmaceutical treatment (20, 21). Such approaches can exert better effect than conventional pharmaceutical therapy or Chinese herbal medicine alone to reduce serum luteinizing hormone/follicle-stimulating hormone, insulin resistance, testosterone, and body mass index (20, 21). Similar to our Cochran review, both papers acknowledged certain biases in the included papers with low power.

In addition to body meridian points, ear points are also widely adopted by Chinese medicine practitioners. In a clinical trial on 45 infertile women with dysfunction of ovulation, ear acupuncture showed a comparatively better effect than conventional medical treatment (e.g. dexamethasone, clomiphene citrate, and gonadotropin) in restore menstruation (22). The pregnant rate was similar between the two groups.

The treatment effect of acupuncture seems to last even after the sessions being completed. Stener-Victorin reported that the effect of electroacupuncture treatment on ovulation induction

lasted for up to three months in two-thirds of the participants with PCOS(23). Same as the most studies in this area, the power was small with only 24 patients. Larger scale clinical trial is needed to confirm this post-effect.

Links between acupuncture meridians and modern physiology

Acupuncture has been considered as a nonspecific physical stimulation, which restores body function by inducing the activation of multiple regulating systems, not the disease itself (24). Clinically, the selection of acupuncture points varies from practitioner to practitioner although they are based on similar traditional Chinese medicine principles. However, scientific studies can still conclude an overall link between acupuncture meridians to neuro-innervation, endocrine and immune functional modulation (24-26).

One theory is that acupuncture induces an inflammatory response in the surrounding tissue which further activates signalling pathways in the neural, endocrine and immune systems (25). It is believed that these three systems work integratory as a network. Via the skin, a neuroimmunoendocrine organ, any exogenous stimuli on the skin can further activate the neuro–endocrine-immune network, in order to neutralise any harmful impact and restore the internal homeostasis (24). Acupuncture certainly firstly stimulate the nervous system by inducing the sensation of soreness, numbness, heaviness, which is different from a random point puncture. Such stimulation can also activate certain brain regions, especially the cortex, which further affect the innervation to the treatment targeting area/organ (24-26).

In addition to the classical neurotransmitters (eg. catecholamine, and acetylcholine) released by central and peripheral nerves, acupuncture can also affect the endocrine system via the hypothalamus–pituitary–adrenal axis, hypothalamus–pituitary–gonadal axis, and hypothalamus–pituitary–thyroid axis. Mayer et al. proposed that acupuncture may stimulate the production of endorphin, an effect antagonised by naloxone, as the mechanism of providing analgesic effects (27). The presence of beta-endorphin was found in the follicular fluid from both normal and polycystic ovaries (28), which has been found to be increased during ovulation in healthy women, which is follicular fluid specific (29). Studies in both animal model and humans with PCOS have shown that acupuncture can modulate central and peripheral beta-endorphin production and secretion, to affect the release of GnRH and gonadotrophin (30). Different non-randomised clinical studies have also provided the evidence that acupuncture can stimulate the release luteinising hormone, follicle-stimulating hormone, progesterone, and

oestradiol in normally ovulating women, however, normalise their levels in women with ovulating dysfunction, including those with PCOS (31-33). This may be related to the impact of acupuncture stimulation to normalise the hypothalamic-pituitary ovarian axis, which in turn restore the menstruation cycle pattern in women with PCOS (24, 25, 34).

Conclusion

From limited evidence-based studies, acupuncture does show some efficacy in managing PCOS-related symptoms, including the induction of ovulation and restoration of menstruation, without the evidence on promoting pregnancy rate. However, most studies had a small sample size and no comparable sham controls. Future studies are still needed and take into consideration of these issues in the experimental design.

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Conflicts of interest

The authors declare no conflict of interest.

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* of special interest

** of outstanding interest

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