SOUTH BAYLO UNIVERSITY

The Use of Acupuncture in the Treatment of Polycystic Ovarian Syndrome (PCOS) – A Review

by

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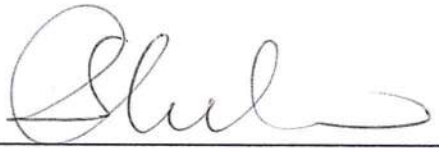

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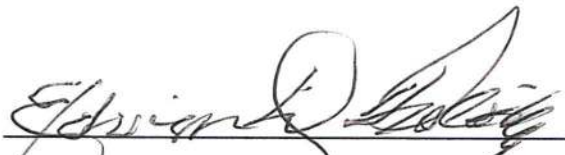

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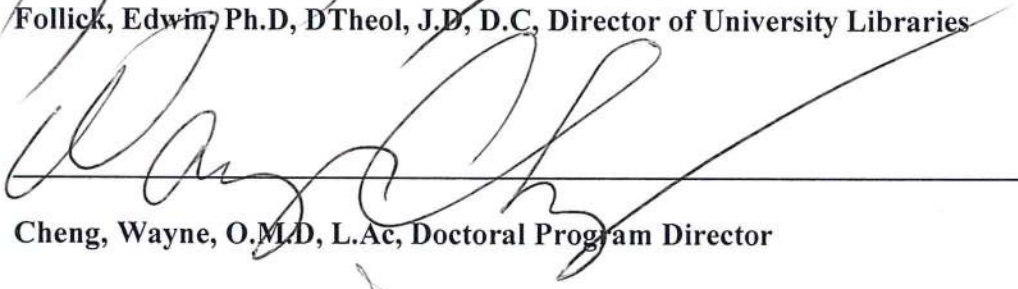

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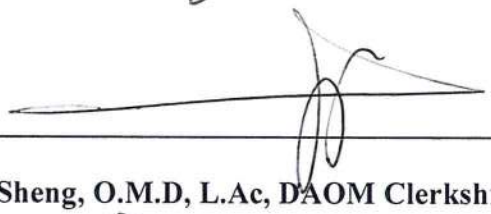

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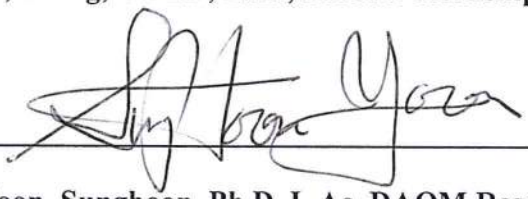

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Abstract

Polycystic Ovarian Syndrome (PCOS) is the most common endocrine related disease in reproductive age women. PCOS hinders many women's ability to conceive and puts women at a higher risk for metabolic disorders and certain cancers. The purpose of this study is to evaluate existing research on the treatment of PCOS using acupuncture as it pertains to menstruation, ovulation, hormone levels, and fertility. A narrative review was conducted by performing a comprehensive search for existing research on four major electronic databases. This review resulted in determining that several studies showed acupuncture can improve ovulation rate, menstrual frequency, and improve hormone levels. These results can have positive implications for fertility problems in women with PCOS. While there is some significant evidence that acupuncture can positively affect these factors, more thorough and well-designed randomized control trials are needed.

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During my seven year journey at South Baylo University, I have come across many great teachers, mentors, colleagues, friends, and patients as I navigated through both the Masters and Doctoral programs in the wonderful world of Oriental Medicine. I can honestly say I have learned so much from the unique collection of people with whom I have crossed paths during this great journey.

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I would not have had the strength, will, and courage to accomplish all that I have without the loving support of my entire family. I wholeheartedly thank my wife, Danae, without whom I would not have been able to push through all these years of academic life. I also thank my brother Roy who is a critical piece to our little family unit.

I dedicate this work to my wife and my son, Kaison, who may not even be here had I not gone through the wonderful journey of learning Acupuncture and Oriental Medicine. You are my inspiration.

Table of Contents

I. Introduction

Polycystic ovarian syndrome (PCOS) is defined by the Mayo Clinic as an endocrine disorder that occurs in women of reproductive age. The onset is usually soon after menarche. Sufferers of PCOS typically have enlarged ovaries that contain follicles, or small collections of fluid (Mayo Clinic, 2014). The most common characteristics of PCOS include irregular menstruation (amenorrhea, oligomenorrhea), anovulation, hirsutism due to hyperandrogenism and polycystic ovaries. PCOS is the most common endocrine disorder in the world, affecting as much as 15-20% of the female population (Sirmans & Pate, 2014; Goodman et al., 2015). Treatment of PCOS primarily relies on the prescribing of synthetic hormones using oral contraception. Because many women with PCOS do not have regular ovulation or menstrual patterns, it greatly affects reproductive age women's chances of conceiving. It would be prudent to offer the public less invasive alternatives such as acupuncture and Chinese Herbal Medicine (CHM). This literature review is to summarize and evaluate existing research on the use of acupuncture in the treatment of menstrual and ovulatory dysfunctions in women with PCOS.

The primary physiological identifiers for PCOS are insulin resistance and elevated luteinizing hormone (LH). These two factors seem to work together, causing ovarian overgrowth, ovarian cyst formation and hyperandrogenism (Pannill, 2002). Other symptoms as a result of hormonal and endocrine dysfunction include signs such as infertility, anovulation, hirsutism and dysglycemia. 50-70% of women with PCOS display insulin resistance, which lead to other issues such as diabetes, hypertension, hyperlipidemia and weight gain (Sirmans & Pate, 2014; Goodman et al., 2015). Acne, alopecia, depression and anxiety are also commonly experienced. Infertility is one of the larger concerns for reproductive-age women who hope to conceive.

Western Diagnosis and Treatment

In diagnosing PCOS, it is important to first look at family history and genetics. Approximately 20-40% of PCOS patients have first degree relatives that have PCOS (Rotstein, 2012). A family history of hirsutism, acne, alopecia, menstrual irregularities, or infertility can be important clues toward a possible diagnosis. When looking at hirsutism, however, ethnicity should be considered as some groups tend to have more hair than other groups. For example, normal Mediterranean women may have more hair in their face, torso and extremities, whereas Asian women usually have very little hair in those same areas (Pannill, 2002). A personal medical history of menstrual irregularities, pregnancies and miscarriages should also be considered.

Diagnostic methods include physical exam, pelvic exam, blood tests and ultrasound imaging. A pelvic exam may result in finding clitoromegaly and pelvic masses where bilateral masses would be consistent with PCOS. Unilateral masses may point toward possible neoplasms (Pannill, 2002). PCOS patients' blood tests show elevated LH levels and decreased Follicle Stimulating Hormone (FSH) levels. Normally, the LH to FSH ratio should be 1:1. The LH to FSH ratio in PCOS women can be up to 3:1 (Pannill). This high ratio can contribute to elevated androgen production. Transvaginal pelvic ultrasound is used for radiologic identification of cysts. It should be noted that not all women with PCOS demonstrate polycystic ovaries. Conversely, healthy women who don't have PCOS may present with cysts. The normal volume of ovaries is between 4.7-5.3 cm^3. The volume in PCOS women is usually more than 10 cm^3 (Pannill).

Diagnostic standards have been provided by three groups: the National Institutes of Health/National Institute of Child Health and Human Disease (NIH/NICHD), the European

Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) and the Androgen Excess and PCOS Society (Sirmans & Pate, 2014). While all three provide similar parameters, they do offer slightly different requirements. This results in slightly different epidemiological prevalence reports, depending on the standards being used.

A differential diagnosis is important so that other diseases are ruled out as causes for key PCOS symptoms. Pituitary (pituitary adenoma) and thyroid dysfunction/disease (hyperthyroidism, hypothyroidism) should be ruled out as the cause of irregular menstruation by testing for prolactin and Thyroid Stimulating Hormone (TSH) levels. Neoplasms, which can increase androgens, should be ruled out before a PCOS diagnosis. Specifically, elevated testosterone and dehydroepiandrosterone sulfate (DHEAS) are caused by androgen-producing neoplasms. DHEAS is mainly released by the adrenal glands. Levels > 800 mcg/dL suggest a virilizing adrenal tumor. Testosterone levels of > 200ng/dL are not usually seen in PCOS and may point toward a virilizing tumor (Pannill, 2002). Cushing's disease should be ruled out as a possible cause of hirsutism. Other disorders that can be associated with menstrual irregularities that should be ruled out include pregnancy, premature ovarian failure, rapid weight loss, extreme physical exertion and low body mass index (BMI) from eating disorders (Pannill).

Treatment for PCOS focuses on the management of androgen related symptoms by using oral contraception (OC), which helps decrease the production of androgens. The progesterone in OC helps protect the endometrium from unopposed estrogen. OC suppresses ovarian, adrenal, and peripheral androgen metabolism, which results in reduction of serum testosterone. OC also decreases testosterone levels by suppressing LH levels. Lower LH levels decrease testosterone production in the ovaries. Additionally, OC can help with acne and hirsutism by inhibiting 5 alpha-reductase in the skin, Women who are not good candidates for OC (hypertensive,

smokers), may be prescribed progestin. Progestin will help protect the over-exposure of the endometrium to estrogen (Pannill, 2002).

Because of the close tie of insulin resistance and PCOS, many doctors prescribe metformin, a medication usually prescribed for type II diabetes. It is important to note metformin does not directly treat polycystic ovaries. Instead, it is applied to target symptoms that coexist with PCOS. Metformin lowers insulin levels, helps increase insulin sensitivity and ultimately decrease androgen levels (Sirmans & Pate, 2014). In one case series, Zelija (2013) evaluated the effects of metformin treatment on the endocrine system in women with PCOS. In this study (uncontrolled, non-random), it was reported that there was a reduction of women with oligo/amenorrhea from 69% of participants down to 20%. Zelija concluded that metformin significantly improved insulin resistance, hormone levels (PRL, LH, LH to FSH ratio), hirsutism, and menstrual frequency. In a systematic review and meta-analysis by Lord, Flight, and Norman (2013), they found that metformin is an effective first-line treatment for anovulation in PCOS women. In their review, however, Lord et al. found metformin was linked to a high rate of side effects. Metformin is linked to some unpleasant side effects such as gastrointestinal disturbances, weight loss and headache. It can also lead to more serious side effects such as lactic acidosis, anemia and hypoglycemia (Slowiczek, 2016).

Reproductive age women with PCOS who have issues with ovulation/menstruation and hyperandrogenism may have some difficulty with conception. Infertility is of great concern for women who fit this description. Treatment of infertility in women with PCOS usually entails promoting ovulation activity, primarily using clomiphene (Sirmans & Pate, 2014). Aside from women who may be resistant to clomiphene, it may produce side effects such as abnormal bleeding, headache, digestive disturbances, pelvic or abdominal pain. Serious side effects include

ovarian hyperstimulation syndrome (OHSS), shortness of breath, seizures, strokes or chest pain. (Cunha, 2016) Clomiphene also increases the likelihood of multiple births.

Ayaz, Alwan, and Farooq (2013) performed an RCT comparing clomiphene treatment of infertility with PCOS versus a combination treatment of metformin with clomiphene. While both treatments succeeded in helping women conceive, the group that received the combination treatment displayed higher rates of conception than the group that received just clomiphene (62% versus 29%, respectively). The combination group also displayed higher ovulatory and menstruation rates than the clomiphene group. Based on their RCT, Ayaz et al. suggest using the combination of the two drugs as first line therapy. However, the researchers were vague in the reporting of side effects.

TCM and PCOS

In TCM gynecology, ovarian cysts fall under the general category of abdominal masses. According to the "*The General Treatise on the Etiology and Symptomatology of Diseases*", AD 610 (Maciocia, 1998), abdominal masses are caused generally by poor regulation of hot and cold. Abdominal masses can be classified into qi, blood or phlegm types. Qi masses change location and involve distending pain that comes and goes. Blood masses are immovable with fixed stabbing pain. Phlegm masses are soft masses in a fixed location but do not involve any pain. All masses involve an underlying qi deficiency that is characterized by the inability to carry out the transportation and transformation function of qi, which sets the stage for the accumulation of qi and blood (Maciocia, 1998).

The etiology of abdominal masses includes emotional stress, diet and external pathogenic factors. Emotional stress stagnates liver qi, which then impairs blood and causes blood stasis. Eating cold and/or greasy foods will lead to damp and eventually phlegm. Cold can invade the lower abdomen which will then impair blood circulation, eventually leading to liver blood stasis. Damp can invade channels of the lower leg, which eventually can become phlegm. This phlegm accumulation becomes a mass. Ovarian cysts, specifically, are caused by external pathogen attack during menstruation or following childbirth, especially attack from damp heat or phlegm, both of which lead to blood stasis. With ovarian cysts, the treatment approach is to resolve phlegm and damp, clear heat, invigorate blood, eliminate stasis and soften hardness (Maciocia, 1998).

When considering polycystic ovarian disease, it is associated with underlying kidney yang deficiency. When a woman's body is deficient in kidney yang, the body is unable to warm and transport fluids in the lower burner. This lack of water movement leads to accumulation of damp, and eventually phlegm. The accumulation of damp or phlegm eventually becomes a cyst. If the cyst formation disrupts blood circulation, it may turn into a blood type cyst. General pathology of ovarian cysts and polycystic ovarian cysts are the same with the added background of kidney yang deficiency in PCOS. Maciocia (1998) states that PCOS is mainly identified by a constitutional deficiency of the kidneys, which is at the root of the development of cysts.

While kidney yang deficiency is associated with most PCOS patients, further differentiation needs to be made. First, there can be kidney yang deficiency with dampness/phlegm. According to Maciocia (1998), signs and symptoms may include amenorrhea, history of infertility, scanty periods, obesity, hirsutism, a feeling of oppression of the chest, heavy sensation in the abdomen, excessive vaginal discharge, a pale tongue with a sticky-white

coating, and a weak and slightly slippery pulse. In such cases, the treatment principle is to warm and tonify kidney yang, while resolving dampness and phlegm. Secondly, there can be kidney yang deficiency with phlegm and blood stasis. This pattern shares all the same symptoms except with the key added symptom of pain in the abdomen. This pain is in a fixed location and the quality is sharp or stabbing. The tongue will be pale purple or bluish purple, with sticky and white coating. The pulse will also be weak and slightly slippery. The treatment principle is to warm and tonify kidney yang, while resolving phlegm, invigorating blood and removing stasis. The main ways to differentiate between the two patterns are the tongue and the presence of sharp abdominal pain (Maciocia).

As described above, some of the options for treatment of PCOS with conventional western medicine involve pharmaceutical drugs with unpleasant side effects. It is important to treat PCOS because women with PCOS are at a higher risk for metabolic disorders (diabetes mellitus, dyslipidemia, CAD) and certain cancers (ovarian, uterine). Diagnosis is difficult, and the cause is usually idiopathic. This results in a diagnosis which rely on the exclusion of other diseases. It is worth exploring using Traditional Chinese Medicine (TCM) philosophies as an alternative to hormone altering and side effect inducing pharmaceuticals. Either acupuncture, Chinese Herbal Medicine (CHM) or a combination thereof, may be a safer alternative to side effect causing drugs, especially to women who desire to conceive.

In this narrative review, existing research that studied acupuncture in treatment of ovulatory, menstrual and fertility problems in women with PCOS was evaluated. This study provided a summary of treatment protocols and results to practitioners who may treat patients

with PCOS. The primary significance and purpose of this study is to provide an updated review on the current evidence of using acupuncture to treat PCOS.

II. Literature Review

Randomized Controlled Trials

In an RCT performed by Johansson et al. (2013), they investigated whether acupuncture had an effect on improving/increasing ovulation frequency in women with PCOS. Because elevated Luteinizing Hormone (LH) levels are closely tied with anovulation, the main outcome measurements used were changes in LH secretion and pulsatility, and ovulation frequency. Secondarily the team also looked at changes in sex steroid hormone levels. In this trial, researchers randomized treatments for 32 qualifying women over a 10-13 week period.

Because sham acupuncture has been shown to be an ineffective control (Johansson et al., 2013), study administrators randomly assigned study participants to meet with a therapist to serve as the control group. The rationale for selecting this as a control was so the control group would receive the same amount of attention as the experimental group. Participants were selected based on inclusion criteria such as confirmed polycystic ovaries, oligo/amenorrhea and hyperandrogenism related symptoms of hirsutism and excessive acne. After baseline measurements were taken, each participant underwent an intervention period of 10-13 weeks. Measurements were taken again at the end of the intervention period.

Participants in the control group met with therapists for 30 minutes, twice a week, where they were treated with similar amounts of attention as the acupuncture group. The acupuncture group was treated for 30 minutes, twice a week, with two alternating treatments. The same two alternating treatments were performed throughout the study. Low frequency electroacupuncture or manual stimulation was performed on select points. The first set of points included electrical stimulation on Conception Vessel (CV) 3, CV 6, Stomach (ST) 29, Spleen (SP) 6, and SP 9. Manual acupuncture was applied to Governing Vessel (GV) 20 and Large Intestine (LI) 4. The

second set of points included electrical stimulation on ST 25, ST29, SP 6, and Liver (LR) 3. Manual acupuncture points used were CV 3, CV 6, Pericardium (PC) 6, and GV 20. Because there was no decrease in LH, it could not be linked to the increased frequency of ovulation in the acupuncture group (Johansson et al., 2013). Instead, an overall decrease in androgens (testosterone) was linked to the increase in ovulation frequency.

Pastore, Williams, Jenkins, and Patrie (2011) evaluated whether acupuncture increases ovulation frequency and normalizes hormones in comparison to sham acupuncture in women with PCOS. This study was a randomized, double blind, controlled clinical trial. Reproductive-age women diagnosed with PCOS, and who have not had any hormonal interventions in the last 6 months, were chosen for the study. Biological testing and questionnaires were administered at baseline, every week during the two-month active portion of the study, and three months after completion of the study. The measurement outcomes included LH, Follicular Stimulating Hormone (FSH) levels, and ovulation frequency.

The same acupuncture points were applied to all patients in the acupuncture group. Electrical stimulation was performed on Bladder (BL) 23, BL 28, SP 6, and SP 9. Manual stimulation acupuncture was performed on PC6, Triple Energizer (TE) 5, and GV 20. For the sham-controlled group, standard points on non-meridian, non-acupuncture point locations were applied. 84 qualified participants completed the study: 40 in the acupuncture group and 44 in the sham-acupuncture group. All participants received treatments twice a week for the first 4 weeks, then weekly treatments for the following 4 weeks, for a total of 12 treatments.

This study by Pastore et al. (2011) did not show any difference in results between true acupuncture and sham acupuncture. However, women in both groups overall saw an increase in both ovulation and menstrual period frequencies. In a systematic review by Johansson and

Stener-Victorin (2013), they referenced the Pastore et al. study results, saying the results showed that sham acupuncture application was not inert, and did not necessarily display a lack of response to true acupuncture.

Rashidi, Tehrani, Hamedani, and Pirzadeh (2012) investigated whether acupuncture can improve the success rate of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in women with PCOS. This RCT studied 62 women, 31 women in the control arm and 31 women in the intervention arm. Both groups treated with standard infertility practices of ovarian hyperstimulation, ovum pick-up (OPU) and IVF/ICSI procedures. The intervention group received acupuncture as an adjunct to the aforementioned procedures.

A total of 5 acupuncture treatments were performed on all 31 women acupuncture participants. The 1st treatment was performed on day 21 of the menstrual cycle. The 2nd treatment was on the first day of ovarian stimulation, the 3rd treatment was performed 2 days before OPU, and the final two treatments were performed immediately before and after embryo transfer. The points used in the first three treatments were LI 4, SP 6, LR 3, CV 4, GV 20, ST 36, and auricular ovary and uterus points. For the last two treatments, the pre-embryo transfer (ET) and post-ET treatments, the acupuncture points used were LR 3, SP 10, PC 6, ST 29, and the auricular shenmen point. All points in both treatment sets were applied bilaterally. While the authors reported applying electroacupuncture, they did not specify the specific points nor the frequency at which it was applied.

Based on results, Rashidi et al. (2012) were able to conclude that acupuncture may help with embryo quality, which may be beneficial to IVF patients. They recommended, however, that prolonged acupuncture treatment 3-4 months prior to starting assisted reproductive

technology treatments. The additional treatments may result in improvements in other parameters that were considered in this study.

In an RCT, Jedel et al. (2011) compared the effects of low-frequency electroacupuncture on hyperandrogenism and oligo/amenorrhea versus physical exercise and no intervention in women with PCOS. A total of 84 women participated in the study. Participants in the three arm RCT were treated for 16 weeks, with pre and post intervention observations. Those in the electroacupuncture group were given 14 treatments over 16 weeks with varying frequencies: twice a week for 2 weeks, weekly for 6 weeks and biweekly for 8 weeks. Low frequency electroacupuncture (2Hz) was applied to the following points: CV 3, CV 6, ST 29, SP 6, and SP 9. Needles were inserted into LI 4 and PC 6 without electroacupuncture. They were manually stimulated every 10 minutes during needle retention. With the exception of CV 3 and CV 6, all points were applied bilaterally. The outcome measurements were menstrual frequencies and concentrations of total testosterone, estrogen, androgens, androgen precursors and androgen metabolites.

Overall, the low-frequency electroacupuncture intervention was more effective than physical exercise in increasing menstrual frequency and in reducing testosterone. Both interventions were more effective than no intervention in increasing menstrual frequency and in reducing testosterone, although any changes in the no intervention group were not significant.

Case Series

In a case series (uncontrolled, prospective) study performed by Stener-Victorin et al. (2000), 26 women were treated with electroacupuncture over a course of 8-10 weeks. They were treated twice per week for the first 2 weeks, then weekly for the remaining weeks. They were

given the following uniform treatment: low frequency electroacupuncture stimulation (2 Hz) on BL 23, BL 28, SP 6, and SP 9 acupuncture with manual stimulation on PC 6 (unilateral), TE 5 (unilateral), and GV20. Blood samples were taken from all participants in 3 different time points: 1 week before the first treatment, 1 week after the last treatment and 3 months after the last treatment. Blood samples were tested for levels of LH, FSH, cortisone, testosterone, SHBG, insulin, TSH, T3, and T4. The study results concluded that electroacupuncture may help women increase ovulation frequency.

Qualitative Study

Billhult and Stener-Victorin (2012) performed a qualitative study to describe the experience of acupuncture for women who were subjects in the RCT by Jedel et al. (2011) that was reviewed above. They recruited 8 women from that study to participate in an interview approximately 6 months after the last electroacupuncture treatment. They interviewed the women independently and recorded their experience. Study administrators concluded that the 8 women who were interviewed had overall positive experiences by participating in the RCT, invoking feelings of hope and accountability.

Systematic Review & Meta-analysis

In a systematic review, Lim et al. (2010) evaluated the effectiveness and safety of acupuncture in treating oligo/anovulation in women with PCOS. They evaluated 5 RCTs that included a combined total of 413 women. The studies included a variety of parameters that included clinical pregnancy, ovulation rate and menstrual frequency. While their primary measurements included live birth rates and ovulation, they did not encounter any studies that

recorded live birth rates. Lim et al. concluded that only a limited number of RCTs have been published and that there is not enough significant evidence to suggest the use of acupuncture to treat ovulatory disorders in women with PCOS.

Jo, Lee, and Lee. (2017) administered a meta-analysis and systematic review on existing studies that examined the use of acupuncture, electroacupuncture or a combination thereof, in treatment of PCOS and its related dysfunctions. The type of RCT studied made comparisons of treatment acupuncture to groups with either no treatment, pharmaceutical intervention or sham acupuncture. The majority of evaluated studies were reported in Chinese.

Jo et al. (2017) found no significant results for ovulation in sham-controlled studies. In acupuncture versus no treatment, they found evidence for improvement in ovulation rates, menstruation rates and testosterone levels in the acupuncture groups as compared to the groups with no treatment. In comparing acupuncture versus pharmaceutical intervention studies, none studied and compared ovulation rates. There was a low level of evidence of improvement in menstruation rates and testosterone levels in the acupuncture group in comparison to the groups that only received metformin treatment. In studies where all participants were medicated, acupuncture groups were compared to sham acupuncture groups. These studies also did not evaluate ovulation frequencies. Studies found evidence of improved LH levels, LH to FSH ratios and insulin levels in the acupuncture groups. Lastly, Jo et al. compared studies that tested acupuncture with medication versus just medication alone. None tested for ovulation or menstruation frequencies. These studies yielded significant improvement in LH levels, LH to FSH ratios and testosterone levels.

Jo et al. (2017) concluded the evidence for supporting benefits of using acupuncture to improve ovulation and menstruation is weak. They site poor reporting and methodologies as

reasons for weak evidence. While the object of the study was to evaluate acupuncture for effects of acupuncture on ovulation and menstrual rates, they found that not many studies evaluated those parameters specifically. For those studies that did show improvement in ovulation and menstrual rates, it was at a low level of evidence. They also found some benefit to hormonal levels when acupuncture was used as supporting treatment to medication. However, evidence was either at a low or very low level. They used GRADE guidelines to determine the quality of evidence.

Jo and Lee (2016) performed a meta-analysis and systematic review to investigate the effectiveness of helping women with PCOS achieve pregnancy with acupuncture as an adjunct therapy to IVF or ICSI. Jo and Lee selected 4 RCT that met their inclusion criteria. 3 out of 4 were reported in Chinese. Primarily, they looked at clinical pregnancy rate (CPR) and live birth rate (LBR) as outcome measures. Secondary measures looked at Ongoing Pregnancy Rates (OPR) and OHSS rates.

Jo and Lee (2016) found that all 4 studies collectively showed a significant increase in LBR in the acupuncture intervention groups versus the non-acupuncture groups. Due to the restriction in number of studies, they were unable to significantly report the benefit of acupuncture with increasing CPR. Additionally, they compiled significant data that showed acupuncture improves OPR and decreases OHSS rates.

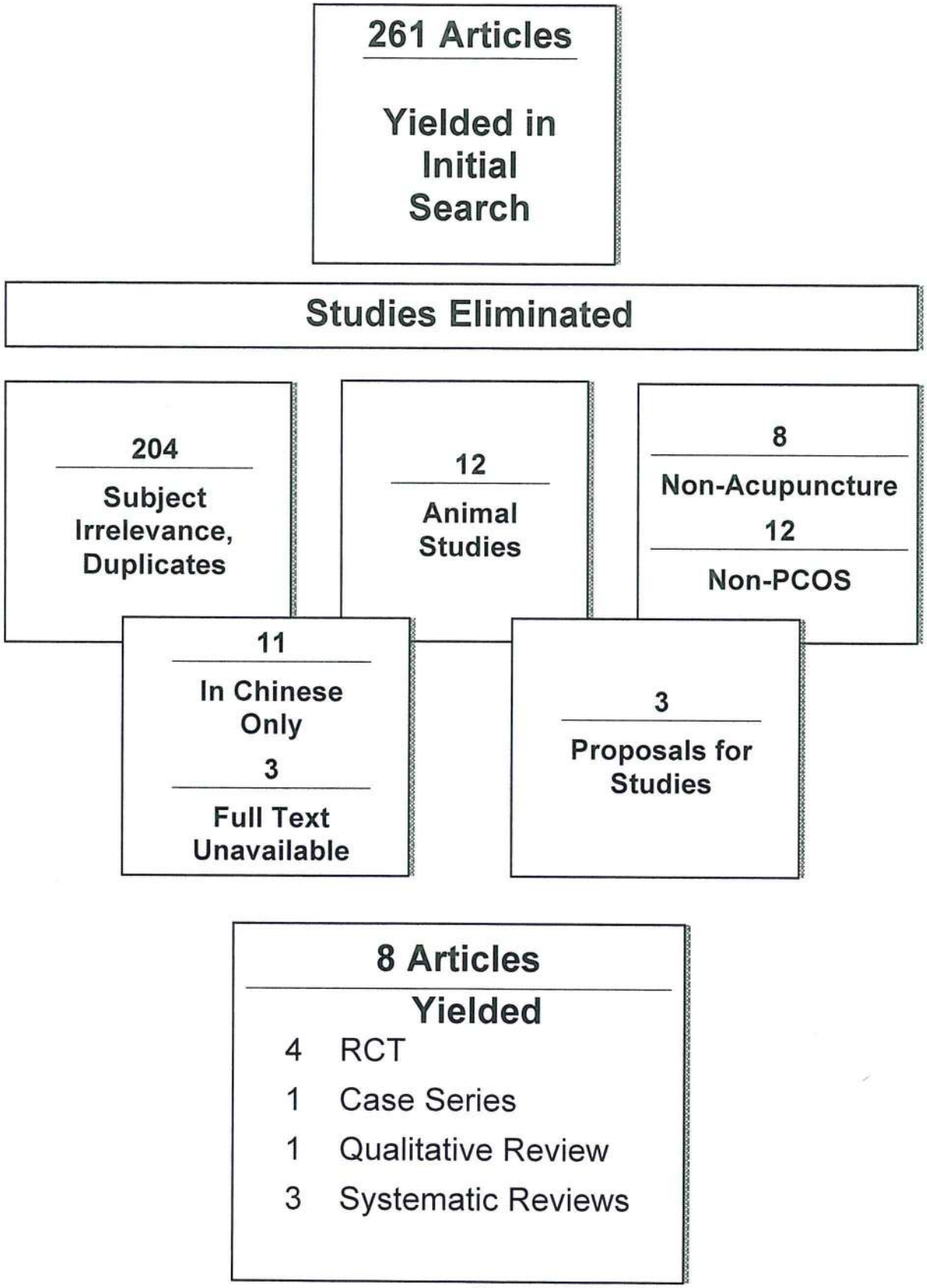
III. Materials and Methods

Literature Search Strategy

Four electronic databases were used for literature selection: the Cochrane Central Register of Controlled Trials, PubMed, EBSCO and Alt Health Watch. A comprehensive search of databases was executed using the key words "polycystic ovarian syndrome and acupuncture," "polycystic ovarian syndrome and TCM," "PCOS and acupuncture, and "PCOS and TCM."

The initial search yielded 261 total articles. Many articles that came up in the search had no relevance to acupuncture. From an initial scan on article titles and abstracts, 204 were eliminated based on subject relevance. Duplicates were also eliminated. Of the remaining 57 articles, 12 animal studies were eliminated. 8 others were PCOS eliminated because they did not involve acupuncture. An additional 12 were excluded because the studies were not about PCOS. Of the remaining 25 articles, 11 were available only in Chinese and full text versions were not available for 3 articles. Of the remaining 11, 3 were only proposals for future RCTs and were without study results. A final total of 8 relevant studies were identified and chosen for this review. Of the 8 articles, 4 of them were RCTs. 1 uncontrolled trial/experimental case series was also chosen. A total of 4 reviews were included: 3 systematic reviews (2 of them meta-analyses) and 1 qualitative study. See Figure 1 for a summary of the selection process.

Figure 1. Article selection flow chart



Inclusion Criteria

The types of studies that were allowed in the search process included RCTs, uncontrolled clinical trials, prospective case series/studies, systematic/meta-analysis reviews, literature reviews and qualitative studies. Only English language studies were included. There was no discernment made between manual acupuncture and electroacupuncture studies as both types of interventions were included. In summary, the inclusion criteria were studies performed between January 2007 and September 2017, studies reported in full text English articles that were peer-reviewed and studies involving human subjects who were treated with acupuncture or electroacupuncture for PCOS related symptoms.

Exclusion Criteria

Studies more than 20 years old were excluded. Studies from articles without full text availability (abstract only) were also excluded. Although some animal studies provided some interesting insight and results, they were excluded from this review. Any opinion articles, blog entries and non-scientific, non-peer reviewed articles were excluded. Studies involving laser acupuncture, acupressure or auricular acupuncture were excluded. Additionally, studies involving gynecological issues other than PCOS were excluded. A total of 3 promising protocols for randomized control trials (RCT) were found. However, since the data from the studies had not yet been reported at the time of search, they were not included.

Study Evaluations

The study design is a narrative review. Based on the exclusion and inclusion criteria, full-texts of the eligible studies were obtained from one of the four aforementioned databases and

reviewed. They were categorized based on their study types: RCTs, systematic reviews/meta-analyses, case series, and qualitative studies. The data of the studies were extracted and compared. The following items were extracted and reported: author(s), study design, number of subjects, publication year, outcome measures and major results (with p value).

IV. Results and Discussion

Randomized Control Trials

In the study by Johansson et al. (2013), ovulation frequency at baseline did not differ between the acupuncture and control groups. After interventions were applied, study administrators found that the acupuncture group displayed higher ovulation frequency than the control group. The acupuncture group displayed 0.76 ovulations per month while the attention group displayed 0.41 ovulations per month. Johansson et al. showed that women who received acupuncture treatments resulted in higher ovulation frequency than women who did not receive acupuncture treatments, and only received therapy sessions. However, there was no significant change in LH levels throughout the study.

Johansson et al. (2013) hypothesized the acupuncture treatments would decrease LH levels, which would therefore increase ovulation frequency. While the study resulted in slightly lower LH levels (-6%) and LH to FSH ratio (-18%), they were not significant. However, improvements in testosterone and free testosterone levels decreased significantly 23% and 33%, respectively. Based on these results, it may be concluded that the acupuncture intervention improved ovulation frequency as a result of the decrease in testosterone levels, and not as a result of the decrease in LH levels.

The study by Pastore et al. (2011) did not result in differing ovulation frequencies between the control and experimental groups. The rate of ovulation in the acupuncture group was 0.37 ovulations per month, and 0.40 ovulations per month in the sham acupuncture group. The menstrual rate between the two groups did not differ much either, both showing improvement over the course of the study. The acupuncture group showed an improvement from 0.5 cycles per month to 0.6 cycles, but was not statistically significant. The sham acupuncture group showed an

improvement from 0.42 cycles per month to 0.6 cycles, and was statistically significant. LH levels decreased similarly in both groups, thus improving the LH to FSH ratio.

LH levels decreased significantly 41% in subjects in the Pastore et al (2011) study. The LH to FSH ratio also improved significantly 32%. Because the increase in menstrual rate was not significant in the acupuncture group, it could not be correlated with the significant improvements in LH levels and the LH to FSH ratio. Although not significant, the LH levels and LH to FSH ratio decreased 37% and 32%, respectively, in the sham acupuncture group. The menstrual rate significantly improved 43% in the sham acupuncture group, versus just 20% in the true acupuncture group. Testosterone was not measured in this study.

Because of the mixed data, there cannot be a significant conclusion from the Pastore et al (2011) study in connecting lower LH levels to higher menstrual or ovulations rates. The large improvement of menstrual frequency in the sham acupuncture group brings to question the usefulness and inertness, or the lack thereof, of a sham acupuncture controlled study.

After 16 weeks of intervention in the Jedel et al. (2011) study, the low-frequency electroacupuncture group showed a significant increase in menstrual frequency from 0.28 to 0.41. The total testosterone decreased by 25% and total free testosterone decreased by 30%. Results for both measurements were statistically significant. At the 16 week mark in the physical exercise group, the menstrual frequency decreased from 0.26 to 0.14 but was not significant. Change in total testosterone was not significant but the free testosterone was significant with a 16% decrease. Any changes in the non-intervention group were not significant.

At the 32-week mark, the low-frequency electroacupuncture group displayed a significant increase in menstrual frequency from 0.28 (baseline) to 0.33. Significant changes in both testosterone (-18%) and free testosterone (-25%) occurred from baseline to the 32-week mark.

For the physical activity group at the 32-week mark, any change in menstrual frequency was not significant. Change in total testosterone was not significant but the free testosterone was significant with a 10% decrease. Changes in the non-intervention group were not significant.

Based on the results of the study by Jedel et al (2011), it can be concluded that acupuncture is more effective in increasing menstrual frequency and in reducing testosterone than both physical exercise and no intervention. However, a link cannot be made between LH levels and increased menstrual rates. Their data seems to point to a significant inverse relationship between decreased testosterone levels and increased menstrual rates. Further studies should be conducted to confirm or disprove the connection between testosterone levels and menstrual rates.

In the study by Rashidi et al. (2012), there were no significant results in all the outcome measurements with the exception of embryo quality. The embryo quality in the acupuncture group was significantly better than in the control group by 7%. The study did not result in any significant difference between the control group and intervention groups in number of oocytes, fertilization rates, pregnancy rates, or birth rates. The embryo quality was determined on a 0-4 scoring scale based on the shape of cells and fragmentation. This may not be considered a truly objective measurement as the quality score was determined by an observing examiner and not by an actual measurement. However, as the researchers suggested, a more meaningful study would involve prolonged treatment course prior to any assisted reproductive treatments.

Case series

The Stener-Victorin, et al. (2000) study resulted with 38% (n=9) of participants experiencing improved ovulation frequency. The baseline ovulation rate was 0.15 ovulations per month (per

woman). In the women who responded positively, the ovulation rate significantly increased to 0.66 ovulations. In the remaining 62% (n=15), there were no changes in ovulation frequencies. The mean LH levels decreased in all women throughout the study, although it was not statistically significant. However, the LH to FSH ratio decreased and was statistically significant. The rate decreased from 1.7 to 1.47 in all women. This can be an important indicator that even women whose ovulation frequency did not improve, continued treatment may have decreased their LH levels further and eventually increased ovulation frequency. This same treatment protocol was later reproduced in the sham-controlled RCT by Pastore et al. (2011).

It is important to emphasize that this study was not randomized or controlled. However, these type of studies can provide important guidance to subsequent RCTs. This study points to a possible correlation between increased ovulation rates with improved LH to FSH ratio and/or testosterone levels. While changes in LH and FSH levels were not significant, it is possible the LH to FSH ratio may be more important in inducing ovulation than the absolute values themselves. The results by Stener-Victorin, et al. (2000) points to that possibility.

Qualitative Study

The Billhult and Stener-Victorin (2012) qualitative study produced generally positive results. Some women experienced and reported skepticism that the acupuncture treatments had anything to do with improvement of symptoms. Others expressed surprise their bodies responded positively to the treatments. Another experience reported was the notice of a change in the symptoms associated with PCOS. Participants reported feeling like there were improvements in symptoms such as acne, mood, hair growth and menstrual bleeding. Some women expressed relief their body was closer to functioning normally by having regular menstrual periods. As they

experienced positive change, some expressed a sense of responsibility. Because diet and lifestyle can lead to obesity or being overweight, a common characteristic of women with PCOS, positive results instilled in some participants a sense of responsibility in their own well-being. They now felt they had to do more for a healthier lifestyle. The most impactful change was one of feeling hopeful that PCOS related symptoms could be managed or even eliminated. One notable aspect in feeling hopeful was in the prospect of being able to bear children.

A qualitative study like the one performed by Billhult and Stener-Victorin (2012) does not provide any useful numerical data to the medical research community. However, it may still be a valuable reference tool. For example, it may serve as an important reference when a potential human study is considered by an ethical review board. Additionally, it may serve as a tool to help educate PCOS patients when considering the various options for treatment. It can be especially important when there are patients who have displayed allergic or other adverse reactions to conventional pharmaceutical therapies.

Data Summary

With the exception of the RCT by Rashidi et al. (2013), all RCTs and case series included in this study utilized acupuncture points based on anatomical location and innervation. Though Rashidi et al reported using TCM style acupuncture, they did not offer further explanation of the selected points. Stener-Victorin et al. (2000) explained that many of the acupuncture points they selected were in areas common to the innervation of the ovary and uterus (Th12-L2, S2-S4). In addition, none of the studies followed the revised (STRICTA) Standards for Reporting Interventions in Clinical Trials of Acupuncture (MacPherson et al., 2010) guidelines in explaining the rationale of point selection. However, it is evident that western anatomy was applied in the point selection process.

Stener-Victorin (200) et al listed all the acupuncture points applied along with the segmental innervation and muscle location. For example, BL 28 is innervated by L4-5 and S1-3. The muscle locations are fascia thoracolumbalis and m. erector spinae lumbosacralis (Stener-Victorin). Pastore et al (2011) used the same exact treatment intervention as Stener-Victorin et al. Jedel et al (2011) reported the point selection using western anatomy per STRICTA guidelines but did not offer further rationale. Johansson et al. (2013) also listed their point selection based on innervation and muscle location. A summary of the points, innervation, and muscle locations reported by Stener-Victorin et al., Pastore et al., and Johansson et al. is included in Appendix B.

The following points were used in all five human studies examined in this review: SP 6 and PC 6. GV 20 and SP 9 were selected in four of the five studies. There were several other points that were used in three of the studies. While the points were selected based on western anatomy, it is highly likely TCM applications were considered. Firstly, the points use TCM

acupuncture nomenclature. Secondly, the majority of the points used for the studies are points many TCM practitioners may use to treat gynecological diseases such as PCOS. For example, both SP 6 and CV 3 is used in TCM to treat many gynecological diseases such as menstrual irregularities (dysmenorrhea, amenorrhea, menorrhagia), infertility, vaginal discharge, uterine bleeding and pain in the lower abdomen (Cheng, 2008). While these are just two examples, most of the points selected can be justified by TCM for the treatment of PCOS related disorders. A summary of the point selections used in all the studies reviewed above is shown in Table 1.

Table 1. Point selection for each study.

Study	Stener-Victorin et al. (2000)	Pastore, et al. (2011)	Jedel et al. (2011)	Rashidi, et al. (2012)	Johansson et al. (2013)
Points Selection – 1ST Set	BL 23*	BL 23*	CV 3*	LI4	CV 3*
	BL 28*	BL 28*	CV 6*	SP 6	CV 6*
	SP 6*	SP 6*	ST 29*	LR 3	ST 29*
	SP 9*	SP 9*	SP 6*	CV 4	SP 6*
	PC 6	PC 6	SP 9*	GV 20	SP 9*
	TE 5	TE 5	LI 4	ST 36	LI 4
	GV 20	GV 20	PC 6		GV 20
Point Selection – 2nd Set				LR 3	ST 25*
				SP 10	ST 29*
				PC 6	SP 6*
				ST 29	LR 3*
					CV 3
					CV 6
					PC 6
					GV 20

* Low frequency (2Hz) electro-stimulation was applied.

The RCTs reviewed above yielded in mixed significant outcome laboratory outcome measures of LH, LH to FSH ratio, testosterone level, ovulation frequency, and menstruation frequency. The Stener-Victorin et al (2000) study resulted in significant ovulation rate improvement in only 38% of the study subjects, and saw a significant overall improvement of the LH to FSH ratio. Although Pastore et al (2011) produced significant values of LH levels and LH to FSH ratio, they did not see significant changes in ovulation or menstrual rates. In contrast, Jedel et al (2011) saw significant improvements in testosterone and menstrual frequencies but not in LH levels or LH to FSH ratio. Johansson et al (2013) saw a significantly higher ovulation rate in the acupuncture group versus the control group. Their studied showed significant improvement in testosterone levels but no in LH levels or LH to FSH ratio. No specific patterns in data significance were observed across the studies from which a conclusion can be drawn about specific impact of acupuncture on PCOS related factors. A summary of statistically significant results in the experimental acupuncture groups for the studies reviewed above is shown in Table 2. A summary of significant and non-significant results of acupuncture and control groups for the studies reviewed above is shown in Table 3.

Table 2. Statistically significant results in acupuncture groups

Study	Significant Results
Stener-Victorin et al. (2000)	- Ovulation rate increased from 0.15 to 0.66 ovulations per month in 38% of participants (p=0.004) - LH/FSH ratio decreased from 1.7 to 1.47 in all women (p=0.042)
Pastore, et al. (2011)	- LH level from 10.2 mIU/ml to 6.0 mIU/ml (p=0.004) - LH:FSH ratio improved from 1.9 to 1.3 (p=0.001)
Jedel et al. (2011)	- Menstrual frequency increased from 0.28 to 0.33 cycles per month (p=0.003) - Testosterone decreased 18% (p=0.020) - Free Testosterone decreased 25% (0.004)
Rashidi, et al. (2012)	- Embryo quality: acupuncture group vs control group (3.75 vs. 3.5, p=0.004)
Johansson et al. (2013)	- Ovulations rate: acupuncture group vs control group (0.76 vs 0.41 ovulations/month, p=0.002) - Testosterone decreased 23% (p=0.018) - Free testosterone decreased 33% (p=0.004)

Table 3. Results Summary for experimental and control groups.

Study	Study Type	# of Parti-cipants	Measurement Outcome	Acup-uncture group	Signifi-cance (p value)	Other Inter-vention	Signifi-cance (p value)	Con-trol Group	Signifi-cance (p value)
Stener-Victorin, et al.	Case Series	26	Ovulation Rate	+340%	S (0.004)				
			LH	-15%	NS				
			FSH	0%	NS				
			LH:FSH Ratio	-14%	S (0.042)				
			Testosterone	0%	NS				
Jedel, et al.	RCT	84	Menstrual Rate	+121%	S (0.003)	+42%	NS	-17%	NS
			LH	-20%	NS	+17%	NS	+6%	NS
			FSH	-4%	NS	+7%	NS	-5%	NS
			LH:FSH Ratio	-9%	NS	+2%	NS	-11%	NS
			T	-18%	S (0.020)	4%	NS	+9%	S (0.049)
			FT	-25%	S (0.004)	-10%	S	+9%	NS
Pastore, et al.	RCT	84	Ovulation Rate	0.37	N/A[1]			0.40	N/A[1]
			Menstrual Rate	+20%	NS			+43%	S (<0.001)
			LH	-41%	S (0.004)			-37%	NS
			FSH	-10%	NS			+4%	NS
			LH:FSH	-32%	S (0.001)			-32%	NS
Johansson et al.	RCT	32	Ovulation Rate	0.76	S (0.002)			0.41	S (0.002)
			LH	-6%	NS			+35%	NS
			FSH	+14%	NS			-5%	NS
			LH:FSH Ratio	-18%	NS			+30%	NS
			T	-23%	S (0.018)			+93%	S (0.018)
			F``T	-33%	S (0.004)			+24%	S (0.004)

				% Difference Between Acu vs Control	Significance
Rashidi, et al.	RCT	62	Oocytes Retrieved	-6%	NS
			Fertilization Rate	+14%	NS
			Embryos Transferred	+10%	NS
			Pregnancy Rate	+37%	NS
			Embryo Quality	+7%	S (0.004)

1. Change in ovulation rate over the course of the study was not reported. The number reported is the mean rate over the course of the entire study period.

Limitations in Acupuncture Trials

One of the major hurdles of studying PCOS treatment is the complicated nature of the disease. The various factors such as lifestyle, weight, metabolic profile, neuroendocrine complications and hormonal influences make it very difficult design the perfect RCT. Various aspects of PCOS, such as androgens, insulin and other factors, aggravate and influence each other. This makes it very difficult to design a study to focus on only a few measurement outcomes.

The existing studies on fertility and menstrual rates ovulation rates have limited sample sizes and lack follow up beyond 32 weeks. It is important to note that none of the studies include a maintenance treatment program. Because acupuncture treatments are seen as having a cumulative effect, the long-term benefits of continued treatments have not been considered or studied. Current studies only look at a small snapshot of time with limited number of treatments. The earlier evaluated studies show improvement of menstrual and ovulatory function and may therefore also improve pregnancy rate in women with PCOS.

The manner in which the studies are designed does not allow for any individualization in the acupuncture points used in the acupuncture interventions. For example, if a patient was showing signs of deficiency and could benefit from moxibustion, there was no allowance for adding it to a specific patient's intervention. Alternatively, if a participant was displaying signs of a phlegm heat pattern, there would be no way to include points for address phlegm and heat issues. In the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA), it is allowed to conduct treatments that are fully individualized or partially individualized, a combination of standard acupuncture points with some flexibility in the use of

other acupuncture points. However, the authors state that such variations are more befitting of pragmatic studies (MacPherson et al. 2010).

To recruit participants in a study that involved fully individualized treatments based on a TCM approach, they would also have to be diagnosed with PCOS using the criteria discussed earlier. Using fully individualized treatments within the construct of an RCT presents a whole new set of problems. One of the first issues is the consistency in TCM diagnoses. Diagnoses can vary between various acupuncturists based on experience level, different styles/schools of thought, and current presentation of disease. A patient's presentations may change in the midst of a study, thus changing the TCM diagnosis. This also brings up the question of whether or not there should even be a control group for each TCM diagnosis group.

Ongoing Studies

There are currently two studies that are evaluating the efficacy of acupuncture in promoting pregnancy in infertile women with PCOS. Kuang et al. (2013) described their study as a multicenter, randomized, double-blind, controlled, 2 by 2 factorial clinical trial. In this trial in China, participants will be placed into one of four treatment arms: (1) true acupuncture and clomiphene citrate, (2) control acupuncture and clomiphene citrate, (3) true acupuncture and placebo clomiphene citrate, and (4) control acupuncture and placebo clomiphene citrate. They will be using the western medical anatomy based protocol used by Jedel, et al (2011) and Pastore, et al (2011). While it will not affect the treatment protocol, they will make a TCM diagnosis for each participant. The primary outcome will be LBR. Secondarily, they will look at other parameters such as ovulation rate, change in hormonal profile, multiple pregnancy rate, and pregnancy rate.

Li et al. (2016) are conducting an RCT in China to explore if pretreatment with electroacupuncture followed by letrozole administration versus letrozole alone leads to a higher LBR in anovulatory women with PCOS. Letrozole is a drug used to help induce ovulation in anovulatory, and therefore infertile, women. They will be using a combination of Western medical acupuncture and TCM acupuncture for their treatment protocol. The acupuncture pretreatment intervention group will be given a series of 4 cycles of letrozole after 16 weeks of acupuncture sessions. The control group will only be given 4 cycles of letrozole. The primary outcome measure will be LBR. Some main secondary outcomes include, but are not limited to ovulation rate, ongoing pregnancy rate (in first trimester), multiple pregnancy rate, hormone profile and metabolic profile.

Thus far, there have not been many studies in which LBR was the primary outcome measurement. The two above studies are important because it directly addresses fertility issues in women with PCOS and they use and integrative approach, combining western and eastern treatment modalities.

Future Studies

While the existing research for using acupuncture to treat infertility in women with PCOS is scarce, there are many existing animal and human studies to guide future researchers in developing relevant and robust studies moving forward. Animal studies, though not evaluated in this review, demonstrate that acupuncture produces changes in endocrine, the metabolic and the sympathetic nervous systems (Napadow et al. 2008). This will be a very important development for many women, as PCOS is affected by all of those systems.

An animal study with rats (Stener-Victorin, Kobayashi, Watanabe, Lundeberg, and Kurosawa, 2004) resulted with researchers showing that electroacupuncture increased ovarian blood flow in rats with polycystic ovaries. In an animal study by Ma, Zhou, Fang, Yang, and Qu (2011), researchers showed that a combination of acupuncture with *Salvia miltiorrhiza* (Dan Shen) can significant lower the Testosterone levels and LH to FSH ratios in rats with PCOS. It should be considered in future human studies to combine herbal and acupuncture therapies. In a separate study with rats, Manneras, Cajander, Lonn, and Stener-Victorin (2009) showed that the combination of electroacupuncture and exercise can improve ovarian morphology in rats with PCOS. In a study by Qu et al. (2015), researchers found that transcutaneous electrical acupoint stimulation alleviates PCOS related hyperandrogenism. Results from all 3 of these animal studies, and many more like it, should help with the design of future animal and human studies.

The existing research in support of the use of acupuncture to treat PCOS and its associated dysfunctions in still in its early stages. With the exception the Rashidi et al. IVF/ICSI study, none of the studies evaluated in this review measured LBR or CPR. However, studies were chosen based on other parameters that have a direct influence on fertility; ovulation rates, menstrual rates and corresponding hormonal changes. The existing pool of trials can used as preliminary research that can help dictate the direction toward more robust studies in the future.

Menstrual/ovulation irregularities and irregularities in hormone levels all factors that directly influence the fertility of a woman with PCOS. The impact PCOS has on a woman's fertility can be of great concern to a reproductive age woman. Because first line pharmaceutical treatments can lead to sometimes serious adverse side effects, it is important for reproductive age women to be given less harmful alternatives. Current first line therapies, such as oral

contraceptives, are not viable options for women with PCOS who wish to conceive. Therefore, it can be a significant contribution to the medical community to have conclusive evidence that acupuncture can provide an alternative to current first line therapeutics with minimal negative side effects.

The study design of previous RCTs that examined acupuncture in treatment of PCOS were flawed in several ways. First, the studies involved samples sizes that were fairly small. Second, the usefulness and quality of the control groups were varied and questionable. Lastly, data collection was limited to a short amount of time. To be truly useful, data and treatment should be administered and collected over an extended period of time. Future studies should be designed to examine the effects of prolonged treatment that run 9 to 12 months with data collection before and several months after intervention. It would be beneficial to design a robust multi-arm RCT that examines the relationship between the aforementioned hormones, LBR, and CPR.

V. Conclusion

While it cannot yet be concluded that acupuncture definitely improves menstrual/ovulation rates and hormone levels, the studies reviewed indicate there is a significant correlation between them. Specifically, the reviewed studies displayed a correlation between menstrual/ovulation rates and decreased LH levels, decreased LH to FSH ratios, and/or decreased testosterone levels. By improving hormonal levels and menstrual and ovulation rates, fertility can therefore be positively influenced by acupuncture treatments. Some studies resulted in improved only menstrual and ovulation frequencies, and not in other outcome measures. Other studies displayed improvement only in the level of LH, or LH to FSH ratio, and not in menstruation or ovulation frequencies. This made it difficult to link the effects of the various outcome measures with each other. Therefore, it is still impossible to make any definitive statements on the efficacy of acupuncture in the treatment of acupuncture. Although each study produced some significant and promising results, the overall combination of the studies were mixed. There are poorly designed studies and too few RCTs from which to extract definite correlations. More rigorous and well-designed RCTs are recommended to study the effectiveness of acupuncture in treatment of PCOS related disorders involving menstruation, ovulation, hormone levels, and fertility.

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VII. Appendices

Appendix A. Definitions of Terms

amenorrhea	The absence of menstrual periods
androgen	A steroid hormone which promotes male characteristics, e.g. testosterone
clitoromegaly	Enlargement of the clitoris
dysglycemia	Any disorder of blood sugar metabolism
dyslipidemia	An abnormal amounts of lipids and lipoproteins in the blood
hirsutism	Excessive growth of hair in women
hyperandrogenism	Excessive secretion of androgens
hyperlipidemia	Elevated levels of lipids in the blood plasma
oligomenorrhea	Infrequent or very light menstruation
pulsatility	Activity characterized by a rhythmic pulsation
virilizing	Development of male secondary characteristics

Appendix B. Abbreviations

CPR	Clinical Pregnancy Rate
DHEAS	Dehydroepiandrosterone Sulfate
ET	Embryo Transfer
FSH	Follicular Stimulating Hormone
ICSI	Intracytoplasmic Sperm Injection
IVF	*in vitro* Fertilization
LBR	Live Birth Rate
LH	Luteinizing Hormone
OC	Oral Contraceptive
OHSS	Ovarian Hyperstimulation Syndrome

Appendix C. Acupuncture point innervation muscle location

Acupuncture Point	Innervation	Muscle Location
BL 23	C6–8, Th9–12, L1–3	Fascia thoracolumbalis, mm. serratus posterior, erector spinae thoracolumbalis
BL 28	L4–5, S1–3	Fascia thoracolumbalis, m. erector spinae lumbosacralis
SP 6	L4–5, S1–2	Mm. flexor digitorum longus, tibialis posterior
SP 9	S1–2	M. gastrocnemius
PC 6	C8–Th1	M. flexor digitorum superficialis
TE 5	C7-8	M. extensor digiti minimi
GV 20	Nn. trigeminus (V), occipitalis minor (C2) and major (C2–3)	Aponeurosis epicranii
CV 3	L1	Fibrous tissue, linea alba
CV 6	Th11	Fibrous tissue, linea alba
ST 29	Th6-12	M. rectus abdominis
LI 4	C8, Th1	Mm. interosseus dorsalis I, lumbricalis II, adductor pollicis
ST 25	Th6-12	M. rectus abdominis
LR 3	S2-3	M. interosseus dorsalis I

Source: Stener-Victorin et al. (2000), Johansson et al. (2013)