

**The Effect of Chinese Herbal Therapy on Pregnancy Rate When Added to In Vitro
Fertilization (IVF) in Combination with Acupuncture**

A Capstone Project

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Doctor of Acupuncture and Oriental Medicine Degree**

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ABSTRACT

The goal of this retrospective chart review was to analyze if Chinese herbal therapy and acupuncture together with IVF will result in a higher pregnancy rate than acupuncture alone with IVF. Cases were reviewed from a reputable Chinese Medicine clinic that specializes in reproductive medicine. A convenience sampling was applied and patients were placed in separate groups according to the treatment they had received. Group A consisted of women who were treated with Chinese herbal therapy and acupuncture and Group B consisted of women who were treated with acupuncture only. A positive *B*-hCG was measured by a serum blood test to determine pregnancy. A total of more than 700 patient charts were reviewed, 34 of which qualified for this study. Out of the 34 patients, 23 were treated with acupuncture and Chinese herbal therapy, and 11 were treated with acupuncture only while going through IVF. The results showed a significantly higher pregnancy rate in the group that was treated with both acupuncture and Chinese herbs compared to the group that was treated with acupuncture only (82.6% vs. 40.0%, respectively; $p = 0.023$). Exploratory analysis was done on the live birth rate and there was no significant difference between Group A (45.5%) versus Group B (20.0%) ($p = 0.163$). Even though this study showed a significantly higher pregnancy rate with the incorporation of Chinese herbs during IVF, more extensive research is required to further support the integration between these two modalities. Investigating a broader range of outcome measures, such as side effects from IVF stimulation, ongoing pregnancy rates, and live birth rates, may support the results of this study and provide more scientific evidence for the public.

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ONE: INTRODUCTION

Background

Reproduction is a fundamental aspect of all known life. Innately, we know when the time comes, it should be natural and easy to conceive and start a family. So what happens when this natural progression of life presents a shocking challenge to some couples? In the fast paced world we live in today, women are getting pregnant later due to either late marriage or in order to keep up with the work force. Unfortunately the female reproductive system does not go on pause when we are not ready. It continues to mature, hence, leading to difficulties in conceiving. These women are not alone. Approximately 10-15% of couples have trouble conceiving sometimes during their reproductive age (15-44 years) (Centers for Disease Control and Preventions [CDC], American Society for Reproductive Medicine [ASRM], 2008; Manheimer et al., 2008). The number might be even higher due to unreported incidences.

More couples are experiencing infertility with higher prevalence occurring in women over 34 years of age (CDC, 2008). In 2002, it has also been reported that out of 62 million women of reproductive age, about 1.2 million had had infertility related medical applications and an additional 10% received infertility services (CDC, 2008). The number of assisted reproductive therapies (ART) cycles performed in the United States, has doubled from 87,636 cycles in 1999 to 148,055 in 2008. The number of infants born conceived through ART is also increasing steadily between 1999 and 2008 (CDC, 2008). In vitro fertilization (IVF) is the most common ART performed.

A typical treatment cycle of IVF begins when a woman starts taking drugs to stimulate egg production. If enough eggs are produced, they are then retrieved from the ovaries. After the retrieval, the eggs are combined with the sperm with the hope of fertilization. Once fertilized, the selected embryos are transferred back to the uterus through the cervix in 3-5 days (CDC, 2008). IVF was originally developed to treat women with infertility due to blocked, damage or absent fallopian tubes thus bypassing the fallopian tubes.

Since the success of the first IVF baby born in 1978, many more babies have been born through the process of IVF (CDC, 2008). With accumulated clinical advancements throughout the years, IVF has been utilized to treat various causes of infertility – endometriosis, polycystic ovarian syndrome (PCOS) and tubal blockages. Even though IVF has helped many couples achieve their fertility goals, the average delivery rate of IVF per single cycle using fresh, non-donor eggs was only 33% (CDC, 2008). IVF cycles are also expensive, can be lengthy, stressful and can involve some risks. Some of the risks involved in IVF include ovarian hyperstimulation syndrome (OHSS)¹ which if severe can lead to serious complications and increase the likelihood of multiple pregnancies which can lead to preterm birth. Whether or not the medications taken to stimulate the follicles can lead to other health complications has yet to be determined. Due to those reasons, many couples are turning to complimentary medicine to enhance the success of their IVF treatments and to aid in reducing some of the side effects from the IVF medications (Rosenthal & Anderson, 2007).

¹ Ovarian hyperstimulation syndrome (OHSS) – ovaries that are hyperstimulated by medication that led to fluid leakage out to the peritoneal cavity, which can cause sever bloating or abdominal pain, nausea, vomiting, ascities or oliguria (Speroff, 2005).

Traditional Chinese medicine (TCM) has been used in China for centuries to treat and regulate the female reproductive system (Maciocia, 1998; Manheimer et al., 2008; Xu, Yin, Tang, Zhang, & Gosden, 2003). So far, in the realm of TCM and IVF combined therapy, the majority of research has focused on the application of acupuncture only for IVF support (Rubin, 2010). The results of the 2002 Paulus study suggested acupuncture to have a beneficial influence on the pregnancy rate of women undergoing IVF, setting the foundation for many other acupuncture and IVF studies. With greater evidence suggesting that acupuncture can possibly help enhance IVF success rates (Manheimer et al., 2008), more reproductive endocrinologists, though cautiously, have been more open to having their patients include acupuncture as part of their treatment regime. Even though most studies have indicated a significant difference in the increase in pregnancy rate with the addition of Acupuncture to IVF (Paulus, Zhang, Strehler, El-Danasouri, & Sterzik, 2002; Westergaard et al., 2006; Deiterle, Ying, Hatzamann, & Neuer, 2006), other studies have shown that there is no significant difference (Smith et al., 2006; Moy et al., 2011) or some even suggested acupuncture to have a negative effect on the pregnancy rate when combined with IVF (Craig, Criniti, Hanse, Marshall, & Soules, 2007). The details of some of these studies will be presented in the next chapter – literature review. Hence, the definitive role of acupuncture having a positive effect on IVF needs to be further evaluated.

While there are an increasing number of studies examining acupuncture during IVF, there has been minimal number of studies done in the United States on the effects of acupuncture combined with Chinese herbs during IVF. In TCM, Chinese herbs are very effective in treating female reproductive health, infertility and endocrine deficiencies (Maciocia, 1998; Xu et al., 2003). In fact, the use of Chinese herbs is the main treatment modality for fertility in Asia (Xu et

al., 2003). A study conducted by Wing and Sedlmeier (2006) demonstrated that Chinese Herbal medicine increases female fertility, which resulted in a higher rate of successful pregnancy. The majority of the research to date on the effective use of Chinese herbs for fertility has been from non-randomized or poorly controlled studies. Hence, these studies have been criticized by Western physicians for failing to meet the criteria normally required by evidence based Western medicine (Xu et al., 2003).

Generally, in Asia, Chinese herbs and acupuncture are employed synergistically as a holistic treatment modality to treat female reproductive issues. Acupuncture promotes blood circulation to the uterus (Sterner-Victorin et al., 1996), harmonizes the hypothalamic-pituitary-ovarian axis and releases beta-endorphins to help reduce stress (Chang, Chung, & Rosenwaks, 2002). Chinese herbal medicine supplies nutrients to the reproductive system and provides a regulatory effect on the blood circulatory, immune and endocrine systems (Xu et al., 2003). This can lead to an improvement of the ovarian and uterine function and other fertility markers, therefore optimizing the chance of conception and pregnancy (Heese, 2006; Wing & Sedlmeier, 2006,). It is safe to assume that the combination of acupuncture and Chinese herbs would provide optimum results for patients undergoing IVF treatment.

Research Objective

Due to the lack of both scientific studies and general knowledge of the possible interactions between the Chinese herbal medicine and IVF stimulation medications, most reproductive endocrinologists are either hesitant or do not allow their patients to take Chinese

herbs while going through an IVF cycle. From my own clinical experience, the combination of Chinese herbal therapy and acupuncture during IVF appears to be more effective during IVF than just acupuncture alone. To test my clinical experience, a statistical analysis is needed for more clarity regarding this subject matter. Therefore, the goal of this thesis is to investigate the hypothesis that the addition of Chinese herbal medicine in combination with acupuncture during an IVF cycle increases pregnancy outcome.

CHAPTER TWO: LITERATURE REVIEW

Overview

This chapter will begin by reviewing in detail some of the randomized controlled trials (RCTs) regarding the effects of acupuncture as an adjunct therapy for IVF. It is important to look at these studies because they pave the way for the integration of Traditional Chinese medicine and Western fertility treatments. Then we will look into some of the studies that have suggested Chinese herbal medicine to be effective in treating female reproduction and infertility.

Searches for this literature review included a web search in: Pubmed, Google scholar, Cochrane Review, SAGE, Chinese Journal of Integrative Medicine, Journal of Chinese medicine, Fertility and Sterility, and Human Reproduction. Some of the key search words included: Chinese herbal medicine, Chinese herbs, Chinese herbs and fertility, IVF, acupuncture and IVF and Chinese herbs and IVF. The most helpful sites for information regarding Western medicine or Western medicine with acupuncture were the sites of the journals Fertility and Sterility and Human Reproduction. This was due to their library of information from past to present on all topics related to reproduction and fertility. On the flip side, it was a challenge finding information on the subject of Chinese herbal medicine related to IVF. The majority of the data or articles on this subject were in Chinese. The studies that are available on the integration of Chinese herbs and IVF will be reviewed later in this chapter.

There have been several RCTs that involved acupuncture and IVF (Benson et al., 2006; Craig et al., 2007; Dieterle et al., 2006; Domar et al., 2006; Humaidan et al., 2004; Paulus et al., 2002; Paulus et al., 2003; Smith et al., 2006; Stener-Victorin et al., 1996; Sterner-Victorin et al., 2003; Westergaard et al., 2006). Some studies show promising results of acupuncture benefiting IVF (Paulus et al., 2002; Westergaard et al., 2006; Dieterle et al., 2006; Magarelli, Cridennda, & Cohen, 2009), while other studies found acupuncture to be non-effective in conjunction with IVF (Smith et al., 2006; Craig et al., 2007; Moy et al., 2011; Domar, Meshay, Kelliher, Alper, & Powers, 2009). To my knowledge, there has been no RCTs on the effects of the combination of Chinese herbal medicine and ART in the United States. This may be due in part to the vast amount of herbs and herbal formulations currently available on the US market. It would be difficult to research the mechanism of action, indication, effective dosage and concentration of each individual herb in conjunction with the IVF stimulating medications.

Acupuncture and IVF

Four of the most conclusive and frequently visited RCTs (Rosenthal & Anderson, 2007) on the effects of acupuncture and IVF (Paulus et al., 2002; Dieterle et al., 2006; Smith, Coyle, & Norman, 2006; Westergaard et al., 2006) will be the main focus of this literature review. Three of the four RCTs present results suggesting acupuncture can benefit the outcome of IVF (Paulus et al., 2002; Dieterle et al., 2006; Westergaard et al., 2006) while one suggests that there was no significant difference between the acupuncture group and control group (Smith et al., 2006).

Study by Paulus et al. (2002). Paulus et al. (2002) is one of the pioneers that had set forth the motion of incorporating acupuncture into the IVF regime. This RCT had established a foundation for several other large RCTs (Westergaard et al., 2006; Smith et al., 2006; Dieterle et al., 2006). The researchers of this trial randomized 160 patients to receive either acupuncture (n=80) 25 minutes before and after embryo transfer (ET) or a standard IVF protocol with no acupuncture (n=80) but also with 25 minutes bed rest after ET. Paulus et al. (2002) applied acupuncture points CV-6 (Neiguan), Sp-8 (Diji), Liv-3 (Taichong), Gv-20 (Baihui), and St-29 (Guilai), ear point Shenmen and Brain in one ear and Uterus and Brain in the other ear for 25 minutes before ET. Then applied St-36 (Zusanli), Sp-6 (Sanyinjiao), Sp-10 (Xuehai) and Li-4 (Hegu) with ear points switched to the opposite side post ET. The point selections were chosen according to the principles of TCM channel theory. The protocol was selected to increase better blood perfusion to the uterus (Stener-Victorin et al., 1996), to regulate the autonomic nervous system for relaxation, and to stabilize the endocrine system.

The primary focus of this study was clinical pregnancy rate, and only patients with good quality embryos were included in this study. A maximum of three embryos were transferred and luteal support was given in the form of progesterone three times a day vaginally (Paulus et al., 2002). In addition, the pulsatility index (PI) was calculated immediately before and after ET in all patients. The PI measures the blood velocity in a vessel. The clinical pregnancy rate (fetal sac with ultra sound 6 weeks after ET) was significantly higher in the Acupuncture group with 42.5% (n=80) compared to the Control group with 26.3% (n=80) (Paulus et al., 2002). They concluded that acupuncture done before and after ET improves clinical pregnancy rate in IVF/ICSI patients. Realizing that the study could be improved, Paulus et al. (2002) also

recommended that future studies should include a third arm – a placebo group to rule out any psychological or psychosomatic effects of acupuncture.

Taking his own recommendation, Paulus et al. (2003) conducted another study, this time including a placebo-controlled group. This trial was not published but presented in the annual meeting of European Society for Human Reproduction and Embryology (Paulus et al., 2003). Two hundred patients with good embryo quality were randomized into two groups: real and placebo/sham² acupuncture for 25 minutes before and after ET. The acupuncture protocol and technique was the same as the 2002 trial (see above). The outcome showed no significant difference between the two groups (43% real acupuncture vs. 37% sham, $p = 0.39$). Paulus et al. (2003) claims that the reason that the results showed no significant difference was due to the fact that the placebo induced an “acupressure effect”. This means that by simply applying light pressure on an acupuncture point, it can have an impact on the pregnancy rate. This study showed that further investigation on the inclusion on a placebo group is needed. Overall the Paulus et al. (2002, 2003) studies set a solid foundation for other RCTs to emulate.

In 2006, three more RCTs investigated the effect of acupuncture on the reproductive outcome of IVF/ICSI patients at the time of ET: Dieterle et al. 2006, Smith et al. 2006 and Westergaard et al. 2006.

Study by Dieterle et al. (2006). Dieterle et al. (2006) conducted a randomized study involving 225 women (average age 34.9 years) separated into two groups. Group I (study group)

² Placebo or sham acupuncture - retractable needles used so the subject is not aware of whether they are receiving true or sham acupuncture.

had 116 patients who received acupuncture and Group II (control group) had 109 patients. Both groups received two acupuncture treatments, one immediately after ET for 30 minutes and a second one three days later. This treatment plan was different from Paulus et al. (2002) in that acupuncture was done twice both after ET. The points needled immediately after ET were Cv-4 (Guanyuan), Cv-6 (Qihai), St-29 (Guilai), Pc-6 (Neiguan), Sp-10 (Xuehai) and Sp-8 (Daiji). Caryophyllaceae ear seeds were placed on ear Shenmen, Uterus, Brain and Subcortex and retained for two days. The patients were instructed to press the ear seed twice daily for 10 minutes. The authors of this study did not specify in which ear to place the ear seeds in first. Three days after ET, group I (control group) received another acupuncture treatment using the points: Li-4 (Hegu), Sp-6 (Sanyinjiao), St-36 (Zusanli), Kid-3 (Taixi) and Lv-3 (Taichong). In addition, patients were instructed to press the same ear points at the opposite ear twice daily for 10 minutes, with the removal of the seeds after 2 days.

The placebo group also received acupuncture treatments immediately after ET. The points used in the placebo group were designed not to influence fertility: Sj-9 (Sidu), Sj-12 (Xiaoluo), Gb-31 (Fengshi), Gb-32 (Zhongdu), and Gb-34 (Yang ling qua). The placebo group did not have another acupuncture treatment three days after. The primary outcome measured was clinical pregnancy (ultra sound showing at least one gestational sac). The results showed that group I compared with group II not only had a significantly higher clinical pregnancy rate (33.6% vs. 15.6%, $p < 0.01$), it also demonstrated higher implantation rates (14% vs. 5.9%, $p < 0.01$), biochemical pregnancy rates (35.3% vs. 16.5%, $p < 0.01$) and ongoing pregnancy rates (28.4% vs. 13.8%, $p < 0.01$) (Dieterle et al., 2006). This study was also different from the Paulus et al. (2002) original study in that it included a placebo group but did not include a non-treatment

group. When compared with Paulus's et al. (2003) second study, both included a placebo with the difference in the type of placebo. Dieterle et al. (2006) used true acupuncture as placebo or control but on different non-fertility related acupuncture points while Paulus et al.'s (2003) placebo used sham acupuncture on the same acupuncture protocol. This is something to think about because with acupuncture treatments regardless of point location may still illicit some type of response to the body that can possibly effect the pregnancy rate. Overall this was a strong study but could be improved by adding the third group of a non-treatment group.

Study by Westergaurd et al. (2006). Westergaurd et al. (2006) demonstrated findings similar to Paulus et al. (2002) and Dieterle et al. (2006) on the possibility that acupuncture as adjunctive therapy to IVF may increase pregnancy rates. In this study, patients were randomized into three groups: to receive acupuncture on the day of ET (ACU 1, n=95), to receive acupuncture on the day of ET and again two days later (ACU 2, n=91), or to receive no acupuncture (control, n=87). The ACU 2 group was included to see if there would be a difference in receiving acupuncture near implantation time which was thought to improve implantation due to the effect on uterine blood flow (Stener-Victorin et al., 1996). This study design was similar to Dieterle et al. (2006) where they performed acupuncture a few days after ET, except Westergaurd et al. (2006) did not do a comparison between the group who only received acupuncture on the day of ET and the group which received acupuncture on the day of ET as well as a few days after. Similar to the first study conducted by Paulus et al. (2002), there was no placebo group in this study.

The primary focus of the Westerguard et al. (2006) study was to compare rates of positive pregnancy tests, clinical pregnancy rates, and on-going pregnancy rates between the control group and the two groups receiving acupuncture. ACU 1 and ACU 2 received the same treatment protocol: acupuncture 25 minutes before (GV 20, St 29, Sp 8, Pc 6 and Lv 3) and 25 minutes after ET (St 36, Sp 6, Sp 10 and Li 4). The ACU 2 group received additional treatment two days after ET with points: Gv 20, Cv 3, St 29, Sp 10, St 36 and Li 4. All of the points chosen were according to the concepts of Traditional Chinese Medicine (Westerguard et al., 2006). A maximum of three embryos were transferred with luteal support which entailed vaginal progesterone was administered three times a day in combination with estradiol orally twice a day.

The average age of patients in this study was about 38 years of age. There were no differences in the patient's demographic characteristics – age, body mass index, duration of fertility, number of previous IVF/ICSI³ cycles, and causes of infertility. The outcome showed that the rate of positive pregnancy test (positive *BhCG*), clinical pregnancies (ultra sound with at least one gestational sac), and ongoing pregnancy (12 weeks gestation) or delivery were all significantly higher in the ACU 1 group than control group: positive *BhCG* (Beta chorionic gonadotropin) 42% vs. 24% ($p = 0.044$), clinical pregnancy 39% vs. 24% ($p = 0.038$), ongoing pregnancy or delivery 36% vs. 22% ($p = 0.049$). The rates of positive pregnancy tests, clinical pregnancy, and on going pregnancy or delivery in the ACU 2 group compared with the controls were also higher but were statistically insignificant.

³ ICSI (intracytoplasmic sperm injection) – is an IVF procedure in which a single egg is injected into an egg (Speroff, 2005).

Interestingly the percentage of early pregnancy loss appeared to be on average higher in the ACU 2 group (33%) than in the control group (21%) and ACU 1 (15%) (Westerguard et al., 2006). The higher early pregnancy loss in the ACU 2 group might have been due to certain acupuncture points used two days after the transfer. The acupuncture points Sp 10 and Li 4 are both cautioned during pregnancy (Deadman, Al-Khafaji, & Baker, 1998). However, Dieterle et al. (2006) used similar points and did not have this result.

This study design also did not include a placebo. Another aspect of the Westerguard et al. (2006) study that could be improved involves the practitioner who is applying the actual acupuncture treatments. This study had nine different nurses applying the acupuncture treatments, which may have contributed to inconsistencies.

Study by Smith et al. (2006). Another RCT that was designed to examine the fertility outcome of acupuncture performed around the time of ET was Smith et al. (2006). Compared with the other three studies reviewed, this RCT concluded that there was no significant difference in the pregnancy rate between the group that received acupuncture and the group who received the sham (placebo) acupuncture (Smith et al., 2006). This study randomized 228 women into two groups: acupuncture group (n=110) or placebo acupuncture with Streitberger needle (the shaft of the needle collapses into the needle handle) (n=118). In this study the patients were interviewed and a TCM diagnosis for each individual was included. The acupuncture treatment protocol was based on Paulus et al. (2002) protocol with some modifications. This is interesting because the other three studies all included a specific acupuncture protocol regardless of the patient's TCM diagnosis. This study actually took into account the patient's TCM diagnosis then

modified their treatment regime accordingly. Since TCM is an individualized based medicine, one would conclude that this method would provide a more reliable outcome due to the fact that this is how TCM is normally practiced. If every individual was treated according to their specific condition, their body should respond better. It is not so in this case. It would be interesting to know what the diagnosis was and what acupuncture points were used.

The placebo group received placebo needling at points located close to but not at the real acupuncture points. Three acupuncture treatments were given, the initial one on day nine of stimulation injections, the second and the third immediately before and after ET (similar to the previously mentioned three RCTs). This study concluded that the difference in the pregnancy outcome between the acupuncture group (31%) and the placebo group (23%) were statically non-significant. It is unknown whether the Sham acupuncture could have affected the treatment outcome, since no true control group was included in the study.

Based on these four RCTs, it is still unclear whether acupuncture provides a benefit as an adjunct to IVF. However, the research designs have been inconsistent therefore it is difficult to assess and compare the outcomes of the studies. Different studies have different approaches on the acupuncture protocol, number of treatments to perform, different people performing the actual treatment and whether to include a group receiving placebo (sham) acupuncture. The variations can lead to different results. But in the recent two meta-analyses conducted by Manheimer et al. (2008) and Cheong, Ng, and Ledger (2009) both research groups showed that overall, acupuncture improves the pregnancy outcome when administered during ET. Manheimer et al. (2008) included seven RCTs while Choeng et al. (2009) analyzed sixteen RCTs.

Chinese herbal medicine, infertility and IVF

Study by Wing and Sedlmeier (2006). Wing and Sedlmeier (2006) conducted a prospective cohort clinical study that showed Chinese herbal medicine to be effective in improving ovarian function and follicular development, which resulted in higher rate of success for pregnancy. This study aimed to “measure accepted bio-medical factors that affect female fertility and to determine if Chinese herbal medicine (CHM) can improve these factors as well as pregnancy outcome” (Wing & Sedlmeier, 2006). The bio-medical factors that this study looked at were ovarian follicle number and size, uterine endometrium thickness, uterine artery flow, serum follicle stimulating hormone (FSH), serum progesterone levels and corpus luteum development. This study compared the differences in the fertility indicators before and after treatment with Chinese herbal medicine. Study participants were diagnosed and treated not according to their Western medical diagnosis but according to their TCM diagnoses. Herbs or herbal formulations were not revealed in this study because the authors stated that it would be inappropriate to focus on the formulas themselves but to choose to focus on the effect of Chinese herbal medicine in treating fertility in general (Wing & Sedlmeier 2006). Understandably so, TCM is very individually based and the Chinese herbs prescribed are formulated for each person according to their specific needs. The authors also mentioned that the formulations were modified according to the changes that the patients were experiencing. They did not, however, include the amount of herbs these patients were taking or what types of herbs (raw, granules or patent) were prescribed.

The findings in this study revealed in eight out of the fertility indicators measured (FSH levels, follicle size, post-ovulatory endometrial thickness, uterine artery peak systolic velocity, uterine pulsatility index, progesterone level, corpus luteum size and corpus luteum vascularity) showed statistically highly significant results ($p < 0.001$) before and after treatment. (Wing & Sedlmeier, 2006). This study showed the Chinese herbal medicine's ability to lower the FSH, which is recognized as one of the measures of an ovarian response (Speroff, 2005, Wing & Sedlmeier, 2006). It also demonstrated that Chinese herbal medicine can help bring more blood flow and perfusion to the endometrium thus providing a better environment for implantation. This is similar to the results from the Stener-Victorin et al. (1996) study, which suggested acupuncture benefits uterine receptivity, and promotes blood flow to the uterus. Wing and Sedlmeier (2006) further suggested that improving the quality of blood flow to the ovaries and uterus may enhance the outcome of ART, and that Chinese herbal medicine can be used along with IVF stimulating medications to help reduce the strong side effects from these medications. Wing and Sedlmeier also reported that there were no side effects with the Chinese herbal medicine. Overall, the study showed the pregnancy outcome to be 56% with Chinese herbal medicine.

Study by Hua (2008). Another study that showed the effects of Chinese herbal medicine in treating infertility was a study conducted in China by Jin Hong Hua. (2008). This study is different from Wing and Sedlmeier (2006) in that it focused on one particular formulation - *Yi Jing Bu Chong Tang* (Benefit the Jing and Tonify the Chong Decoction) - to treat a specific condition – poor ovarian reserve. Ovarian reserve is a term describing the functional potential of the ovary and reflects the number and the quality of the remaining ovarian follicular pool

(Speroff, 2005). Several tests can be used to help determine a women's ovarian reserve - serum blood test of FSH/E2, antimullerian hormone (AMH), ultra sound of anteral follicle count and inhibin B.

This is a retrospective study of 55 cases of women who demonstrated poor ovarian reserves. Women who were included in this study presented with symptoms of delayed menstruation, scanty menstruation, amenorrhea or infertility with the exclusion of any other internal or external disease. The study included women between 25 and 39 years of age who had experienced these symptoms for 3 to 8 years. Another inclusion criteria of this study was based on the patient's TCM diagnosis. These women had to have poor ovarian reserves due to either kidney qi or kidney yang deficiency. The symptoms of kidney qi deficiency are: scanty menstruation, delayed menstruation, amenorrhea, infertility, low back and knee soreness, dizziness, tinnitus, fatigue, profuse, clear urination, pale tongue, thin tongue coating, and a deep, wiry pulse. The symptoms of kidney yang deficiency are: low libido, cold abdomen and extremities, profuse leucorrhea, lumbago, frequent urination, pale tongue, white coating and a slippery, deep and thready pulse (Hua, 2008).

Other criteria of inclusion included serum FSH level ($<10\text{mIU}$), FSH/LH ratio ($<3.6\%$) and estrogen level ($>80\text{pg/ml}$). According to the author, women who presented with the criteria for one of these three measurements, were diagnosed with diminished ovarian reserve (Hua, 2008). The formula *Yi Jing Bu Chong Tang* was taken one dose per day for three months. The author also explained the indications of each herb in the formulation. The conclusion of this study was that of the 55 cases, the author stated "34 were *cured*, 9 *obviously effective*, 1

improved and 11 *non-effective*” (Hua 2008). In his study, Hua (2008) provided an explanation of what – “cured”, “obviously effective”, “improves”, “non-effective” and “effective implies”. The total “*effective*” (Hua 2008) rate was 80%. The pregnancy rate was 33% of the 80% effective. The levels of FSH, FSH/LH and E2 were also decreased. Therefore, the author concluded that the formula Yi Jing Bu Chong Tang is effective for treating poor ovarian reserve, hence benefiting female fertility.

The strengths of this study are in the strict inclusion and exclusion criteria, clear TCM differential symptoms of kidney qi and kidney yang deficiency and the TCM treatment methodology. In TCM, one will often see the same disease in different patients, which will require different treatment principles and herbal prescription. Jin Hong Hua understands this basic principle. Hence he selected patients that showed signs and symptoms of only kidney qi or kidney yang deficiency. This formula was intended to treat the same pattern of TCM diagnosis in order to stay consistent with the same treatment protocol. He also listed several strict criteria that were excluded from the study to further enhance the control of this study. The author was also able to explain the functions of the individual herbs and how they work together to strengthen the female reproductive function.

Several weaknesses in this study mostly involved the Western clinical measurements. Cycle day 3 serum FSH and E2 concentrations, although the simplest and still most widely applied measurement of ovarian reserve, can be unreliable and misleading (Maheshwari, Fowler, & Bhattachary, 2006). Due to the feedback loop of the hypothalamus/pituitary/ovarian (HPO) axis, FSH and E2 are interrelated and dependent on each other and can therefore give false

readings. If the follicular pool is weak, E2 level decreases and causes a rise in FSH. And if there is an elevated E2, it may suppress the FSH into a normal range, giving it a false-negative FSH result (Visser, Jong, Laven, & Themmen, 2006). A better measurement of the ovarian reserve that can be used in conjunction with the blood serum would be transvaginal ultrasound of antral follicle count (AFC), measurement of the ovarian volume, inhibin-B and anti-mullerian hormone (AMH) (Maheshwari et al., 2006). AFC and AMH have been suggested to be the most predictive, direct tests of ovarian reserve screening (Jayaprakasan et al., 2009). Despite these weaknesses, this study provides some support for the use of CHM in treating female fertility.

Study by Haeberele et al. (2006). In 2006, Haeberele et al., integrated Chinese herbs and acupuncture during the treatment of IVF. What led to this study was an interest that Haeberele et al. (2006) had on the results of Paulus et al.'s (2002) study. Although the trial is only published as an abstract it is still worth mentioning because it is one of the few studies that are available that included CHM in conjunction with ART. This study was a retrospective analysis of all IVF cycles from 2002 to 2005. During that time frame, 1473 IVF cycles were treated without TCM (defined as either acupuncture or acupuncture with Chinese herbs) and 127 IVF cycles were treated with TCM. The TCM treatments consisted of a minimum of 3 acupuncture treatments and some Chinese herbs before and after ET. The acupuncture points selection and Chinese herbal prescription were based on the individual TCM differential diagnosis. The data analyzed were age, causes of primary vs. secondary infertility, patterns of monofactorial vs. multifactorial infertility, IVF with or without ICSI, fertilization rate, number of embryo transferred, clinical pregnancy and implantation rate. The authors concluded that TCM improves the fertilization rate

in cycles IVF/ICSI using non-frozen embryos and that this improvement is significant in the age group of older than 35 years (Haeberle et al., 2006).

Even though this study supported the use of acupuncture and Chinese herbs during IVF, it was a weak study. Since the authors were curious about the outcome of Paulus et al.'s (2002) study, they should follow the Paulus et al.'s (2002) protocol. The question is why they did not follow that protocol. The incorporation of Chinese herbs was also inconsistent. Some patients took herbs and some did not. This weakens the validity of the study. One of the suggestions I recommend for future analysis of this study can be including the patients who took herbs vs. those who did not. Although there were many gaps in this study, it is still a step towards the right direction of investigating the effects of Chinese herbs, acupuncture, IVF and their integration.

Study by Rubin (2010). A recent case study conducted by Rubin (2010) showed that the use of CHM could provide a safe and effective adjunct to IVF. This case study involved a 41-year-old female with secondary infertility due to advanced maternal age and diagnostic diminished ovarian reserve. She requested TCM support in conjunction with her IVF cycle. An assessment of her TCM diagnosis was made during her consultation and her treatment plan was executed accordingly (Rubin, 2010). Her treatment protocol included acupuncture with points that addressed her specific condition and a customized granular herbal formula that was to be taken for three weeks – or throughout the stimulation phase of her IVF cycle and discontinued on the day of the egg retrieval. Each acupuncture point and herbs were described in detail, including reasons why they were prescribed. During her TCM/IVF cycle, her lining was 11mm and ten mature eggs were retrieved and seven fertilized. This case study did not include how

many embryos were transferred back into the uterus. She received acupuncture on the day before her embryo transfer using the Paulus et al. (2002) pre-IVF protocol with one modification. The end result in this case was the delivery of a healthy baby girl.

This case study shows the potential of using both CHM and acupuncture as safe and effective adjuncts to IVF when utilized together. Even though this was a case study, it still demonstrated a stronger validity compared with the Haeberle et al. (2006) study. Haeberle et al. (2006) had several gaps in his study that were not indicated like who received both acupuncture and CHM, or who received acupuncture only. Rubin (2010) was very clear on when the patient took the herbs and the duration of the herbal intake. This study was one of the few studies currently available that integrated Chinese herbs with acupuncture during IVF and is most closely related to this current study among the publications found.

Currently, it is very difficult to find any research on the effects of CHM when used in conjunction with IVF medications. These gonadotropin stimulators (GnRH) are utilized during a specific time during the IVF cycle in a specific dosage. Anything that interferes with this process may disrupt the IVF treatment protocol. Due to the potential function of CHM either stimulating or inhibiting or changing the action of IVF medications (Rubin, 2010), reproductive endocrinologists (RE) are hesitant to add CHM into the IVF regime. Without a doubt, more studies need to be conducted on this subject matter. Future studies should include case reviews that include the previous results of just regular IVF cycle compared with IVF cycles that are combined with CHM and acupuncture.

The hypothesis of this study was that the use of Chinese Herbal Therapy in conjunction with Acupuncture during an IVF cycle would increase pregnancy rates compared to Acupuncture and IVF alone.

THREE: METHODOLOGY

This study was a chart review that used data extracted from currently existing patient charts. Information was extracted from the charts of infertility patients that came in to the Tao of Wellness acupuncture clinic between January 2006 to December 2009 for Chinese Medicine Therapy to enhance their IVF success and achieve pregnancy. These patients were treated with both Acupuncture and Chinese Herbal Therapy for at least two months prior to beginning IVF.

Procedure

The charts of all fertility patients seen at the Tao of Wellness Acupuncture clinic between January 2006 and December 2009 were reviewed to determine those patients who qualify for inclusion in the study (convenience sampling). Once a patient was identified as eligible for inclusion, her chart was reviewed systematically to obtain all data detailed on the attached chart abstraction form.

Sample Size

The sample size needed to be sufficiently large enough to make the outcome statistically meaningful yet achievable within the time frame allocated. The data collection was in a span of four years of charts. The criteria for inclusion were:

- Age range between 34 and 43.
- Women must have been trying to get pregnant with no success for more than 6 months.

- Women must have had at least eight acupuncture treatments and Chinese Herbal Therapy treatment for at least two months prior to beginning In-Vitro Fertilization (IVF).
- Acupuncture/Herbs group continues with Acupuncture and Herbal Therapy during IVF. Acupuncture-Only group stops with herbal therapy at the start of IVF.

Note that patients who were diagnosed with secondary fertility issues such as endometriosis, fibroids, tubal blockage, poor ovarian reserves (high FSH, low AFC, low AMH) and PCOS all can be included.

Inclusion/ Exclusion Criteria

The criteria for exclusion were:

- Women who have had any fertility stimulating medications and/or assisted reproductive technology (ART) at least two month or two period cycles prior to the start of IVF. ART includes –IVF, ICSI (Intracytoplasmic Sperm Injection), GIFT (Gamete Intrafallopian Transfer) and ZIFT (Zygote Intrafallopian Transfer).
- Women who have not had both at least eight treatments of Acupuncture and Chinese Herbs for at least two months prior to the start of IVF.

Once the charts that fit the criteria were pulled, they were further separated into two groups. Group A consisted of patients who continued with both acupuncture and Chinese herbal therapy during their IVF protocol. Group B consisted of patients who continued with acupuncture but

stop their Chinese herbal therapy during IVF protocol. IVF protocol starts when the patients begin their fertility medications.

The outcome variable in this study was pregnancy (yes vs. no) based on the result of a *BhCG*⁴ pregnancy blood test. A positive result of this blood test was interpreted as “yes” for the pregnancy variable. The independent variable was Chinese herbal therapy (yes vs. no) in conjunction with IVF/acupuncture therapy as treatment for infertility. A Fisher’s exact Test was used to compare these two dichotomous variables to determine the efficacy of Chinese herbal therapy in the treatment of infertility. A probability of < 0.05 was used as the criteria for significance.

Instruments

The instruments used in this study were a chart abstraction log and a data collection log. A chart abstraction log was used in order to see whether the patients qualify for the inclusion/exclusion criteria of the study. Information collected from the patient’s charts were: age, occupation, the length of time trying to conceive, history of prior pregnancy, history of abortions, history of life births, history of miscarriages, history of prior ART or fertility medications, number of eggs retrieved, number of fertilized eggs, number of embryos transferred, the patient’s Western medicine diagnosis, traditional Chinese medicine diagnosis, a positive *BhCG* after IVF with either acupuncture or acupuncture with herbs and life birth (see appendix 1). The main outcome measurement was pregnancy rate (positive value of *BhCG*

⁴ *BhCG* (beta human chorionic gonadotropin): a hormone that is produced during pregnancy made by the developing embryo.

measured in the blood). It was important to identify the age of the patient and collect past reproductive/fertility history, due to possible unforeseen patterns that might have arisen to give this study more insight.

In the data collection chart, two groups were separated: IVF, acupuncture and herbs (Group A) and IVF and acupuncture (Group B). Each group was coded with individual numbers. Once the data were collected from the charts, pregnancy outcome was tested using one-sided Fisher's exact test.

FOUR: DATA ANALYSIS/RESULTS

Data Overview

A total of more than 700 patient's charts were reviewed for this study. Out of the 700 charts, 34 qualified to fit the inclusion and exclusion criteria for this study. Out of the 33 patients, 23 received acupuncture and Chinese herbs during IVF while 10 received acupuncture only during IVF.

Table 1 displays summary statistics for the continuous history variables of the women in the study. Skewness and standard error of mean values were calculated for all continuous variables in order to assess the normality of the distributions. As shown in Table 1, all values of skewness divided by their standard errors were within reasonable limits, indicating that the distributions were sufficiently normal to proceed with comparative statistics. The average age of the women was 39 and they had been trying to conceive an average of 19.8 months. The number of TCM treatments they received before their results were an average 27 treatments. The mean number of eggs retrieved was 11.5, the mean number of fertilized eggs was 6.5 and the mean number of embryos transferred was 3.3. The majority of the women in the sample were professionals with the exception of one homemaker. The jobs that they reported ranged from support staff (receptionist, administration assistance) to lawyers and physicians (see appendix 1).

A comparison of the continuous history variables between women treated with acupuncture and herbs during IVF versus those treated with acupuncture only were analyzed (see

table 2). This was to show that the results were not due to any history variables but were due to the treatments alone. The average age for the women treated with both acupuncture and herbs was 39 and the average age for the acupuncture only group was 38. The comparison was done using t-test and the results showed there was no significant difference between the two groups.

Table 3 displays summary statistics for the dichotomous history variables. The dichotomous variables include: history of prior pregnancy, history of abortions, prior life births, prior miscarriages, fertility medications and history of ART. This information was gathered to see if the history variables would make a difference to the result of the study.

The hypothesis of this study was that the use of Chinese Herbal Therapy in conjunction with Acupuncture during an IVF cycle would increase pregnancy rates compared to Acupuncture and IVF alone. Since the hypothesis was directional, it was tested using a one-sided test. Since the minimum expected cell count was less than 5, a Fisher's exact test was used instead of a Pearson's chi square analysis.

The results showed a significant difference between the two treatment groups. The analysis showed that the pregnancy rate for the acupuncture/herbal therapy group is considerably higher than the acupuncture only group. The acupuncture/herbal therapy group had 82.6% positive *B*-hCG tests compared to a 40.0% rate in the acupuncture only group ($p = 0.023$). The results can be seen in Table 3.

A set of two-tailed *t*-tests and additional Fisher's exact tests (two-tailed) were conducted to rule out the possibility that the difference in outcome (*B*-hCG positivity) was partly due to variations in the history variables. The variables compared using *t*-tests included the following continuous variables: age, number of months trying to conceive, number of eggs retrieved, number of fertilized eggs, number of embryos transferred and number of treatments the patients received before the results. The findings showed no significant difference between all the patients (see Table 4). The variables compared using Fisher's exact tests included the following dichotomous were: prior pregnancy, history of abortion, prior spontaneous abortion, any prior live births, history of fertility medications and history of assisted reproductive therapies. There were no significant differences on these history variables between those who were *B*-hCG positive and those who were negative (see Table 6).

One additional analysis was conducted to compare the live birth rate between women who received acupuncture and Chinese herbs versus acupuncture only. Although the live birth rate for women who took herbs (45.5%) was more than twice that of the women who had acupuncture only (20.0%), a one-tailed Fisher's exact test showed this difference was not significant ($p = 0.163$). See Table 7.

Another analysis was performed using *t*-test to compare the number of eggs retrieved and fertilized between the two treatment groups (see Table 8). The findings did not find a significant difference.

FIVE: DISCUSSION

Summary of Findings:

The hypothesis of this study was that the use of Chinese herbal therapy in conjunction with acupuncture during an IVF cycle would increase pregnancy rates compared to acupuncture and IVF alone. The data collected is in support for the hypothesis. The data confirmed that there was a significantly higher pregnancy rate in the group that was treated with both acupuncture and Chinese herbs versus acupuncture only (82.6% vs. 40.0%; $p = .023$). All the continuous variables were calculated in order to calculate the skewness and standard error of mean values to assess the normality of the distribution. The skewness of the variables verifies the normality of the distribution therefore allowing the t -test to be conducted. The t -test has a normality assumption that needs to be met for the test to be valid.

Implications of Results for Theory

The purpose of this study was to investigate whether the incorporation of Chinese herbal therapy during IVF is beneficial to the patients who are going through IVF. Medical doctors are concerned about combining stimulating drugs – gonadotropins (GnRH) with Chinese herbs because one, the mechanism of action is unclear and two, there had been no randomized controlled trials (RCT) on the use of Chinese herbal therapy in IVF (Cheong et al., 2010).

Specific dosing of the GnRH with close monitoring of the patient is critical during IVF. From the reproductive endocrinologist's point of view, any "outside" influences can influence the direction of the IVF cycle (Rubin, 2010). Therefore, Chinese herbs can be perceived as something that can potentially interfere with this delicate process. This study was aimed to investigate whether by including Chinese herbs into the IVF process it would benefit the patients by increasing pregnancy rate. Hence, patients, physicians and Chinese medicine practitioners can have the scientific evidence to have the confidence to integrate Chinese herbs during the IVF/acupuncture regime.

IVF and Traditional Chinese Medicine studies so far have been mainly focused on acupuncture only (Cheong et al., 2009). Acupuncture had been proven to have beneficial effects on female reproduction in some studies, like providing a better uterine environment for implantation to improving ovarian function (Sterner-Victorin et al., 1996, Chang et al., 2002, Xu et al., 2003, Wing and Sedlmeier, 2006, Heese, 2006). Even though some studies show acupuncture increases pregnancy rates and live birth rates other studies suggested that there were no significant differences (Smith et al., 2006; Craig et al., 2007; Domar et al., 2009; Moy et al., 2011). Therefore despite the increased number of studies on acupuncture as an adjunct to IVF, the results still remained inconclusive and further trials need to be conducted. Regardless of the unclear conclusions, these studies had opened the doors for the integration of Chinese medicine and Western medicine.

In Traditional Chinese Medicine, Chinese herbs play an imperative role in the practice of Traditional Chinese Medicine (TCM). Chinese herbs, whether used alone or in combination to

form an herbal formula, had been known to preserve reproductive health and treat infertility (Xu et al., 2003). The design of the herbal formula combination is used to help correct the functional or organic problems that caused infertility (Zhou & Qu, 2009). Hence, it is important to incorporate the herbs during fertility treatments in order to further support the patient while they are in the process of IVF treatment. According to my research and also according to Xu et al. (2003), there have been few high quality control trials due to poor randomization, which failed to meet the criteria for evidence-based Western medicine. With that, it leads to more challenges for the study of Chinese herbs in combination during an IVF cycle.

It is difficult to study Chinese herbs and show how they affect each patient while they are going through IVF due to several reasons. First, different women can respond differently to the IVF stimulation. Therefore their herbal formulation would need to be adjusted. This would be challenging to measure. Second, Chinese herbal therapy is prescribed to patients according to their TCM diagnosis. Therefore, every patient coming in for fertility treatments will receive a different formulation based on their TCM diagnosis. One possible way of standardization is to conduct a trial by grouping the patients together according to their TCM diagnosis and prescribe the same formula according to that diagnosis. Hua (2008) conducted a study similar to that idea in that he only included patients that had a particular diagnosis and prescribed the same formula for all of them. Hua's (2008) study investigated whether Chinese herbs can help with infertility especially for women with poor ovarian reserves. The details of Hua (2008)'s study are mentioned in the literature review chapter. Future studies on the effects of Chinese herbs with fertility can possibly follow the concept of Hua (2008)'s study.

With the challenges of conducting a valid study on Chinese herbs by itself already, it is perceived to be even more of a challenging task when combined with the IVF medications. Hence to my knowledge, there have been very few numbers of studies (Haeberle et al., 2006; Rubin 2010) on the combining Chinese herbs with IVF.

Similar to the Wing and Sedlmeier (2006) study, the acupuncture point selection and herbal formulations used for the patients of my study were not mentioned because the focus of this study was to analyze the effects of Traditional Chinese Medicine in general along with IVF and not on a specific point combination and the herbal formula. To use a specific formula or specific point combination would be appropriate for a different research question where the focus would be on a particular type of a formula or a specific point combination used during IVF.

Even with the different herbal formulations and point combinations prescribed to each individual patient, the results of this study showed a significant difference. This further supports the hypothesis of this study.

It was interesting to note that regardless of the patient's secondary fertility issues – polycystic ovarian syndrome (PCOS), endometriosis, fibroids, tubal blockage, or poor ovarian reserves (high FSH, low AFC or low AMH) – the results still showed a significant difference between the treatments. The result further encourages the usage of Chinese herbal therapy during the IVF process. There have been some studies and suggestions that are supporting the use of Chinese herbal therapy in the treatment of endometriosis, PCOS and poor ovarian reserves (Lin

et al., 2006; Hua, 2008; Elliott, 2009; Zang et al., 2010; Flower et al., 2011; See et al., 20011).

The outcomes from some of these studies may perhaps influence the patients who have other secondary fertility issues, which in turn might benefit them in their IVF cycle.

Exploratory Analysis

Considering that herbs did significantly increase pregnancy rate, which confirmed the hypothesis, one might suspect that also the live birth rate might be different between the two treatment groups. Thus live birth data were extracted from the charts for an exploratory analysis. As Table 6 shows there was no significant difference between treatments.

The numbers of eggs retrieved and fertilized were also explored (table 7). The average number of eggs retrieved in acupuncture/herb/IVF group was 12 while the acupuncture IVF group was 6.9. A 2-tailed fisher's exact test was performed and the results did not show any significant difference between treatments ($p= 0.646$). The mean number of the eggs fertilized also showed no significant difference between treatments ($p= 0.448$). This result was unexpected. Based on the outcome of this study, one might have also hypothesized that the patients would have produced more eggs leading to a higher fertilization rate. Though other factors need to be taken account as well when analyzing these data, such as the age of the women, their ovarian reserves and the quality of the male semen, all these factors can contribute to the number of eggs retrieved and fertilized.

Limitation of the Current Study

The sample size was not as large as originally anticipated. This was due to the fact that it was challenging to find a large enough sample size for the group that used acupuncture only. The majority of the patients seen at the Tao of Wellness used herbs in addition to acupuncture with an exception of a few who only used acupuncture. The ones who chose not to include herbs during the stimulation phase of IVF was either due to the request of their reproductive endocrinologist (RE) or to the fact that the patient themselves were not comfortable taking herbs. Another reason for not having a larger sample size was due to the exclusion/inclusion of this study. The age range in this study was ranged between 34-42 years of age. This particular age range was selected because according to the CDC (2008) women at the age of 34 and above showed a decline of their fertility and this was also the age range that is most often seen clinically at the Tao of Wellness.

All women included in this study had to receive acupuncture and Chinese herbal therapy for a minimum of eight acupuncture treatments within two month prior to starting IVF. This sets a base line for both groups so that one group does not have an advantage or disadvantage over the other. Ideally, 12 treatments three months or three menstrual cycles of pre-treatment are advised in preparing the body for IVF (Lyttleton, 2004). Due to the possibility of not having enough cases accommodating the inclusion criteria, the decision was made to have the pre-treatment as no less than eight acupuncture treatments within two months.

There were some patients who received acupuncture only but did not fit the criteria for inclusion. Most of them did not receive enough acupuncture treatments before the IVF stimulation or were just coming off from another fertility treatment. There were some patients who sought treatments right in the beginning of their IVF cycle or right in the middle of the IVF stimulation process therefore they were starting too late to fit the inclusion criteria. Their decision to come in for treatment during that time was either due to the suggestions by their reproductive endocrinologist (RE) RE, their friends, due to learning of acupuncture being helpful or due to prior failed IVF cycles. Some of the acupuncture/IVF trials are definitely making an impact on the TCM practice. From my clinical experience more REs are referring their patient to seek acupuncture treatment as an adjunct to IVF.

Another limitation to this study is the possible inconsistency in the treatment plan implemented by the different practitioners at the Tao of Wellness. At the time of the study, there were eight practitioners practicing at the Tao of Wellness. Even though the majority of the patients all came from one main practitioner, there are still inconsistencies with the acupuncture protocol and the herbal formulations. Different practitioners might make different diagnosis based on their own TCM practice and experience. For instance, patients that are diagnosed with the same TCM condition like kidney yin deficiency with liver qi stagnation might not be treated with the same herbal formulations and acupuncture points. For future studies, women should be grouped according to their TCM diagnosis (e.g. kidney yin deficiency) and be treated with a standard protocol of acupuncture points and herbal formulations for that diagnosis. This would create a stronger validity to the study.

The women included in the study were going to different REs, which can result in some inconsistencies. Different REs are likely to use different IVF stimulation protocols (down regulating, micro flare or antagonist). Some women require different IVF techniques (ZIFT, ICSI) due to their condition. The majority of the women went through a standard IVF technique where they extract the eggs and fertilize them with sperm in a petri dish then transfer back to the fertilized embryo. Some women also did ICSI and had the sperm manually injected in the egg to ensure fertilization. Even with this broad range of IVF techniques used, the results showed a significant difference between the treatment groups, which further supports the strength of the outcome.

Frozen embryo transfer (FET) was not included in the study. Including FET would not have made sense because some of the FET could be from the stimulation from the previous IVF stimulation cycle. This previous stimulation could be from patients with untreated TCM treatments therefore could not qualify for the study. The results would be skewed because we would not know if the pregnancy or non-pregnancy came from the TCM treatments.

Further Discussion and Recommendations for Future Research

There are strengths and weaknesses within this study that need to be addressed. The variables of the patient's fertility/reproductive history, background, and present reproductive health all were included as co-variables in this statistical analysis. The strength of the study is indicated by the fact that even when the co-variables were considered, the outcome variable showed significant difference between the two treatment groups. The results for the comparison

of the history variables between the two groups (herbs vs. no herbs) showed no significant difference. This further strengthens the study by showing that with regards to the history variables, the two groups were similar. For instance the mean age group of the women treated with both acupuncture and herbs was 39, while the mean age group of women treated with acupuncture only was 38. The results of the pregnancy rate were more likely to be caused by the administration of herbs and not due to any history variables.

Strictly following the inclusion and exclusion criteria further strengthens this study. The patients included all started at the same starting point. They all had to have at least eight acupuncture treatments within the two months along with herbal medicine prior to IVF and no ARTs or fertility medications were allowed two months prior to IVF treatment. This standardized all women to receive the same TCM pre-treatment before IVF.

This study is a pilot study. Therefore some weaknesses have been encountered. One of the weaknesses of this study is the small sample size. Even though more than 700 cases were reviewed, only 33 patients fit into the inclusion and exclusion criteria of this study. This can be explained by the fact that this particular TCM clinic prescribes herbal therapy to majority of their patients. Hence, it was challenging to find patients who were treated with only acupuncture. Another reason for the limited sample size is the time frame of this study. If more time were permitted, more patient charts from previous years could have been explored. Also for future research, the chart review can be expanded to other TCM clinics as well in order to pool from a larger selection.

Another weakness of this study is the frequency and length of the TCM treatments patients received prior to the start of the study. This showed some inconsistencies. Prior to the study, some patients received TCM treatments two times a week while others were treated only once a week. Some patients also received TCM treatments for one year or more before the start of the study while others received as little as one week to none prior to the study. Even the prior history of IVF was different among the women included in this study. Some women had multiple IVF treatments prior to the IVF in the current study and others had only one. This inconsistency should be addressed in future research. Ideally, only women who historically had a set number of IVF treatments or none at all should be included in order to make the study more specific.

Future studies may include conducting a randomized controlled study (RCT). RCT may potentially have a stronger validity. Though it might be difficult to find women wanting to be in a trial where they might fall under the placebo group. This and other considerations would need to be well thought out before taking on this major task.

Since herbal therapy is the main variable in this study, it is important for more research to be conducted on the effects of Chinese herbal medicine for fertility and the interactions of it with fertility medications. Once we get a better understanding, we can utilize Chinese herbal medicine to its utmost potential. The women of this study all had different herbal formulations based on their own TCM diagnosis. Ideally, to increase the study's validity it would be better to prescribe the same formula to all the women. Unfortunately, it would be a challenging task due to the fact that one of the strengths of TCM is that it treats every person as individual. Therefore, the herbal formulation is prescribed accordingly. Further thoughts would be needed regarding this subject.

The potential of this study is to ignite an interest in both TCM practitioners and allopathic physicians in the field of fertility to be open to the possibility of using Chinese herbs during IVF. This type of study can help to inform TCM practitioners, reproductive endocrinologists and patients that combining both therapies provides an effective treatment in improving pregnancy rates.

Conclusion

This study showed that there was a significantly higher pregnancy rate in the group that was treated with both acupuncture and Chinese herbal therapy during IVF compare to the group who was treated with acupuncture only. In conclusion, I am proposing further research on the integration of TCM and IVF. More studies on this subject need to be conducted in order to proof to patients that integrating TCM and IVF, can increase their chances of conceiving.

The only studies to the author's knowledge that are similar to this study are from Wing and Sedlmeier (2006) and Rubin (2010). Both studied measured live birth whereas with this current study, the pregnancy rate was the main outcome measured. Future research should include additional outcome measures including live birth rates along with the pregnancy rates as the outcomes. The more studies that are available regarding the integration of acupuncture, Chinese herbs and IVF, the narrower the gap between Chinese medicine and allopathic medicine, and the stronger evidence we will have for providing our patients with a better chance of realizing their dreams of becoming parents

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Table 1. Summary Statistics for Continuous Patient History Variables

Variable	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>Minimum</i>	<i>Maximum</i>	<i>Skewness (SK)</i>	<i>Std. Error of Skewness (SE)</i>	<i>SK/SE</i>
Years of age	33	38.82	2.21	34	42	-0.38	0.41	-0.93
Months trying to conceive	27	19.81	14.02	4	54	1.22	0.45	2.72
N of eggs retrieved	32	11.56	7.80	2	34	1.43	0.41	3.45
N of fertilized eggs	31	6.55	4.21	1	17	0.75	0.42	1.78
N of embryos transferred	33	3.33	1.80	1	8	0.77	0.41	1.89
N of treatments before results	33	27.09	12.83	13	67	1.27	0.41	3.11

Table 2. Comparison of Continuous History Variables Between Women Treated with Acupuncture and Herbs During IVF Versus Those Treated with Acupuncture Only

	Treatment						<i>t</i>	<i>df</i>	<i>p</i> (2-tailed)
	Acupuncture + Herbs			Acupuncture Only					
	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>N</i>	<i>Mean</i>	<i>SD</i>			
Years of age	23	39.13	2.12	10	38.10	2.38	1.24	31	0.225
Months trying to concieve	20	21.05	13.13	7	16.29	16.91	0.77	25	0.450
N of eggs retrieved	22	12.00	8.95	10	10.60	4.62	0.46	30	0.646
N of fertilized eggs	21	6.95	4.86	10	5.70	2.31	0.77	29	0.448
N of embryos transferred	23	3.61	1.99	10	2.70	1.06	1.35	31	0.186
N of treatments before results	23	28.61	14.29	10	23.60	8.21	1.03	31	0.310

Table 3. Summary Statistics for Dichotomous History Variables

	No		Yes	
	<i>f</i> *	%	<i>f</i>	%
History of prior pregnancy	14	42.4%	19	57.6%
History of abortions	19	57.6%	14	42.4%
Prior live births	27	81.8%	6	18.2%
Prior miscarriages	31	93.9%	2	6.1%
Fertility medications	4	12.1%	17	51.5%
History of ART	17	51.5%	16	48.5%

* *f* = frequency

Table 4. Comparison of Beta hCG Positivity (one-sided Fisher's exact $p = .023$) Between Women Treated with Acupuncture and Herbs During IVF Versus Those Treated with Acupuncture Only

	Beta hCG					
	Negative		Positive		Total	
	<i>f</i>	%	<i>f</i>	%	<i>f</i>	%
Herbs	4	17.4%	19	82.6%	23	100.0%
No Herbs	6	60.0%	4	40.0%	10	100.0%
Total	10	30.3%	23	69.7%	33	100.0%

Table 5. Comparison of Continuous Patient History Variables by Beta hCG Positivity

	Beta hCG						<i>t</i>	<i>df</i>	<i>p</i> (2-tailed)
	Negative			Positive					
	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>N</i>	<i>Mean</i>	<i>SD</i>			
Years of age	10	38.70	2.21	23	38.87	2.26	-0.20	31	0.843
Months trying to conceive	10	19.10	16.80	17	20.24	12.65	-0.20	25	0.844
N of eggs retrieved	10	8.80	3.65	22	12.82	8.88	-1.37	30	0.181
N of fertilized eggs	10	5.10	2.02	21	7.24	4.82	-1.34	29	0.191
N of embryos transferred	10	3.30	1.70	23	3.35	1.87	-0.07	31	0.945
N of treatments before results	10	20.30	7.04	23	30.04	13.76	-2.01	31	0.053

Table 6. Comparison of Dichotomous Patient History Variables by Beta hCG Positivity

	Bhcg							<i>Fisher's exact p (2-sided)</i>
	<i>Negative</i>		<i>Positive</i>		<i>Total</i>			
	f	%	f	%	f	%		
History of prior pregnancy	no	5	50.0%	9	39.1%	14	42.4%	.707
	yes	5	50.0%	14	60.9%	19	57.6%	
History of abortions	no	8	80.0%	11	47.8%	19	57.6%	.131
	yes	2	20.0%	12	52.2%	14	42.4%	
Prior live births	no	8	80.0%	19	82.6%	27	81.8%	1.000
	yes	2	20.0%	4	17.4%	6	18.2%	
Prior miscarriages	no	9	90.0%	22	95.7%	31	93.9%	.521
	yes	1	10.0%	1	4.3%	2	6.1%	
Fertility medications	no	1	10.0%	3	13.0%	4	12.1%	1.000
	yes	9	90.0%	20	87.0%	29	87.9%	
History of ART	no	5	50.0%	12	52.2%	17	51.5%	1.000
	yes	5	50.0%	11	47.8%	16	48.5%	

Table 7. Comparison of Post-Treatment Live Birth Rate (one-sided Fisher's exact $p = .215$) between Women Treated with Acupuncture and Herbs during IVF versus those treated with Acupuncture only.

	Live Birth					
	No		Yes		Total	
	<i>f</i>	%	<i>f</i>	%	<i>f</i>	%
Herbs	12	54.5%	10	45.5%	22	100.0%
No Herbs	8	80.0%	2	20.0%	10	100.0%
Total	20	62.5%	12	37.5%	32	100.0%

* *f* = frequency

Table 8. Comparison between Women treated with Acupuncture and Herbs during IVF (*t*-test) versus those treated with Acupuncture only on of number of eggs retrieved and number of eggs fertilized

	Treatment						<i>t</i>	<i>df</i>	<i>p</i> (2-tailed)
	Herbs			No Herbs					
	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>N</i>	<i>Mean</i>	<i>SD</i>			
N of eggs retrieved	22	12.00	8.95	10	10.60	4.62	.464	30	.646
N of fertilized eggs	21	6.95	4.86	10	5.70	2.31	.769	29	.448

Appendix 1

Id	G AB	Bhcg	age	occupation	months conceive	prior preg	abortions	livebirths	miscarriages	Fertility Meds	ART	eggs retrieved	fertilize degg	embryos transf	live birth post tx	n#txb4 results
1	1	1	39	actor	14	0	0	0	0	1	1	24	17	3	1	41
2	1	1	37	publicist	12	1	1	0	0	1	0			2	0	16
3	1	1	40	at home mom	18	1	1	1	0	1	0	10	5	3	1	36
4	1	1	35	location scout	18	1	1	0	0	1	0	17	12	2	1	13
5	1	0	41	Art consultant	12	1	1	0	0	1	0	8	6	6	0	35
6	1	1	38	Receptionist	12	1	1	0	0	0	0	4	3	3	0	16
7	1	0	39	Fashion designer	36	0	0	0	0	1	1	5	1	1	0	13
8	1	1	41	Admin Assist	36	1	1	0	0	1	1	5	5	1	1	28
9	1	1	41	Writer	12	1	1	0	0	1	1	3	2	2	0	20
10	1	0	36	public health mar	36	0	0	0	0	1	1	14	7	6	0	19
11	1	0	37	physician	5	1	0	0	1	1	1	6	4	3	0	19
14	1	1	41	real estate agent	12	1	1	0	0	1	1	4	3	3	0	20
15	1	1	39	Lawyer		1	1	0	0	1	0	15	11	5	1	15
16	1	1	39	Homemaker	48	1	1	1	0	1	1	34	na	3	1	30
17	1	1	39	tv producer	24	1	1	0	0	1	0	2	2	2	1	25
18	1	1	41	psychologist	12	1	0	1	1	1	0	10	6	6		17
19	1	1	41	Self employed	6	1	1	0	0	1	1	33	14	6	0	43
20	1	1	35	Graphic designer		0	0	0	0	1	1	15	9	4	1	53
21	1	1	42	Accountant	12	1	0	1	0	1	0	7	2	2	0	67
22	1	1	40	Music business		0	0	0	0	1	0	12	10	6	1	47
23	1	1	42	N/a	48	0	0	0	0	1	1	16	13	8	0	21
24	1	1	37	Pharmaceutial sa	24	0	0	0	0	1	1	5	1	1	1	38
25	1	1	40	Sales	24	1	1	0	0	1	1	15	13	5	0	26
26	2	1	38	Sr. Recruiter		0	0	0	0	1	1	19	10	4	1	21
27	2	0	42	DVD Producer	12	1	1	0	0	0	0	12	8	2	0	22
28	2	0	30	Marketing	30	0	0	0	0	1	1	18	15	3	0	36
29	2	0	36	Lawyer	12	1	0	1	0	1	1	7	5	4	0	14
30	2	0	37	Production	54	0	0	0	0	1	0	7	5	4	0	19
31	2	1	37	Antique Dealer		0	0	0	0	1	0	11	7	3	0	40
32	2	1	38	Executive		0	0	0	0	0	0	6	2	2	1	30
33	2	0	40	psychologist	4	1	0	1	0	1	1	9	7	3	0	20
34	2	1	34	Marketing	12	0	0	0	0	0	0	15	5	1		28
35	2	0	38	Analyst	12	0	0	0	0	1	0	15	4	2	0	29
36	2	0	41	Specail project	8	0	0	0	0	1	0	5	4	2	0	13