Effectiveness of Acupuncture and Chinese medicine herbs in lowering FSH level of a thirty-nine year old female: A case study

A Capstone Project

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By

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ABSTRACT

The current study engaged single case study method to explore the effectiveness of acupuncture and Chinese herbs in lowering follicle stimulating hormone (FSH) level in a 39 year old female. Data gathered from the retrospective chart review manifested a decrease from FSH level of 23.64 to 7.65 reading after three months of treatments. Coincident with the decrease in the FSH level, improvements were also observed in menstrual cycle length, pulse quality and tongue quality according to Traditional Chinese Medicine (TCM) criteria. It was concluded that acupuncture and Chinese herbal treatments may be instrumental in the observed improvements, it is important to mention further single blinded studies for acupuncture and double blinded studies in case of herbs are required to investigate the effects of acupuncture and Chinese herbs on FSH levels. Implications were discussed regarding the potential for patients with advanced maternal age and initially high FSH readings to respond to in vitro fertilization (IVF) procedures.

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Chapter 1: Introduction

In industrial societies such as United States, many women choose or are forced to have children at an older age. They postponed the decision to have children for economical reasons, finding a suitable partner, advancing in their career or their education. As the result of this phenomenon, women are trying to conceive at older ages (late 30s to early 40s) which contributes to problems with their fertile capability.

According to American Society of Reproductive Medicine (ASRM), the optimal physiological age range for pregnancy for a woman is between the early 20s to early the 30s. Formal evaluation of infertility is generally indicated in women attempting pregnancy who fail to conceive after a year or more of regular, unprotected intercourse (The practice Committee of the ASRM; 2006).

Earlier evaluation and treatment is indicated for women who meet one or more of the following criteria:

- Age over 35

- History of oligomenorrhea (irregular menstruation) or amenorrhea (lack of menstruation)

- Known or suspected uterine/tubal disease or endometriosis

- A partner known to be sub-fertile (Katz et al., 2007, The practice Committee of the ASRM., 2006).

Relevant history for an infertile woman includes:

- Gravidity, parity, pregnancy outcome, and associated complications

- Age at menarche, cycle length and characteristics and onset/severity of dysmenorrhea

- Methods of conception and coital frequency

- Duration of infertility and results of previous treatments

- Past surgeries, injuries, STDs (sexual transmitted diseases), PID (pelvic inflammatory disease), and unusual childhood disorders

- Pap smear history and treatments

- Current medications and allergies

- Occupation

- Tobacco, alcohol, and other drug use

- Family history of birth defects, mental retardation, reproductive failure

- Symptoms of thyroid disease, pelvic or abdominal pain, galactorrhea (abnormal breast secretions), hirsutism (abnormal hair growth), and dyspareunia (pain during intercourse) (Katz et al., 2007, The practice Committee of the ASRM., 2006).

It has been proven that as women age, the quality and responsiveness of the follicles produced by their ovaries are compromised, which can be measured via few different blood tests. The follicle stimulating hormone test (FSH) is on the most commonly used blood tests that may indicate ovarian reserve and responsiveness to ovarian stimulation. FSH is measured via serum level on day 2-3 of menstrual cycle (Elliot et al., 2009).

FSH is produced by the anterior pituitary gland, and is a gonadotropin with a function of ovarian stimulation. During the follicular phase of the menstrual cycle, FSH is secreted by the pituitary gland and stimulates the production of ovarian follicles and estradiol (E2). When E2 levels peaks, this causes the pituitary gland to increase the production of luteinizing hormone (LH), which triggers ovulation to occur. If the ovaries

respond poorly to FSH, and the level of E2 does not rise sufficiently, the pituitary gland recognizes this and secretes more FSH to further stimulate the ovaries. In this feedback system the FSH level rises as the ovaries become less responsive (Elliot et al; 2009).

In healthy women the FSH level varies based on the age. For a woman in her reproductive age, normal FSH level should be 3.5-12.5 IU/L. Elevated or pre-menopausal FSH level is between 12.6-25.7 IU/L, and post menopausal FSH is 25.8-148.8 IU/L (Elliot et al., 2009). According to Elliot (2009) women with higher FSH level (>12) tend to suffer from aging ovaries, poor quality follicles, and poor response to the ovarian stimulation medications that are used during In Vitro Fertilization (IVF).

FSH consists of two subunits: an alpha subunit includes a molecule of 92 amino acids and a beta subunit includes a molecule of 118 amino acids. FSH molecule has four carbohydrate side chains two on each subunit. The initial half-life of FSH is 3-4 hours (Speroff & Fritz, 2005). The gene for alpha subunit is shared by FSH, LH, Human Chronionic Gonadotropin (HCG), and Thyroid Stimulating Hormone (TSH). It is located on chromosome 6q12.21, a single promoter site that is subject to multiple signals and hormones. Transcription of the alpha gene is regulated in both the placenta and the pituitary. The alpha subunit gene is expressed in several different cell types, but the beta subunit gene is restricted in cell type (Speroff & Fritz, 2005). The gene for the FSH beta subunit is located on chromosome 11p13, and is expressed in the pituitary. It is influenced by Activin (a hormone released by ovaries which enhances FSH synthesis and secretion). Although FSH and LH both require gonadotropin releasing hormone (GnRH) stimulation, the FSH beta gene is unique in that its response to GnRH is dependent on Activin. With GnRH stimulation, the role of Activin is increasingly repressed by its

binding protein, follistatin, the secretion of which is also stimulated by GnRH and Activin. Activin is further antagonized by Inhibin (a hormone released by the ovaries which down-regulates FSH synthesis). It is the first factor that is recognized to suppress FSH secretion (Speroff & Fritz, 2005, Katz et al., 2007).

The level of FSH and its effect on the follicles differ throughout the cycle. The primordial germ cells originate in the endoderm of the yolk sac, allantois, and hindgut of the embryo, and by 5-6 weeks of gestation, they migrate to the genital ridge. After mitotic multiplication, which begins at about 6-8 weeks of pregnancy and continues to 16-20 weeks of pregnancy, the maximum number of oocytes in both ovaries is 6-7 million (Speroff & Fritz, 2005). Primordial follicles begin to grow and undergo atresia (cell death) under all physiologic circumstances, from infancy to around menopause. This process will cause a decrease in the number of follicles from 6-7 million during gestation to 1-2 million at birth, to 300,000-500,000 follicles at menarche. Only 400-500 follicles will ovulate during a woman's reproductive years (Speroff & Fritz, 2005).

FSH has an important function in regulating the menstrual cycle and therefore in regulating fertility. The following is a summary of the menstrual cycle and the function of FSH over time.

- **The follicular phase**: This phase lasts 10-14 days during which a leading follicle is chosen to mature and ovulate. First the pre-antral follicles (immature follicles) are chosen by FSH stimulation, which rescues a cohort of follicles from apoptosis (programmed cell death). FSH induces the aromatization of androgens to estrogens in the granulosa cells. This process is explained by the two-cell, two-gonadotropin mechanism, which allows the

critical creation of an estrogen dominant micro-environment. Together, FSH and estrogen increase the FSH receptor content of the follicles and stimulate the proliferation of granulosa cells. Selection of a dominant follicle is established during day 5-7 of the cycle, and peripheral levels of estradiol begin to rise by day 7 of the cycle. This rise of estrogen via a negative feedback suppresses FSH release, but has a positive feedback effect on LH secretion. An increased level of LH causes stimulation of androgen production in the theca cells, optimizing the final maturation and function of the dominant follicle. This follicle responds to FSH, thereby producing more estrogen. FSH also induces the appearance of LH receptors on granulosa cells. FSH stimulation causes granulose cells to produce and secrete inhibin-B, which directly suppresses pituitary FSH secretion (Speroff & Fritz, 2005, Katz et al., 2007).

- **Pre-ovulatory phase**: Estrogen production becomes sufficient to achieve and maintain a LH surge; LH initiates luteinization and progesterone production in the granulosa cells. At this point the production of progesterone has a positive feedback action on estrogen and may be required to induce the mid-cycle FSH peak. At this time, theca cells of unsuccessful follicles secrete androgen which explains the mid-cycle raise in androgen levels (Speroff & Fritz, 2005, Katz et al., 2007).

- **Ovulation phase**: The LH surge initiates the continuation of meiosis in the oocyte, luteinization of the granulosa, and synthesis of progesterone and prostaglandins within the follicle. Progesterone enhances the activity of

proteolytic enzymes (enzymes that break down protein molecules) that in combination with prostaglandins aid to digest and rupture of the follicular cell wall. The progesterone induces a mid-cycle rise in FSH that frees the oocyte from follicular attachments, and to ensure that sufficient LH receptors are present to allow an adequate normal luteal phase (Speroff & Fritz, 2005, Katz et al., 2007).

- **Luteal phase:** Normal luteal function requires adequate pre-ovulatory follicular development (especially adequate FSH stimulation) and continued LH support. Early in the luteal phase, active angiogensis and new vessel growth is held in check by angiopoietin-1, working through its receptors Tie-2 on endothelial cells. Regression of the corpus luteum is associated with a decrease in vascular endothelial growth factor (VEGF), and angiopoietin-1 expression and an increase in angiopoietin-2 activity. At this phase, progesterone, estradiol, and inhibin-A act centrally to suppress gonadotropins and new follicular growth. In early pregnancy, HCG rescues the corpus luteum, maintaining luteal function until placental steriodogensis is able to maintain the pregnancy (Speroff & Fritz, 2005, Katz et al., 2007).

According to western medicine, increased levels of FSH could be due to the following:

- Pre-menopause

- Premature ovarian failure (POF)

- Poor follicle quality

- Polycystic Ovarian Syndrome (PCOS) (Speroff & Fritz, 2005)

In Traditional Chinese Medicine gynecology texts, the section on female infertility is usually found in the last chapter as one of "eight miscellaneous diseases". According to these texts, the major etiologies of female infertility include:

- Kidney deficiency: Which includes kidney jing deficiency, kidney yin deficiency, kidney yang deficiency, or simultaneous kidney yin and yang deficiency

- Heart and liver Qi stagnation

- Blood stagnation

- Damp phlegm accumulation (Lyttleton & Clavey, 2007, Maciocia & Kaptchuk, 1998)

Although Chinese medicine texts do not specifically discuss the etiology of a rise in FSH level, any of the above could cause a high FSH level. Elliot (2009) discusses the main differential diagnoses of high FSH levels according to Traditional Chinese Medicine (TCM). They are as follows:

- Kidney yin deficiency with empty heat

- Liver blood deficiency leading to yin deficiency

- Liver and heart qi stagnation

- Liver fire

- Blood stagnation

- Kidney yang deficiency

Some studies have shown the effectiveness of acupuncture and Chinese herbal medicine in various gynecological problems and fertility issues where FSH levels were measured

before and after treatments. However few studies have been done with sole purpose of measuring the effects of acupuncture and Chinese herbs on FSH level (Elliot et al., 2009).

In this study, I will demonstrate the effectiveness of acupuncture and Chinese herbs in lowering the FSH level. This was a retrospective case study based on chart review of a 39 year old woman with a high FSH level due to advanced age, who desired IVF treatment for fertility. The treatments were rendered in an office setting between July to October 2010, after which the patient discontinued her treatments and returned to her reproductive endocrinologist to start her IVF cycle. A case study is a good start for measuring the effects of acupuncture and Chinese herbs in lowering FSH level due to advanced age, since a case study can be effective in exploring the nature of a phenomenon as well as in explaining its dynamics. Case study methods are most effective in the process of providing in-depth analysis of persons, events, decisions and processes. Case study research is often accomplished in advance of more in-depth and more controlled research studies, and often results in the generation of specific hypotheses for future more controlled research (Yin, 2009).

Glossary of Relevant Terms

The following is a glossary of terms and their definitions that provide a common foundation for understanding factors that recur throughout this project.

Activin: A hormone released by ovaries which enhances FSH synthesis and secretion (Speroff & Fritz, 2005).

AMH: Anti-mullerian hormone. AMH is secreted by small antral follicles and in Reproductive age women are expressed by granulosa cells of the ovary (Speroff & Fritz, 2005).

Amenorrhea: No menstruation (Speroff & Fritz, 2005).

Antral follicles: Ovarian follicles during later stages of folliculogenesis, number of antral follicles reflect ovarian reserve (Speroff & Fritz, 2005).

Atresia: Cell death (Speroff & Fritz, 2005).

Clomiphene citrate: Clomophine is a non-steroidal triphenylethylene derivative with both estrogen agonist and antagonist properties, however clinically this drug acts as an estrogen antagonist. This drug is administered orally from third to fifth day of the menses; dosage depends on the body weight (Katz et al., 2007).

CUN: A measurement which acupuncturist use for point location. 1 cun is correspondent to the width of patient's index finger (Zheng et al., 1999).

Dopamine: A neurotransmitter that helps to control the brain's reward and pleasure centers. Dopamine also helps regulate movement and emotional responses, and it enables us not only to see rewards, but to take action to move toward them (Katz et al., 2007).

Dyspareunia: Pain during intercourse (Speroff & Fritz, 2005).

E2: Estradiol, a hormone which is produced by many tissues including developing follicles (Speroff & Fritz, 2005).

FSH: Follicle stimulating Hormone which is produced by anterior pituitary gland and has a function in stimulation and maturation of follicles (Speroff & Fritz, 2005).

Follistim: A recombinant version of human follicle stimulating hormone (Speroff & Fritz., 2005)

Galactorrhea: Abnormal secretions from breasts (Speroff & Fritz, 2005)

GnRH: Gonadotropin releasing hormone which is released by hypothalamus to stimulate pituraty gland (Speroff & Fritz, 2005).

Granulosa cells: Cells surrounding follicles and have a function in hormone production (Speroff & Fritz, 2005).

Gonal_F: A recombinant version of human follicle stimulating hormone (Speroff & Fritz, 2005).

Hirsutism: Abnormal hair growth in women (Katz et al., 2007)

HCG: Human chorionic gonadotropin which is produced by placenta during pregnancy (Speroff & Fritz, 2005).

Inhibin: A hormone released by ovaries which down regulates FSH synthesis (Speroff & Fritz, 2005).

LH: Luteinizing hormone that is produced and released by anterior pituitary gland, and it induces ovulation (Speroff & Fritz, 2005).

Myomas: Uterine fibroids which are located on the uterus wall (Katz et al., 2007).

Norepinephrine: Is both a hormone and a neurotransmitter. As a hormone, secreted by the adrenal gland, it works alongside epinephrine / adrenaline to give the body sudden energy in times of stress, known as the "fight or flight" response (Katz et al., 2007).

Oligomenorrhea: Irregular menstruation (Speroff & Fritz., 2005).

Oligophrenia: Abnormal mental development (Katz et al., 2007).

PCOS: Polycystic ovarian syndrome. It is a gynecological problem which is characterized with oligomenorrhea or amenorrhea, and multiple ovarian cysts and abnormal hormones (Speroff & Fritz, 2005).

Prostaglandins: Any member of a group of compounds derived from fatty acids containing 20 carbon atoms, including a 5-carbon ring. Prostaglandins have a variety of biochemical and physiological effects, including hormonal effects (Katz et al., 2007).

SOAP: Subjective, objective, Assessment, and Plan; standard method of note taking in medical offices (Wikipedia., August 26,2011)

Tibolone: An analogue of the progestin norethynodrel is a drug with tissue-specific effects on receptors and enzymes that influence the synthesis and metabolism of endogenous estrogen, progesterone, and androgen (Qu et al., 2009)

TSH: Thyroid stimulating hormone which is produced by anterior pituitary gland and stimulates thyroid gland (Speroff & Fritz, 2005)

Vascular endothelial growth factor (**VEGF**): Is a signal protein produced by cells that stimulate vasculogenesis and angiogenesis. It is part of the system that restores the oxygen supply to tissues when blood circulation is inadequate (Speroff & Fritz, 2005)

Chapter 2: Literature review

This chapter will establish the background and foundation for the current study by providing a review of literature that pertains to the FSH factor and its impact on fertility. The chapter will begin by reviewing data derived from Western Medicine studies, it will then followed by summaries of studies that have emerged from the field of Traditional Chinese Medicine (TCM) and will include sections that specifically address data derived from studies involving the use of Chinese herbs and acupuncture. The chapter will conclude with a literature review integration section that summarizes the prior studies and leads directly to the need for the current study.

Western Medicine

One of the most commonly used tests in fertility clinics today is serum day 3 Follicle Stimulating Hormone (FSH) level alone, or after that administration of Clomiphene citrate to identify women with poor fertility potential. These tests theoretically identify women with advanced depletion of ovarian follicles, or diminished oocyte quality, which is known as a "decreased ovarian reserve" (Barnhart & Osheroff, 1999). The patho-physiological mechanism of why the day 3 FSH test would be a good predictor of lower fertility potential has not been determined. Nonetheless, because of its simplicity this test has been accepted and used in many fertility clinics to determine if a patient is eligible for Assisted Reproductive technology (ART) (Barnhart & Osheroff, 1999).

Ideally a test for ovarian reserve should be able to identify all patients who are infertile (high sensitivity) as well as to identify correctly all those who are not infertile (high specificity). Since sensitivity and specificity are inversely related, most screening

tests are only able to test one and sacrifice the other aspect. The serum day 3 FSH test has

poor sensitivity of 8% (Barnhart & Osheroff, 1999). Other studies have shown that an

elevated FSH had the highest sensitivity of 11.3% in women >35 (Esposito et al., 2002).

However FSH test has shown a high level of specificity, in one study 90.1% of women

who did achieve a live birth did not have an elevated FSH (Esposito et al., 2002). It is

important to mention that it does not guarantee that all women with a positive test result

truly have poor ovarian reserve (Barnhart & Osheroff, 1999; Esposito et al., 2002).

It is further argued that since this test is done mostly on patients from a specific

population (patients who seek fertility treatments), the predictive values of this test is

directly related to the population who is being tested. It has been emphasized that there is

good evidence to support the predictive value of this test in a population of women at

high risk for failure to become pregnant with the use of standard (Assisted Reproductive

Technology) ART. This high risk population includes women older than 40 years of age,

women with poor ovarian response to ovarian stimulation, and women who fail to

conceive in prior cycles of In Vitro Fertilization (IVF) (Barnhart & Osheroff, 1999).

 However the use of this screening test in a population at low risk for poor ovarian

reserve, such as women <35 years of age, women initiating an infertility workup, women

without history of infertility will yield incorrect interpretation, since the predictive value

of this test in women with low risk of infertility could give false positive (Barnhart &

Osheroff,1999).

Esposito, Coutifaris and Barnhart (2002), published a retrospective chart review

of 293 IVF patients and concluded that a moderately elevated FSH (10-11.4 mIU/ml) was

not statistically associated with pregnancy outcome either independently or after

multivariable analysis, and had a low predictive value of 71%. In this study, chart of 293 patients was reviewed, the FSH level of 12 months was reviewed and the highest FSH level was recorded and used for the study. The researchers also included other information such as age, etiology of infertility, medication used, number of ampoules used, day of Human Chronionic Gonadotropin (HCG) administration, estradiol (E2) concentration of the day of HCG administration, endometrial thickness, whether Intra-cytoplasmic sperm injection (ICSI) was performed, number of oocytes (eggs) retrieved, number of embryos transferred, and pregnancy results. The study found that elevated basal FSH level >11.4 mIU/ml was significantly associated with poor prognosis in IVF. A moderately elevated FSH (10-11.4mIU/ml) was not significantly associated with poor prognosis in IVF and had a limited predictive ability (Esposito et al., 2002).

In another study completed by Abdalla and Thum (2004) it has been argued that women with high FSH could be a heterogeneous group. Some may have true reduced ovarian reserve; others may be due to presence of heterophylic antibodies. Also, FSH receptor polymorphisim could result in high FSH level in patients with otherwise normal ovaries. In this study the authors noted a reduction in pregnancy rate (PR) and live birth rate (LBR) associated with higher levels of basal FSH, but they also found that with young cycling women with high FSH level, there is still a respectable PR and LBR (21.2% in one cycle and 49.2% in three cycles) and IVF is not a contraindication for this patient pool. They argue that the reduction in PR and LBR is due to reduced ovarian reserve rather than poor oocyte quality (Abdalla & Thum, 2004).

In article written by Elliot (2009) the author discussed the importance of FSH measurements in today's fertility clinics. The article described general signs and

symptoms patients with high FSH level would exhibit according to Traditional Chinese medicine (TCM). He further explained that although FSH measurements are used frequently in fertility clinics to predict patient's responsiveness to fertility medications such as recombinant FSH (Follistim, Gonal-F); he also emphasized that FSH levels are by no means are predicting value of ovarian reserve of quality of the follicles. He pointed out two schools of thought about the meaning of FSH levels. One school of thought maintains that elevated FSH levels are a clear indicator that a woman is nearing menopause, and a woman's eggs are as good as her highest FSH level. Another school of thought argues that FSH levels are a measure of the current functioning of the ovaries and therefore on the months that FSH levels are lower, there is a greater chance of stimulating the ovaries successfully (Elliot, 2009).

In amenorrheic (lack of period) women, an FSH level will differentiate patients with ovarian failure (Candidates for donor oocyte recipiency) from those with hypothalamic dysfunction (Candidates for pulsatile exogenous gonadotropin-releasing hormone or exogenous gonadotropin stimulation) (The Practice Committee of the ASRM, 2006). It has been suggested that evaluation of "ovarian reserve" with a cycle day 3 FSH or Clomophine citrate challenge test may provide important prognostic information in women with 1) Age over 35, 2) a single ovary or previous ovarian surgery, or 3) documented poor response to exogenous gonadotropin stimulation (The Practice Committee of the ASRM., 2006).

In a review by Viseer, De Jong, Laven and Themmen (2006) the use of Anti-Mullerian hormone (AMH) has been discussed by reviewing the latest research. AMH is a member of the transforming growth factor B family of growth and differentiation

factors. In the ovary, AMH has an inhibitory effect on primordial follicle recruitment as well as on the responsiveness of growing follicles to FSH. It has been discussed that serum level of AMH decreases with age in premenopausal women. Also AMH levels have a strong correlation with the number of antral follicles, which can suggest that AHM levels reflect the size of the primordial follicle pool. Due to these facts and also since AMH levels do not vary in the cycle; it has been suggested that AMH might be a better measurement of ovarian physiology (Visser et al., 2006)

In a study done by Singer, Barad and Weghofer (2009), it was argued that AMH measurement is more effective in predicting ovarian reserve and responsiveness of the ovaries to fertility treatments. AMH is secreted by small antral follicles and in reproductive-aged women, and it is expressed by granulosa cells of the ovary. It is emphasized that a big potential benefit of measuring AMH over FSH levels as a clinical test, is that AMH levels are stable throughout the menstrual cycle and hence serum can be drawn at any time (Singer et al; 2009). In the study, the correlation of AMH/FSH was studied in a group of patients with poor ovarian reserve undergoing fertility treatments. This study, which was a retrospective chart review analysis of 81 women who underwent fertility treatments at a center in New York between July 2006-November 2007, who had documentation of FSH level and AMH level in their charts prior to In vitro fertilization (IVF) induction (Singer et al., 2009).

Patients were divided to four groups according to their age: <35 years, 35-37 years, 38-40 years, and >40 years. A diagnosis of diminished ovarian reserve was reached when age specific FSH levels were elevated and/or oocyte yield at IVF retrieval was considered insufficient. The first AMH level in the chart was used and the FSH level which had been

measured within six weeks of AMH test date was used for comparison (Singer et al., 2009). The correlation between FSH and AMH data were examined by linear regression, and the result of study indicated that FSH levels raised and AMH levels decreased with increasing female age. It also suggested that serum AMH level, determined at random on any given day of a spontaneous menstrual cycle, is highly predictive of baseline FSH level obtained within 6 weeks. The presumed linkage in the relationship between baseline FSH and random AMH is that both hormones are indicators of ovarian reserve (Singer et al., 2009). The authors argued that AMH is a better tool compare to FSH levels, since FSH levels have to be measured in day 2-3 of menstrual cycle, where as AMH levels can be measured at any time in the cycle. Second point is that the degree of cycle-to-cycle fluctuations in the baseline FSH level depending of E2 levels in blood. However AMH does not exhibit these difficulties and it is relatively stable from month to month; it is not affected by other hormonal variations and for these reasons can be used as reliable biomarkers of ovarian reserve (Singer et al., 2009).

Chinese Medicine

In a review article by Elliot (2009) it was noted that AMH levels can be a more reliable measurement of ovarian reserve, whereas FSH can predict the responsiveness of the ovaries to fertility treatments.

Elliot (2009) has suggested three months treatment duration for the best results. This article, also discussed that main differential diagnosis of high FSH levels according to Traditional Chinese Medicine (TCM), and offered herbs and acupuncture points to lower the FSH based on diagnosis.

- Kidney yin deficiency with empty heat indicates: Elevated FSH, shortened follicular phase, hot flashes, night sweats, malar flush, dizziness, scanty cervical mucus, and vaginal dryness. In this case yin of the body maybe in natural decline due to aging, the empty heat acts as a stimulant to the pituitary gland causing the release of more FSH. This causes ovaries to work harder and faster leading to early egg maturation and early ovulation. Patent herbal formulas used are zhi bai di huang wan, qing jing san, and tian wan bu xin dan. Herbal formula which are effective for this diagnosis are; mu dan pi, di gu pi, bai shao, shen di huang, fu ling, xuan shen, E jiao, Nu zhen zi, Han lian cao, Qing hao, and Huang bai. Acupuncture points used for this condition include: Lu7, Kid6, Ren4, Sp6, Kid2, Kid7, and Ht6 (Elliot, 2009).

- Liver blood deficiency leading to yin deficiency: Elevated FSH, scanty or pale red menstrual flow, a thin endometrial lining, low blood pressure, dizziness, insomnia, poor memory and a dull complexion. This pathology is more common in women younger than 30 years who are underweight or over exercised which causes more release of FSH. Patent herbal formula suggested in this article include: gui shao di huang wan, liu wei di huang wan, si wu tang. Herbal formula used for this condition include: dang gui, sheng di huang, bai shao, chuan xiong, shu di huang, shan zhu yu, fu ling, ze xie, mu dan pi, shan yao, sha yuan zi. Acupuncture points used for this condition include: Lu7, Kid6, St36, Ren4, Sp6, Liv8, BL20, and ST30 (Elliot, 2009).

- Liver and heart qi stagnation: Elevated FSH, emotional instability, anger, anxiety, saw-tooth shape basal body temperature chart during the follicular

phase. In this pathology heat generated from liver and heart qi stagnation causes the pituitary to release more FSH. Patent herbal formula used is Jia wei xiao yao san. Herbal formula used in single herb form include: dang gui, bai shao, fu ling, bai zhu, chai hu, bo he, mu dan pi, shan zhi zi, xiang fu, ye jiao teng, bei he, fu xiao mai, zhi gan cao. Acupuncture points used are: PC6, Yintang, Liv3, Ht7, Ren3, St36, Sp6, and Li4 (Elliot, 2009).

- Liver fire: Elevated FSH, early ovulation, irritability, hot flashes, night sweats, headaches and excessive menstrual flow. In this case excess heat over stimulate the pituitary causing excess release of FSH. Patent herbal formula used for this condition is Jia wei di huang san. The single herbal formula used include: Mu dan pi, Di gu pi, Bai shao, Qing hao, Sheng di huang, Huang bai, Fu ling, Shan zhi zi. Acupuncture points used include: Liv3, Liv2, Ren4, Sp6, Li11 (Elliot, 2009).

- Blood stagnation: Elevated FSH level, painful periods, dark and clotted menstrual flow, pain at ovulation, menstrual spotting before or after the period, a history of endometriosis, fibroid and adhesions. In this pathology the function of ovaries is compromised by surrounding blood stagnation causing pituitary gland to release more FSH. Herbal patent formulas commonly used are: Tao hong si wu tang, and gui zhi fu ling san. Single herbal formula suggested in this paper include: Sheng di huang, dang gui, chi shao, chuan xiong, tao ren, hong hua, dan shen, yan hu suo. Acupuncture points suggested include: SP4, Pc6, Sp10, Liv3, Sp6, Kid14, and St28 (Elliot, 2009)

- Kidney yang deficiency: Elevated FSH, possible diagnosis of polycystic ovarian syndrome (PCOS), elevated LH, delayed menstruation, scanty menstrual flow, dragging pain relived by heat, an-ovulation, water retention, weight gain, abdominal bloating, fatigue, vaginal discharge, dizziness and a feeling of heaviness. In this pattern ovaries are less responsive due to yang deficiency and their function is impaired by surrounding dampness, as the result pituitary releases more FSH. Patent formula used are: you gui wan combined with cang fu dao tan wan, or gui zhi fu ling san. Single herb formula suggested include: shu di huang, rou cong rong, huang jing, bug u zhi, chuan shan jia, gui zhi, zhe bai mu, zao jiao ci. Acupuncture points used are: Lu7, Kid6, St36, Sp6, Kid3, Bl20, Bl23, Sp9, St28 (Elliot, 2009).

Chinese Herbs studies

In a pilot study it was illustrated that a Kampo formula called EH0202 had a positive results of lowering FSH levels in menopausal women with symptoms while relieving menopausal symptoms as well (Ushiroyama et al., 2004). In this study 32 postmenopausal women presenting with menopausal complaints were enrolled in the clinical study. Patients were given herbal supplement EH0202 which include: Nan gua zi, che qian zi, hong hua, and jin yin hua. This herbal supplement was taken at 6gr/day for 6 months. After 6 months of herbal administration, it was found the plasma level of FSH had a significant decrease (p=0.018) (Ushiroyama et al., 2004).

This was a pilot study with low number of participants, although the results of FSH level had been lowered, but the study did not have any follow up FSH levels to determine whether the levels continued to stay low after discontinuation of herbs. The study also did

not mention the dosage of specific herbs given to patients; it also failed to mention the

mechanism of action of these herbs either in biomedical medicine or in TCM terms.

In another study the effectiveness of the herbal formula Unkei-to (Wen jing Tang) was

measured for inducing ovulation and normalizing plasma hormone levels. This study

included 100 patients (21-32 years of age) with ovulatory dysfunction, serum luteinizing

hormone (LH) level of at least 10mIU/ml, and 38 patients out of 100 were diagnosed with

Polycystic Ovarian Syndrome (PCOS). The results indicated that LH level of the

treatment group (which included both PCOS and non-PCOS patients) showed a drop of

30.1% at four weeks, and 51.2% at eight weeks; PCOS patients showed a decline of

38.8% at eight weeks, however the study did not show a significant change in plasma

FSH levels in four or eight weeks of taking the herbal formula (Ushiroyama et al., 2001).

Another study illustrated the effectiveness of Unkei-to (Wen jing tang) on plasma

levels of FSH, LH, and estradiol (E2) in an-ovulatory young women with hyper or hypo-

functioning conditions (Ushiroyama et al., 2003). In this study, the formula used Unikei-

to (Wen Jing Tang) included the following herbs; mai men dong, ban xia, dang gui, gan

cao, gui zhi, bai shao, chuan xiong, ren shen, mu dan pi, wu zhu yu, sheng jiang, and E

jiao. Since in this study patients did not menstruate, that meant that these patients did not

ovulate. Therefore the above formula was used to raise their FSH level and LH level,

causing ovulation and as the result of ovulation eventually menstruation would take

place. In this study among the hyper-functioning first grade amenorrhea patients, an

improvement of FSH level of 71.0% was observed; among the hypo-functioning patients

with first grade amenorrhea an improvement of 69.7% was reported. In patients with

hyper-functioning second grade amenorrhea an improvement in FSH level of 72.7% was

reported and 75.5% improvement was reported in hypo-functioning patients with second-grade amenorrhea. Patient with Hyper-functioning condition the mean FSH level was 4.2+_0.73 and for hypo-functioning patient the mean FSH level was 3.8+_0.81. This indicated that the formula Wen Jing Tang is effective in improving gonadotropin levels in patients with primary and secondary amenorrhea (Ushiroyama et al., 2003).

Another study measured the effectiveness of Wen Jing Tang in plasma level FSH and LH in Polycystic Ovarian syndrome (PCOS) patients. PCOS is a disease developing in women of relatively young age that begins with menstrual cycle abnormality and progress to disturbance of ovulation causing amenorrhea, and infertility. Recent studies had shown that Wen jing tang was effective in decreasing basal plasma LH level and with continued administration, this formula would increase ovulation rate. In this study researchers had randomly picked 64 an-ovulatory women with PCOS. Patients were diagnosed using eight principle pattern identification based on the state of the qi, blood, and water or the five parenchymatous viscera. Based on the diagnosis, 43 patients took dang gui shao yao san, and 21 patients took Gui zhi fu ling wan. After 8 weeks of administration, 54 patients failed to ovulate, from this 54 patient group, 27 patients continued with their previous treatments and 27 patients were given Wen Jing tang. Plasma levels of FSH, LH were measured before the treatment, after the first 8 weeks of treatments and the final 8 weeks of treatments. It was reported that the LH level in patients in second part of the treatments who were switched to Wen Jing tang had a significant drop in LH level; there was no significant change in FSH level (Ushiroyama et al., 2006).

Another Chinese herbal formula Tokishakuyakusan (Dang gui shao yao san) and its effect on luteal phase insufficiency was examined. This study measured the effectiveness of the above formula with patients with luteal phase insufficiency (Progesterone level in luteal phase <5ng/ml), the authors also studied the formula in normal menstruating women to explore the negative side effects of the formula (Usuki et al., 2002). The study showed that this formula is safe if taken by normal menstruating women, it also showed a significant increase in Estradiol-17B (E2) level of 71.4%, and a significant increase in progesterone (P4) levels of 71% in women with insufficient luteal phase (Usuki et al., 2002). Considering this formula has a positive effect in regulation E2 and P4 levels, it can be concluded that this formula has a regulatory effect of FSH as well, since E2 levels are controlled and regulated by FSH levels.

In a study done by Qu, Cai andGu (2009), Chinese formula GNL was used in a randomized controlled trial to determine the effectiveness of this formula in relieving premenopausal depression. In this study a total of 47 patients were randomly divided in two groups. Study group (n=21) received GNL formula which was prepared in 200ml of liquid and then reserved in vacuum bags. Patients took one dose a day for 12 consecutive weeks. The comparison group (n=26) were prescribed oral Livial (2.5gr/tab), one tablet a day for 12 consecutive weeks. The GNL formula included Chinese herbs such as: Zhen Zhu mu 15gr, Suan zao ren 8gr, Bai zi ren 12gr, Yuan zhi 10gr, He huan pi 8gr, huang qi 15gr, dang shen 10gr, bie xie 15gr, tu si zi 15gr, Nu zhen zi 10gr.

In this study, the levels of FSH decreased significantly and levels of E2 increased significantly in both groups (p<0.05), the serum levels of FSH, LH and E2 changed more in the comparison group than the GNL group (P<0.05).

Tibolone, which is the active ingredient in Livial, is an analogue of the progestin norethynodrel is a drug with tissue-specific effects on receptors and enzymes that influence the synthesis and metabolism of endogenous estrogen, progesterone, and androgen. This medication can protect bone and alleviate premenopausal symptoms like estrogen does; it had a protective, progesterone-like effect on the uterus and does not increase breast density or tenderness. Tibolone is effective in improving mood disorders, it works better than HRT since it had a lower chance of vaginal bleeding, lower chance of hyperplasia, no increase in size or volume of myomas, and it also prevents body fat increase and weight gain in post-menopausal women. This medication is not available in the US due to lack of large randomized trials. The side effect of this medication include, stroke in older women with osteoporosis, increase risk of endometrial disease, increased risk of acne, hair loss, hypertension, and recurrent endometriosis (Qu et al., 2009) Considering all the side effects of Tibolone and lack of any reported side effect of GNL Chinese herbal formula, and since in this study it has been shown that both can decreased FSH levels, it can be concluded that GNL formula is not only effective, but a safer alternative. The authors had a detail explanation about their choice of specific herbs.

- Zhen zhu mu: Calms the liver, nourishes yin, and sedates rebellious yang and tranquilize the mind. It has sedative and hypnotic activities and it is used for treating depression, palpation, insomnia, amnesia, dementia, neurasthenia, mental retardation, and infantile oligophrenia (abnormal development) (Qu et al., 2009).

- Suan Zao ren: Nourishes the liver and causes tranquilization, some animal studies showed this herb modulated stress-induced sleep changes in mice and enhanced total sleep in rabbits, and improve immunity in human. Zhen zhu mu and suan zao

ren together have been used together to treat depression, vexation, restlessness, insomnia, and dreaminess (Qu et al., 2009).

- Huang qi: Supplements qi and blood, it builds immune system, stamina and endurance. It has shown to have an immuno-modulatoring effect both in vivo and in vitro (Qu et al., 2009).

- Bi xie: Supplements kidney yin and qi and improves the functions of the spleen, it has antioxidant properties and traditionally used to improve immunity (Qu et al., 2009). It is important to mention that Bi Xie is actually in the category of drain dampness, but in this paper they used this herb as a yin tonic.

- Bai zi ren: Nourishes heart and calms the mind and supplements the kidneys (Qu et al., 2009).

- He huan pi: Tranquilizes the five zang organs, in particular clears the liver, harmonizes the mind, it is often used as a sedative and blood activator for treatment of distractibility, depression, and insomnia (Qu et al., 2009).

- Dang shen: Supplements qi and tonifies blood, it improves immunity, memory, and adaptability of the body and has sedative and hypnotic activities (Qu et al., 2009).

- Tu si zi: Supplements both kidney yin and kidney yang, it has been found that it improves the function of hypothalamic-pituitary ovarian (HPO) axis and improves immunity (Qu et al., 2009).

- In one study, it was found that Dang shen increases ATP synthesis in aged rat brains (Qu et al., 2009).

- Yuan Zhi: Tranquilizes the heart and mind, the active ingredient Tenuifolin has been found to have sedative activities and increases the level of norepinephrine and dopamine, therefore improving learning and memory in aged mice (Qu et al., 2009).

- Nu zhen zi: Supplements the kidney, liver and heart, it has been found to induce ultra-structural changes on the corticotrophs of the rat pituitary gland, it modulates endocrine function and posses' anti-aging activities (Qu et al., 2009).

In a study done by Wing and Sedlmeier (2006), the effectiveness of Chinese medicine herbs was measured in lowering FSH level. In this study a sample group of 50 patients were used with a western diagnosis of unexplained infertility, patients were prescribed Chinese Herbal medicine (CHM) in capsule form for one menstrual cycle; data collection took place over span of three months. Each patient was diagnosed according to Traditional Chinese Medicine (TCM) differential diagnosis and had been prescribed herbs matching their diagnosis and herbal formulas were modified each week based on patient's symptoms. This study failed to mention and discuss the herbs used in the study. The authors measured FSH levels before and after herbal medicine administration, and showed a significant drop of FSH level (1.7, P<0.001) (Wing & Sedlmeier, 2006).

In an interesting study, few Chinese herbs (drugs) and their properties according to TCM were studied in order to measure their affects in GnRH, FSH and LH levels. In this study, it was found that drugs for nourishing yin to reduce pathogenic fire can significantly down-regulate, and the drugs for tonifying the kidney to replenish essence can up-regulate mRNA expression of the hypothalamic GnRH, pituitary FSH, LH.

The herbs used for tonifying yin included: Di hunag, Zhi Bie jia, Huang Bo, Zhi Mu. The herbs to tonify kidney included: Shu di huang, Bie Jia Jiao, Ying Yang huo, and Lu jiao Jiao (Depei & Wei, 2005).

Another study showed that the herbal formula Erxian decoction which is a combination of Wen shen Yi jing recipe (warming the kidney and replenishing essence), Zi yin Xie huo recipe (for nourishing yin and dispersing fire) and Tiao li Chong ren recipe (regulating Chong and ren channel) can increase the FSH and LH levels of primary cultured anterior pituitary cells from female rats (Dong et al., 2007)

In a study, the effect of Chinese formula Bushen Tiaochong recipe (BSTCR) was measured on promoting the expression of mRNA of FSH receptors (FSHR) expression of rat's granulosa cells (GC). This formula included the following herbs: Tu si zi, huang jing, shu di huang, rou cong rou, dang gui, zhi shi ying, chuna xiong, and wu wei zi. This study revealed that BSTCR had a marked dose-dependent effect in increasing FSH receptor (FSHR) messenger RNA (mRNA) expression in ovarian GCs. As the result GCs become more sensitive to FSH stimulation, causing an estrogen dominant environment for these cells which put these cells in advantageous position to grow and develop into primary follicles (Tian et al., 2007). Considering that this herbal formula can increase FSHR on GCs, it can be concluded by increasing number of FSHR on GC more estrogen will be produced and this in turn by negative feed back can lower FSH level.

Acupuncture studies

One study examined the impact of acupuncture in regulating FSH levels. The study measured the effectiveness of Acupuncture in ovulatory dysfunction using the following acupuncture points: Ganshu (BL18), Shenshu (BL23), Guanyuan (Ren4),

Zhongji (Ren3), and Sanyinjiao (Sp6). The reinforcement and reduction of acupuncture stimulation enables it to strengthen liver and kidney, and Chong and ren channel nourishes uterus to adjust the patient's axis function and recover ovulation. Patients in this study had acupuncture for an average of 30 times, the marked effectiveness rate of ovulation was 35.29% and total effective rate was 82.35% (Xiaoming et al., 1993). This study showed that acupuncture treatments had a regulatory effect on the endocrine indices of the hypothalamus-pituitary-ovarian axis (HPO axis), including a bidirectional regulatory effect on FSH, LH, and E2; therefore, acupuncture can either reduce the higher level or raise the lower, to within the normal range (Xiaoming et al., 1993).

In another study acupuncture treatments were done on menopausal women to reduce their symptoms. The acupuncture points used in this study were as follows: Tai-xi (Kid3), Sanyinjiao (Sp6), Shen shu (BL23), Da zhui (GV14= Du14), Fenchi (GB20), Fuliu (Kid7), Zusanli (St36), Qihai (CV6, Ren6), Daling (PC7), Shenmen (Ht7), Taichong (Liv3). The study showed after acupuncture treatments FSH level decreased in 54.54% of patients, the level increased in 18.18% of patients, and FSH levels did not change in 27.27% of patients. The mean FSH level decreased from 86 at baseline to 82 mIU/mL at the end of treatment (95% confidence interval for the difference of 14 to 6; p=0.4) (Dong et al., 2001).

In a study which was done on a normal ovulatory woman, the effects of acupuncture were measured on plasma levels of LH, FSH, progesterone, and estradiol. This study showed that there was a great variation in plasma levels of these four hormones in the pre-ovulatory phase under acupuncture stimulation. Fifteen minutes after acupuncture stimulation the plasma levels of LH, FSH and Estradiol dropped while

progesterone level rose. After 30 minutes, the progesterone level begun to drop while the

LH and FSH levels returned to the normal levels. After 60 minutes of stimulation, the

progesterone level rose while FSH and LH levels dropped and Estradiol levels dropped as

well (Lim & Wong, 2010). The study also concluded that acupuncture has some good

regulatory effects on endocrine indices of the HPO axis, including a bi-directional

regulatory effect on FSH, LH, and Estradiol (Lim & Wong, 2010).

In the same study, female infertility was treated using auricular acupuncture. In this

study, it was observed that acupuncture was able to induce more physiologic regular

menstrual cycle than those by hormone therapy which may also explain the lower

abortion rate in acupuncture patients in the study (Lim & Wong, 2010).

A study examined one acupuncture point, it was shown the after Electro-

acupuncture on SP6 (Sanyinjiao), the FSH and LH levels decreased and E2 level

increased (Qin et al., 2007).

Another study a group of points were examined, the study illustrated that back

Shu and source points seem to have better effects in improving FSH and LH levels. This

study was abstract only, the text was in Chinese and the abstract failed to explain what

the study considers as an improvement in FHS and LH level (increased or decreased

plasma levels of FSH and LH) compared to routine acupuncture group. The points used

in back the study group included: Kid3, Liv 3, Sp3, Sp6, BL23, BL18, BL20, Ren4.

Routine acupuncture points include: Du20, Ren4, BL23, Kid3, Sp6 (Shang et al., 2009).

Literature Review Integration

The role of FSH levels has been established by Western Medicine as an important

factor in fertility medicine (Barnhart & Osheroff, 1999, Esposito at al., 2002, Abdalla &

Thum, 2004, Elliot., 2009, Singer et al., 2009, Viseer et al., 2006). Traditional Chinese

Medical theory has also made a contribution by defining the dynamics of the

reproductive system of women (Elliot, 2009). Additionally, Chinese herbal treatments

have been studied extensively with several formulations being demonstrated as having

some potential impact on FSH levels (Ushiroyama et al., 2001, 2003, 2004, 2006, Usuki,

2002, Qu et al., 2009, Wing & Sedlmeier, 2006, Depei & Wei, 2005, Dong et al., 2007,

Tian et al., 2007). Finally, the Traditional Chinese Medicine (TCM) technique of

acupuncture has been studied regarding its impact on FSH levels (Xiaoming et al., 1993,

Dong, H. et al, 2001, Lim & Wong, 2010, Qin et al, 2007; Shang et al, 2009). The current

study will make a contribution to the field by providing a detailed case study that

demonstrates via the analysis of a wide range of both objective and subjective data the

impact of the combined use of the treatments of acupuncture and Chinese herbs on FSH

levels in women of advanced maternal age.

Chapter 3: Case Study Method

The research objective of this study was to demonstrate through case study data the positive effect that treatments of acupuncture and Chinese herbs had in lowering FSH level in a woman of advanced maternal age. This chapter will specify the method used to accomplish that objective.

The current study was completed using case study research method. Yin (2009) described case study research as involving the multiple perspectives of both exploration and explanation. Case studies can be effective in both exploring the nature of a phenomenon as well as in explaining its dynamics. Case study methods are most effective in the process of providing in depth analysis of persons, events, decisions and processes. Case study research is often accomplished in advance of more in-depth and more controlled research studies, and often results in the generation of specific hypotheses for future more controlled research. Case study data comes from a variety of sources including direct observation, interview, archival records and other documents. A retrospective case study involves the examination of data and information that is historical, meaning that it has been previously gathered and archived. The current study was accomplished with the exclusive use of archived data from the chart of one patient who met the inclusion criteria for participation in this study.

Inclusion/Exclusion Criteria

The inclusion criteria for the case study engaged in the current study specified a number of factors. Those factors include the following:

- The case study subject must be a female
- The case study subject must be of advanced maternal age

- The case study subject must have a history of infertility

- The case study subject must present a history of a high Follicle Stimulating Hormone (FSH) level.

- The case study subject must have no history of previous pregnancy

- The case study subject must have no history of prior acupuncture or Chinese herbal treatment

In order to assure that the resulting data were not complicated by other factors, exclusion criteria were carefully designated and followed through in the selection of the case study subject. The exclusion criteria included the following:

- The case study subject had not other fertility problems

- High FSH level is not attributed to Premature Ovarian Failure (POF), Polycystic Ovarian syndrome (PCOS), Endometriosis or other endocrine or gynecological problems

- The case study subject did not suffer from obesity

This study was a qualitative study. The independent variables may be described as the patient's presenting symptoms, her current status and the treatment techniques of acupuncture and Chinese herbal medicine techniques that were engaged with the patient. The dependent variables included the factors measured in the treatment process and entered into the patient' archived chart. They included the following:

- Changes in presenting symptoms

- Changes in tongue

- Changes in pulse

- Measured FSH levels (via serum blood testing)

The use of retrospective chart review was a prudent way to engage this study since I was able to isolate the cause of infertility as being due to advanced age and high FSH and no other etiologies which could complicate the study.

With the careful application of the inclusion and exclusion criteria, the current study was a retrospective chart review case study of a 39 year old woman with high FSH levels due to advanced age. The case study subject was motivated to go through In Vitro Fertilization (IVF) treatment for infertility. The Acupuncture and Chinese herbal treatments were rendered in an office setting between July 31, 2010 and October 28, 2010, at which point the patient discontinued her treatments and returned to her reproductive endocrinologist to start her IVF cycle. The retrospective recording of data from the patients chart was accomplished in a home office setting starting in February of 2011 and concluding before the end of August 2011.

In this study information and data were collected as per the SOAP schema (Subjective, Objective, Assessment and Plan). The SOAP schema is a method of documentation commonly employed by health care providers to provide structure in the entry of notes in patient charts. The SOAP Schema from chart notes and blood tests (all collected prior to the onset of the study) constitute the data gathered from the archived chart of the designated case study patient (Wikipedia., August 26,2011) .

The data collected week to week during the designated time period (July31-October 28, 2010), included subjective and objective chart data that describe the patient's current status (see Tables 3A, 3B and 3C). The subjective and objective patient status data were compared and contrasted with patient "interview" data (INT) which included patient's signs and symptoms," Observation 1" data (OB1), which included Traditional Chinese

Medicine (TCM) tongue diagnosis, "Observation 2" data (OB2), which included TCM

pulse diagnosis, and "Observation3" data (OB3), which included FSH levels tested on

day two or three of the patient's menstrual cycle.

The following is a summary of the categories of data that were included in the chart

that was reviewed for this study.

- **INT:** On every visit, patient's symptoms had been recorded which was described

  in this study as an Interview (INT). These questions include changes to sign and

  symptoms on each visit.

- **OB1**: On every visit changes to the tongue according to TCM had been noted and

  recorded, in the study these changes were mentioned as OB1. These Changes

  include changes in tongue color, shape, coating, coating color, and moisture.

- **OB2:** On every visit changes to pulse according to TCM had been recorded and in

  the study which was discussed as OB2. Changes to the pulse include the depth,

  strength and speed of the pulse in each pulse location reflecting the affected organ

  system.

- **OB3**: Once a month of day 2 or 3 of her cycle, patient had a blood test which

  measured her Follicle stimulating hormone (FSH) level and her Estradiol level

  (E2), changes in FSH level and E2 level via the blood test was recorded as OB3 in

  the study.

Previous discussed data from the patient's chart was recorded according to her menstrual cycle as following:

- **Week 1:** Post-menstruation

- **Week2:** Ovulation

- **Week3:** Post-ovulation

- **Week4:** Menstruation

Patient received Acupuncture treatments and Herbal prescription every week, once a week for period of July 31/2010 to October 28/ 2010.

Table 1: Treatments/blood tests received on weekly basis for the patient

Month of July/August 2010	Acupuncture/herb week 3	Acupuncture/herb week 3	Acupuncture/herb week 4	Acupuncture/herb week 1
INT	+	+	+	+
OB1	+	+	+	+
OB2	+	+	+	+
OB3	+			+

*Weeks indicate where patient was in her menstruation

Month of September 2010	Acupuncture/herb week 4	Acupuncture/herb week 1	Acupuncture/herb week 2-3	Acupuncture/herb week 3
INT	+	+	+	+
OB1	+	+	+	+
OB2	+	+	+	+
OB3		+		

*Weeks indicate patient menstrual cycle

Month of October 2010	Acupuncture/herb week 4-1	Acupuncture/herb week 2-3	Acupuncture/herb week 3	Acupuncture/herb week 3
INT	+	+	+	+
OB1	+	+	+	+
OB2	+	+	+	+
OB3	+			+

*Weeks indicate patient menstrual cycle

In this study the three instruments of measurements were subjective and open to different interpretations. These include, first patient interviews (INT), at which point she reported the changes in her symptoms, secondly changes in tongue (OB1) and changes in pulse (OB2) which can be interoperated differently by different acupuncturists. Because of these factors, it was difficult to demonstrate the validity of the recorded data due to the subjective nature of the responses. Since the study had only one practitioner who treated the patient, there was no possibility of obtaining inter-rater reliability data. However, it should be emphasized that for this study, the most important measurements were the FSH data, which were obtained from subjective clinical test processes, as the result FSH data have high validity and reliability.

The questions asked and treatment protocol depended on the week of treatment which was based on patient's menstrual cycle. In each visit the same questions were asked from the patient (Table 3); therefore the questions were consistent. During ovulation time and menstrual time, more questions regarding ovulation day and menstruation were asked.

The data in the file were collected and recorded by a licensed professional who upholds the standards and ethics of the profession. As a result the data are likely to be true and honest. Professionals who do not record data honestly in patient charts run the

risk of being sued, having their licensed suspended or revoked, and censure from the licensing board. Hence the data that are in those files is likely to be valid and reliable. The data were recorded carefully each visit by the same licensed acupuncturist, there was a minimum chance that the recorded data were incorrect or false. This factor will minimize the external threats to reliability.

Internal threats to the validity and reliability of the data included the possibility that there were mistakes in data collection or/and data entry. In order to minimize this problem, I double checked every entry myself, and I could ask a colleague to collect a sample of data (perhaps two or three data collection sheets) independently, and I could compare the data collection of my colleague with my own data collection, and will demonstrate a high level of consistency, this will minimize the internal threats to the study.

Acupuncture:

Each visit patient was interviewed and assessed according to TCM criteria, acupuncture points were prescribed according to TCM protocol. Needles used were from Cloud and Dragon brand, one Cun (inch) 36 gauge, depth of insertion depended on location varying 0.2 inch to 0.75 inch. Needles were retained in patient for about 45 minutes each visit, there was also an ultraviolet heat lamp placed close to the needles during the treatment to keep the patient warm and comfortable.

Herbal Prescriptions:

Herbs prescribed were processed by Evergreen Herbal Company; the herbs were prescribed and taken in powder from. Dosage has been calculated to be taken on daily

basis three spoons three times a day for a total of 10.5g/day converted to powder dosage
with ratio of 1:5 (raw: powder).

Tables 2A through 2C reflect the Acupuncture points and Herbal prescription
which was administered to the patient.

Table 2A: Acupuncture points and herbs administered in month of July and August

MONTH OF JULY-AUGUST	WEEK 3 (CYCLE DAY 17). JULY 31	WEEK 3 (CYCLE DAY 22) AUG 5
Acupuncture point	Kid3, Kid7, St36, Ren12, Moxa on Ren 4, 6, Liv3, Li10 , Du 20, Yin tong	Kid3, Kid7, St36, Ren12, Moxa on Ren 4, 6, Liv3, Li10 , Du 20, yin tong, Li11
Herbs + dosage	Tu si zi 9gr, Du zhong 6, Xu duan 7.2, Shu di huang 6, Ban xiao 6, Dan shen 4.8, Bai shao 7.2, Dang shen 7.2, Dang gui 6, Wu wei zi 8, Fu pen zi 7.2, Chuan Xiong 6.8	Tu si zi 9gr, Du zhong 6, Xu duan 7.2, Shu di huang 6, Ban xiao 9.2, Dan shen 4.8, Bai shao 7.2, Dang shen 7.2, Dang gui 6, Wu wei zi 8, Fu pen zi 7.2, Chuan Xiong 6.8
Diagnosis	Kid yin def, liver qi yu, sp qi def causing phlegm accumulation	Kid yin def, liver qi yu, sp qi def causing phlegm accumulation

MONTH OF JULY-AUGUST	WEEK 4-1 (CYCLE DAY 1) AUG 16	WEEK 1-2 (CYCLE DAY 10) AUG 25
Acupuncture point	Li4, Liv3, Sp8, 10, Ren4, Ren6, St36, Kid 6 (L), Lu7 (R), Pc6 (L), Sp4 (R), Kid 3, Liv14, Du 20, Yin tong	Sp10, 8, St36, Lu7 (R), Kid6 (L), Ren4, Ren6, St 29, Zi gong xue, Du20, Ren 17, Ren15, Li4, Liv3, Li11, Du20, yin tong, Li 11
Herbs + dosage	Qing hao bie jao tang 20gr, Chi Hu7.2, Tao ren7.2, Hong hua 7.2, Sha ren 6gr, Dang gui 7.2, Shan zhu yu 7.2, Tu si zi 9.2. Nu zhen zi 7.2, hunang lian 4.8	Qing hao bie jao tang 20gr, Chuan Xiong 7.2, Dang gui 7.2, Xu duan 7.2, Sheng di hunag 6.8, Tu si zi 7.2, Gou qi zi 6.8, Nu zhen zi 7.2, Wu wei zi 7.2, Fu pen zi 7.2, Sha ren 7.2, Bai shao 7.2, Gan cao 4.8
Diagnosis	Kid yin def, slight blood and qi yu, Sp qi Yu	Kid yin def, sp qi def

*Weeks indicate where patient was in her menstruation

Table 2B: Acupuncture points and herbs administrated in month of September

MONTH OF SEPTEMBER	WEEK 4 SEPT 1 (DAY 1 OF CYCLE)	WEEK 1 SEPT 8 (DAY 8 OF CYCLE)
Acupuncture points	Sp10, Sp8, Ren3, Sp6, St36, Li4, Liv3, yin tong, Du20, Kid6 (L), Lu7 (R), Sp 4(R), Pc6(L), Li 11	Sp10, 8, St36, Lu7 (R), Kid6 (L), Ren4, Ren6, St 29, Zi gong xue, Du20, Ren 17, Ren15, Li4, Liv3, Li11, Du20, yin tong
Herbs & dosage	Qing hao bie jao tang 15gr, Chi Hu7.2, chuan xiong 7.2 sheng di huang 7.2 Tao ren7.2, Hong hua 7.2, Zhi zi 6, Sha ren 6gr, Dang gui 7.2, Shanzhu yu 7.2, Tu si zi 9.2. Nu zhen zi 7.2, Ban xia 9.2, Fu shen 7.2 He huan pi 6, Bai zhu 7.2, Huang jing 7.2	Same formula of Week 4
Diagnosis	Kidney yin deficiency, blood and liver qi yu, sp qi deficiency	Kid deficiency, liver qi yu, sp qi xu

MONTH OF SEPTEMBER	WEEK 2-3 SEPT 15 (DAY CYLE15)	WEEK 3 SEPT 22 (DAY CYCLE22)
Acupuncture points	(E red)Ren3, (E black) zi gong xue, (E red) ren 6, (E black) zi gong xue. Kid 3,6, 7, Lu 7, yin tong, Du20, St36,40, ren 17, ren12	Kid 3, 7, St 36, 40, sp 9 Ren 17, yin tong, du 20, Moxa on Ren 4, 6, sp3
Herbs& dosage	Shu di huang 7.2, Chi shao 7.2, dan shen 7.2, Huang jing 7.2, bai shao 7.2, xu duan 6.8, tu su zi 9.2, nu zhen zi 9.2, fu pen zi 7.2, gou qi zi 7.2, Dang gui 7.2, Ban xia 7.2,	Du zhong 7.2, xu duan 7.2, tu si zi 7.2, gou qi zi 7.2, nu zhen zi 7.2, shan zhu yu 7.2, bai shao 7.2, huang jing 7.2 gan cao 4.8
Diagnosis	Kid deficiency (overall), liver qi yu, sp qi deficiency	Kidney deficiency, sp qi deficiency

* Weeks indicate where patient was in her menstruation

Table 2C: Acupuncture points and herbs administrated in month of October

MONTH OF OCTOBER	WEEK 4-1 OCT 5 (DAY 3 OF CYCLE)	WEEK 2-3 OCT 13 (DAY 11 OF CYCLE)
Acupuncture points	Li4, liv3, Sp10,8, Ren 4, 6, St36,40, Sp 6,9 Kid 3,6. Liv14. Lu 7, Li 11	(E red)Ren3, (E black) zi gong xue, (E red) ren 6, (E black) zi gong xue. Kid 3,6, 7, Lu 7, yin tong, Du20, St36,40, ren 17, ren12. liv 14
Herbs and Dosage	Sheng di huang 7.2, mu dan pi 6.8, shan zhu yu 7.2, tu si zi 7.2, Dang gui 7.2 bai shao 7.2, Chuan xiong 7.2, Tao ren 6.8, hong hua 6.8, Chi shao 6.8, bai zhu 7.2, ban xiao 7.2, fu shen 6.8, sha ren 6.8	Chai hu 9.2, Sang ji sheng 7.2, dang gui 7.2, Chi shao 7.2, dan shen 7.2, Huang jing 7.2, bai shao 7.2, xu duan 6.8, tu su zi 9.2, nu zhen zi 9.2, fu pen zi 7.2, gou qi zi 7.2, Dang gui 7.2, fu ling 6.8,
Diagnosis	Liver qi stagnation, sp qi deficiency	Liv qi yu, kid deficiency

MONTH OF OCTOBER	WEEK 2 OCT 20 (DAY CYCLE 18)	WEEK 3, OCT 28 (DAY CYCLE 26)
Acupuncture points	Kid 3, 7, St 36, 40, sp 9 Ren 17, yin tong, du 20, Moxa on Ren 4, 6, sp3	Kid 3, 7, St 36, 40, sp 9 Ren 17, yin tong, du 20, Moxa on Ren 4, 6, sp3, UB23, 24
Herbs and Dosage	Tu si zi 9gr, Du zhong 6, Xu duan 7.2, Shu di huang 6, Ban xiao 9.2, Dan shen 4.8, Bai shao 7.2, Dang shen 7.2, Dang gui 6, Wu wei zi 8, Fu pen zi 7.2, Chuan Xiong 6.8	Same as last week
Diagnosis	liv qi yu	liv qi yu, slight Kidney deficiency

*Weeks indicate where patient was in her menstruation

Human Subjects Ethical Considerations

The current study was engaged exclusively by the collection and analysis of data

collected from the archived chart of the designated case study patient. No new data were

collected, nor were any additional interviews or observations of the patient made.

Additionally all data were collected, managed and reported anonymously with no

possibility of identification of the case study subject. As a result, this study is exempt

from Institutional Review Board (IRB) procedures. Nonetheless, the proposal for this

research project was presented to the Yo San University IRB in February of 2011.The Yo

San University IRB review resulted in a response letter which affirmed the exempt status

of the study. A copy of the IRB response letter is included in Appendix A**.**

Chapter 4: Results

Data gathered in this study were recorded from the archived chart of the designated case study patient and included both subjective and objective current status factors, changes in tongue and pulse pathology, as well as FSH levels. Most data were gathered on a weekly basis between July 29 and October 28, 2010. Tables 3A, 3B and 3C provide a summary of the subjective and objective data.

A review of the data in Tables 3A, 3B, and 3C manifests improvements in the patient's status reports of sings and symptoms (INT) over the course of treatment. Over the course of treatment, the patient reported fewer episodes of hot flashes and night sweats, more overall energy level, more ovulatory cervical mucus during ovulation, and less general cold feeling. Additionally, positive changes are observed regarding the OB1 (Changes in tongue) and OB2 (changes in pulse) factors. The tongue and pulse factors were evaluated using standard TCM criteria by the same practitioner. Table 4 and Table 5 respectively indicate the changes in tongue and pulse.

Table 3A: Objective and subjective data collection for month of July-August

Month of July 31st 2010-August 25th 2010	Week 3 (cycle day 17). July 31	Week 3 (cycle day 22) Aug 5	Week 1 (cycle day 1) Aug 16	Week 2 (cycle day 10) Aug 25
INT	Night sweat/hot flashes. yes	Night sweat/hot flashes: none	Night sweats/hot flashes: slight night sweats	Night sweats/hot flashes: none
	E level: 7/10	E level: 6/10	E level: 5/1	E level:7/10
	BM/appetite: QD	BM/appetite: QD	BM/appetite: slight. Loose stool	BM/appetite: QD
	Breast tenderness: none	Breast tenderness: none	Breast tenderness: none	Breast tenderness: none
	Spotting: none	Spotting: none	Spotting b/f or after: one day before	Spotting: none
		Cervical mucus: none		

	Cervical mucus: none Stress/emotional state: high General cold/heat: cold Other changes: N/A	Stress/emotional state: high General cold/heat: cold Other changes: N/A	Bleeding days: 4 Clots: first day Color: bright red Cramps: day before and first day PMS/Emotional changes: yes/anger Stress/emotional state: high General cold/heat: slight. heat Other changes: N/A	Cervical mucus: none Stress/emotional state: less stressed OPK: not yet (+) on day 13-15) General cold/heat: none Other changes: N/A
OB1	Tongue color= dusky, pale, teeth marks Tongue coating= thick white	Tongue color= Dusky, pale Tongue coating= thick and white	Tongue color= dusky slightly red tip and sides Tongue coating=thick, slightly yellow	Tongue color= pale, dusky Tongue coating= thick, slight yellow in MJ and LJ
OB2	Right pulse= thin, weak, chi position deep Left pulse= wiry, slippery, chi position weak	Right pulse= slightly slippery, weak, chi position deep Left pulse= wiry, thin and slightly rapid. Chi position deep and weak	Right pulse= slippery, weak Left pulse= wiry, thin and slightly rapid. Chi position weak and deep	Right pulse= Slippery, slight rapid Left pulse= Wiry and thin, chi position deep and weak
OB3	Day 2 of cycle July 16th FSH: 23.64 E2: 22.31		Day 2 of cycle August 17th FSH: 14.20 E2: 21.49	

*Weeks indicate where patient was in her menstruation

As it is evident from Table 3A, patient's symptoms such as hot flashes and night sweats improved over the treatment course. She ovulated on Day13-15 of her cycle, no ovulatory cervical mucus was reported, and her energy level and stress level remained unchanged.

Table 3B: Objective and subjective data collection for month of Sept 2010

Month of Sept. 1 to 22nd 2010	Week 4. Sept 1 (DC1)	Week 1. Sept 8 (DC8)	Week2-3 Sept15 (DC15)	Week 3. Sept 22 (DC22)
INT	Night sweat/hot flashes. yes E level: 5/10 BM/appetite: QD Breast tenderness: none Spotting: yes b/f period for one day Bleeding days: 4 Clots: first day PMS/emotional state: yes/anger Color: dark red Cramps: one day before, and first day Cervical mucus: none Stress/emotional state: high General cold/heat: slightly heat Other changes: N/A	Night sweat/hot flashes: none E level: 6/10 BM/appetite: QD Breast tenderness: none Spotting: none Cervical mucus: none Stress/emotional state: high General cold/heat: ok Other changes: N/A	Night sweats/hot flashes: none E level:7/10 BM/appetite: slight. Loose stool Breast tenderness: none Spotting: none Cervical mucus: none OPK: (+) ovulation date DC13-15 Stress/emotional state: high General cold/heat: slight. heat Other changes: N/A	Night sweats/hot flashes: none E level:7/10 BM/appetite: QD Breast tenderness: none Spotting: none Cervical mucus: none Stress/emotional state: less stressed General cold/heat: none Other changes: N/A
OB1	Tongue color= dusky, slightly pale, red tip and red sides Tongue coating= thick slightly yellow	Tongue color= Dusky, pale, slight red tip Tongue coating= thick and slightly yellow	Tongue color= slightly red tip and sides Tongue coating=thick, slightly yellow	Tongue color= slightly dusky, flabby Tongue coating= thin white
OB2	Right pulse= wiry, slippery, chi position deep Left pulse= thin, slightly rapid wiry, chi position weak	Right pulse= slightly slippery, weak, chi position deep Left pulse= wiry, thin and slightly rapid. Chi position deep and weak	Right pulse= slippery, weak Left pulse= wiry, thin and slightly rapid	Right pulse= Slightly slippery, slight. rapid Left pulse= think, slightly rapid and slippery

OB3		Sept. 10th FSH: 13.43 E2: 72.50		

* Weeks indicate where patient was in her menstruation

As it can been seen from Table 3B, patient continued to repot improvement in her hot flashes and night sweats symptoms, she ovulated on day 13-15 of her cycle but no cervical mucus was reported. During her period, she reported some menstrual cramps, and her overall stress level remained unchanged.

Table 3C: Objective and subjective data for month of October 2010

Month of October 2010	**Week4-1. Oct 5. (DC3)**	**Week2-3. Oct 13 (DC11)**	**Week 2. Oct 20 (DC18)**	**Week 3 . Oct 25 (DC26)**
INT	Night sweat/hot flashes. Slight night sweat E level: 7/10 BM/appetite: QD Breast tenderness: none Spotting: yes b/f period for one day Bleeding days: 4 Clots: first day PMS/emotional state: yes/anger Color: dark red Cramps: slight cramp first day Cervical mucus: none	Night sweat/hot flashes: none E level: 6/10 BM/appetite: QD Breast tenderness: none Spotting: none Cervical mucus: slightly egg white mucus seen OPK: (+) Stress/emotional state: high General cold/heat: cold Other changes: N/A	Night sweats/hot flashes: none E level: 7/10 BM/appetite: QD Breast tenderness: none OKP= (+) ovulated day 14 Cervical mucus: + Stress/emotional state: slightly less General cold/heat: slight. heat Other changes: N/A	Night sweats/hot flashes: none E level:7/10 BM/appetite: QD Breast tenderness: none Spotting: none Cervical mucus: none Stress/emotional state: less stressed General cold/heat: none Other changes: mild cramps

	Stress/emotional state: high General cold/heat: pt is slightly warm Other changes: N/A			
OB1	Tongue color= dusky, pale Tongue coating= slightly thick white	Tongue color= Dusky, pale Tongue coating= thin and white	Tongue color= dusky, slightly red tip and sides Tongue coating=thin, and slightly yellow	Tongue color= slightly dusky pale, some teeth marks Tongue coating= White slightly thick in LJ
OB2	Right pulse= thin, weak, slight. slippery Left pulse= wiry, slippery,	Right pulse= slightly slippery, wiry Left pulse= wiry, thin	Right pulse= slippery, weak Left pulse= wiry, slightly thin	Right pulse= slightly slippery Left pulse= Slightly wiry and thin
OB3	October 5th 2010 FSH: 16.14 E2: 12.95			Nov 3rd 2010 FSH: 7.65 E2: 42.25

*Weeks indicate where patient was in her menstruation

In Table 3C, it can be seen that patient did not report any more hot flashes and night sweats, ovulation occurred on day 14 of her cycle and she reported small amount of ovulation cervical mucus. Her menstrual cramps during her period was less, however her stress level remained high.

In Table 4, I have detailed the changes in pathological tongue over time. Each month the patient had 4 visits (approximately one visit a week). For example, in month of July/August, the patient presented with dusky tongue on each visit; therefore, dusky tongue pathology was 100% for the month of July/August. As it can be seen from the Totals in Table 4, the pathological tongue quality decreased from 42.86% to 25% over

the course of treatment. It can be interpolated that Acupuncture and Chinese Herbal medicine may have a role in reducing the pathological tongue quality over time.

Table 4: Changes in Tongue Pathology

Month	July/August	September	October
Dusky	4/4 (100%)	2/4 (50%)	3/4 (75%)
Pale	3/4 (75%)	1/4 (25%)	2/4 (50%)
Thick white coating (TWC)	2/4 (50%)	0/4 (0%)	1/4 (25%)
Thick Yellow coating (TYC)	2 /4(50%)	3/4 (75%)	0/4 (0%)
Red sides/ tip (RST)	0/4 (0%)	1/4 (25%)	0/4 (0%)
Flabby	0/4 (0%)	1/4 (25%)	0/4 (0%)
Teeth marks (TM)	1/4 (25%)	0/4 (0%)	1/4 (25%)
Total	12/28 (42.85%)	8/28 (28.57%)	7/28 (25%)

* note that the qualities which had been described as slightly were not considered as pathology.

Pulse pathology was measured by the following qualities: thin, weak, deep, slippery, slightly rapid, and wiry. These pulses were measured and recorded on both the right hand and left hand. The overall quality of pulses independent of position of depth was recorded; slightly slippery, and slightly weak and slightly thin were not considered pathology since pulses are very subjective in nature. For example, if the patient presented with a thin pulse on each visit in month of July/August on each hand a total of 8 thin pulses would be recorded. In the month of July/August the patient presented with a total of 4 thin pulses which gave us a value of 50%. As it can be seen from the Totals in table 5, the frequency of pathological pulses decreased over time from a value of 54.16% in the first month to a 20.83% at the end of the treatment period, suggesting that Acupuncture and Chinese Herbal medicine may have an effect in reducing pathological pulses and harmonizing the overall pulse system.

Table 5: Changes in Pulse Pathology

Month	July/August	September	October
Thin	4/8 (50%)	4/8 (50%)	2/8 (25%)
Weak	7/8 (87.5%)	5/8 (62.5%)	2/8 (25%)
Deep	5/8 (62.5%)	3/8 (37.5%)	0/8 (0%)
Slippery	3/8 (37.5%)	3/8 (37.5%)	2/8 (25%)
Slightly Rapid	3/8 (37.5%)	5/8 (62.5%)	0/8 (0%)
Wiry	4/8 (50%)	4/8 (50%)	4/8 (50%)
Total	**26/48 (54.16%)**	**24/48 (50%)**	**10/48 (20.83%)**

The only laboratory derived data in this study was OB3 ($2^{nd\ or\ 3rd}$day FSH level) which was measured at reproductive Endocrinologist's office and results were faxed and recorded in patient's chart. Table 6 shows the changes in FSH and E2 value before the onset of Acupuncture and Chinese Herbal Medicine treatments to the last value after 3 months of treatments had been rendered and before IVF protocol had started.

Table 6 FSH level from July 2010 to November 2010

	FSH level mIU/ml	E2 level pg/ml	TSH level uIU/ml	Cycle length
July 16th 2010	23.64	22.31	1.051	35
August 17th 201	14.20	21.49		32
September 10th 2010	13.43	72.50		24
October 5th 2010	16.14	12.95		26
November 3rd 2010	7.65	42.25		29
Normal Value	<12	40	0.8-2.5	28-32

As it is evident above, it can be seen that Acupuncture and Chinese Herbal Medicine had a positive impact in FSH levels over the course of treatment. Patient was introduced with a FSH level of 23.64 and E2 level of 22.31. FSH level was too high and E2 level was too low and her cycles were irregular ranging from 36-35 day in pervious months according to patient's history. Through the course of treatment with Acupuncture

and Chinese Herbal Medicine, it is evident that her FSH level has gradually decreased to a desired value of <10 (FSH: 7.65), E2 level of 42.25 which is within normal range and her cycle length has normalized.

In consideration of all the above reported values, FSH, E2, cycle length, changes in patient's sign and symptoms and changes to her tongue and pulse, it can be concluded that Acupuncture and Chinese Herbal Medicine decreased FSH level and might have an effect in the overall health of this patient.

Chapter 5 Discussion

Summary of findings

The current study was a case study of a 39 year old woman with a history of infertility and high Follicle Stimulating Hormone (FSH) levels. It was shown that acupuncture and Chinese herbal treatments decreased FSH level. The FSH level at onset of treatments was 23.64 mIU/ml and after three months of treatments the level had dropped to 7.65 mIU/ml. There was also some improvement in cycle length of patient which was a little irregular at the beginning (24-35 days) and at the end of treatments (27-29 days). Also some improvement in tongue and pulse qualities according to Traditional Chinese Medicine (TCM) criteria was reported. At the beginning of treatments pathological quality of tongue was recorded was 42.85% at first month of treatment and at the last month of treatment was 25%. Pathological pulse recording were at 54.16% at first month of treatment and it dropped to 20.83% at the last month of treatment.

Implications for theory

Via current case study, it has been demonstrated that acupuncture treatments have a regulatory effect on the endocrine indices of the hypothalamus-pituitary-ovarian axis (HPO), including a bidirectional regulatory effect on FSH, luteinizing Hormone (LH), and Estradiol (E2); therefore, acupuncture can either reduce the higher level or raise the lower, to within the normal range (Xiaoming et al., 1993). In some studies, it was seen that certain acupuncture points can decrease FSH levels (Dong et al., 2001, Oin et al., 2007, and Shang et al., 2009). In another study it was shown that acupuncture has a regulatory effect in FSH levels (Lim & Wong, 2010). The exact mechanism of how acupuncture is able to lower FSH level is not known. A theory, which was suggested by

P. Magarelli (Personal communication, August 5, 2011) suggested that acupuncture may increase the blood flow and neuro-vascularization to the eggs which are located in the cortex of the ovaries, therefore increasing the access to these eggs. As a result of stimulation of these follicles, there is an increase in estrogen levels, which lowers FSH levels. This is a viable theory and consistent with the data observed in the current study. As the patient's FSH level decreased, her E2 levels (estrogen) increased.

It has been proven that FSH induced aromatization of androgen in the granulosa cells results in the production of estrogen. This process is explained by the two-cell, two-gonadotropin mechanism which allows the critical creation of an estrogen dominant micro-environment. Together, FSH and estrogen increase the FSH receptors content of the follicles and stimulate the proliferation of granulosa cells (Speroff et al., 2005). In one study it was shown that herbal formula Bushen Tiaochong recipe can increase the number of FSH receptors on granulosa cells (Tian et al., 2007). In the perspective of the current researcher, the process is further explained by the hypothesis that persistent FSH stimulation and lack of estrogen production from follicles may desensitize FSH receptors on granulosa cells, which in turn will cause higher FSH production. Similar to the theory of insulin resistance, in the process of lowering the FSH level, the FSH receptors on granulose cells become more sensitive to FSH stimulation.

Chinese Herbs seemed to have a regulatory effect on FSH levels, in cases which FSH levels are low Chinese herbs seem to increase FSH levels (Ushiroyama et al., 2003, Dong et al., 2007). In cases which FSH levels were high the herbs were able to decrease FSH (Ushiroyama et al., 2002, 2004, Qu et al., 2009, Wing & Sedlmeier, 2006, Depei & Wei, 2005, Tian et al., 2007).

In my study the Chinese herbs used were able to decrease the FSH level without a dramatic increase the E2 levels. It is difficult to study the exact mechanism of how Chinese herbs are able to lower FSH. Since each formula has many herbs and each herb contains many chemicals, it difficult to measure how these chemicals interacts with each other and how they affect the body on the cellular level. One theory which has been suggested by Western medical community is that some of Chinese herbs have estrogenic effect which by negative feed back lowers the FSH levels. This is a valid explanation since the estrogenic effects of certain herbs can have a negative feedback on FSH level, this can be in form on estradiol, estrone, or other estrogen forms which could bind to estrogen receptors in hypothalamus and pituitary gland and suppress FSH level.

Implications for practice

According to studies which have been mentioned above FSH is not an effective indicator of ovarian reserve or oocyte quality since FSH is produced and secreted by pituitary gland, and FSH levels tend to fluctuate every month and it can only be measured on a specific time (Barnhart & Osheroff, 1999, Esposito et al 2002). It has been suggested that Anti Mullerian hormone (AMH) is a more effective way in measuring the oocyte quality and ovarian reserve since it is secreted by small antral follicles and in reproductive-aged women is expressed by granulosa cells of the ovary. It is mentioned that a big potential of measuring AMH over FSH levels as a clinical test is that AMH levels are stable throughout the menstrual cycle and hence serum can be drawn at any time (Singer et al, 2009).

Although FSH levels do not reflect the quality and the ovarian reserve, but for patients who desire to undergo In vitro fertilization (IVF) treatments, it is important to

have low FSH levels for better response to stimulation medications. This group of patients can benefit from acupuncture and Chinese herbs to lower their FSH levels.

In this study, it was illustrated that acupuncture and Chinese herbs may be effective in lowering FSH level which was high due to advanced maternal age. Patient's treatments were designed according to her TCM diagnosis and her menstrual cycle time (Tables 2A-2C, Appendices C-E). On the menstruation phase, moving, cooling, and regulating qi and blood Chinese herbs and acupuncture points prescription were used to move qi and blood for better menstrual flow. During the follicular phase, many yin nourishing, qi nourishing, some qi regulating and a small amount of yang tonifying Chinese herbs were used. In the follicular phase yin tonics and qi tonics had a function of nourishing the developing follicles and small amount of yang tonics ensured better growth of the developing follicles. Acupuncture points that were used during this period were mostly to tonify kidney and spleen and regulate Chong and Ren channels. At the ovulation phase, qi moving, qi regulating, some blood moving herbs, and yang tonifying herbs were used in her herbal prescription to ensure better ovulation. Also, acupuncture points followed the same principle for promoting ovulation, using local points on abdomen with electro-stimulation to promote ovulation. In the luteal phase, more yang tonic herbs were used to tonify yang, ensure the health and quality of the corpus luteum, promote a consistent level of high progesterone level, and promote implantation. At the luteal phase, kidney yang and spleen yang tonifying acupuncture points were used to promote implantation and hold the possible pregnancy; points that are classically forbidden during pregnancy were omitted at this time.

At the end of treatment period it was observed that patients showed improvements in signs and symptoms such as an increase in ovulatory cervical mucus, reduction of hot flashes and night sweats, there was also an improvement in overall energy level. Patient's menstrual length was also regulated, there were improvements in tongue quality and pulse quality, and most importantly FSH level was reduced over the course of treatments. The primary diagnosis for this patient at the onset of treatments was Kidney yin deficiency, and this diagnosis was resolved by the end of the treatment course since patient showed improvement in her Kidney deficiency symptoms, but I suspect she continued to have a general Kidney deficiency due to her age. These improvements in her condition prepared the patient for IVF procedure and increased her chances of better outcome.

According to Traditional Chinese Medicine (TCM), kidneys dominate reproduction, kidney Jing which corresponds to sperm/egg, kidney yin, and kidney yang correspond to hormones. Other organs such as liver, spleen, heart, and lung also play important roles. Smooth flow of liver qi is required to ensure optimal follicular development, ovulation, and menstruation, liver also moves and stores blood which nourishes the developing follicles and uterus. Spleen needs to be in harmony since spleen provides the post natal qi and this in turn nourishes the kidneys, also the transform and transport function of spleen will provide nutrition (blood) to the ovaries and uterus. Heart is involved via bao mai in regulating hypothalamus-pituitary-ovarian axis (HPO axis), also heart moves blood which ensures better circulation to the uterus and ovaries. Lung governs qi and lifting action of lung qi is important during implantation and pregnancy (Lytteleton & Clavey, 2007)

Channels which greatly involved in female reproduction are Chong and Ren and it is important to keep these channels open and have a smooth flow of qi during follicular phase to better follicular development. Du channel is important during ovulation time, and Dai is important for better communication and free flow of qi between Middle Jiao and lower Jiao. Other channels which play a key role in reproduction include Bao Mai which connects heart and Bao Gong (uterus) and Bao Luo which connects Kidney and uterus; this ensures smooth and open HPO axis (Lyttelton & Clavey, 2007) Considering the importance of these organs, it can be seen that most of herbs and acupuncture points used are to ensure optimum function of these organs which will result in better reproductive potential.

I can theorize that acupuncture and Chinese herbs may improve follicular quality by improving the hormonal environment in the ovaries, improve follicular recruitment, increase FSH receptors on follicles causing better respond to stimulation, and improve hormonal environment in ovaries which in turn will improve follicular quality. These are all theories and more studies need to examine how acupuncture and Chinese herbs might affect hormones and follicular development.

Limitations

Several limitations regarding the current study can be identified. First and foremost is the limitation inherent in the case study method engaged in the current study. As a case study the current study involved only one subject. While the data collected and analyzed regarding the single subject were diverse, extensive and in-depth, the nature of qualitative case study research method is limited as there are no average data points across a number of subjects that can be engaged for comparison. Secondly, because case

study method is lacking the factors of randomization and the potential for blind

application of treatments and procedures, the possibility for the emergence of statements

of cause and effect are extremely limited. Thirdly, while current theory explains the

impact of acupuncture on FSH levels as a function of the influence that acupuncture has

on the hypothalamic-pituitary-ovarian axis by increasing endorphin levels and thereby

enhancing sympathetic nerve stimulation, the exact mechanisms are not known. There

are no empirically based studies or data to explain exactly how acupuncture impacts FSH

levels. As a result studies regarding the acupuncture FSH connection are in the early

stages of development. As a result, while the data and observations from the current study

are convincing, they must be tempered with the awareness that the findings are at best

tentative and need to be followed up with further case studies, case series and eventually

controlled and randomized quantitative/empirical research.

A further factor that constitutes a limitation in the current study as well as in all

Acupuncture research models is the issue of point prescription, point location and the

exact methods of insertion. Different locations, different insertion levels and different

means of stimulation can yield different results.   Because of the spectrum of styles that

result form a range of theory and training models in Traditional Chinese Medicine, it

must be kept in mind that treatment is likely to differ when engaged by different

acupuncture practitioners. As a result, replication of the current study is likely to be very

limited.

The factor of herbal treatment likewise raises a further limitation of the current

study. The relationship between TCM diagnosis and the requisite herbal prescription in

most cases is an art and only beginning to approach the level of science. Within the

practice of the profession there is a good deal of variability regarding the precise herb(s) prescribed, the dosage and the frequency of herbal ingestion. Additionally, the issue of patient compliance must also be considered as a factor that in case study research and in most controlled studies remains an unknown fact. In the current study, while it is clear what herbs, in what amount and at what frequency were prescribed, there is no way that patient compliance could be precisely monitored or controlled.   Finally, in the arena of the herbal factor, is the issue of the quality of herbs provided to the patient. It is widely known that herbs used in TCM treatments vary greatly regarding the batches the exact geographic area of their origin, the season of harvesting, and the post-harvesting processing. Again, in the current study, it is impossible to assure standardization regarding the quality of the herbs utilized by the patient.

Recommendations for future research

As a qualitative single subject case study, the current research study might be considered ground breaking with substantive observations emerging. However, the observations and conclusions that emerged from the current study must be considered preliminary. Those preliminary observations derive some of their value in pointing the direction for future research studies. It is obvious that further research should be undertaken as a follow up to the results of the current study. It would decidedly be beneficial to conduct one or more studies that engage the same factors that were explored in the current study (acupuncture/herbal treatment/FSH levels) using more controlled empirical quantitative methods. Such studies should be carried out with randomization, blind and double blind controls in effect to explore the same variables engaged in the current study. Additional studies should be conducted to examine the effects of birth

control pills, vs. Chinese herbs on FSH levels. Even further randomized and controlled studies should be engaged to explore the impact of acupuncture and herbal treatments on pregnancy and live birth rates.

More specific research is also warranted regarding the impact of acupuncture and herbal treatments on oocyte quality and on the processes for improving the number of antral follicles. Likewise further controlled research is needed regarding the impact of acupuncture and herbal treatments on Anti-Mullerian Hormone (AMH), another factor that is suspected to have strong links to oocyte quality and the ability of the female to successfully conceive. All of the above mentioned potential research studies will be vital to continue the path of fertility research at a higher and more conclusive level that is characterized by the preliminary and tentative conclusions of the current study.

Conclusion

As demonstrated from the analysis of case study chart review data, the combined use of acupuncture and Chinese herb treatments appears to have the potential to lower FSH levels. However further studies that engage controlled randomized clinical trial methods are needed to further affirm the observations that emerged from the current study.

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Appendix A: IRB letter

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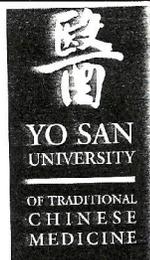
February 8, 2011

Sharareh Daghighi
15120 Magnolia Blvd., Apt 102
Sherman Oaks, CA 91403

Dear Sharareh,

Your Claim for Exemption from the Institutional Review Board (IRB) has been reviewed. Your research proposal will be approved with the following recommendations:

Under the heading Appropriateness of instruments, please change "where she reports" to "where she reported".

Under the heading Information on Reliability, please change "few months after completion of the study" to reflect the information being collected during the time of the study.

Please provide us with an updated copy of your IRB and Capstone Thesis Proposal outline.
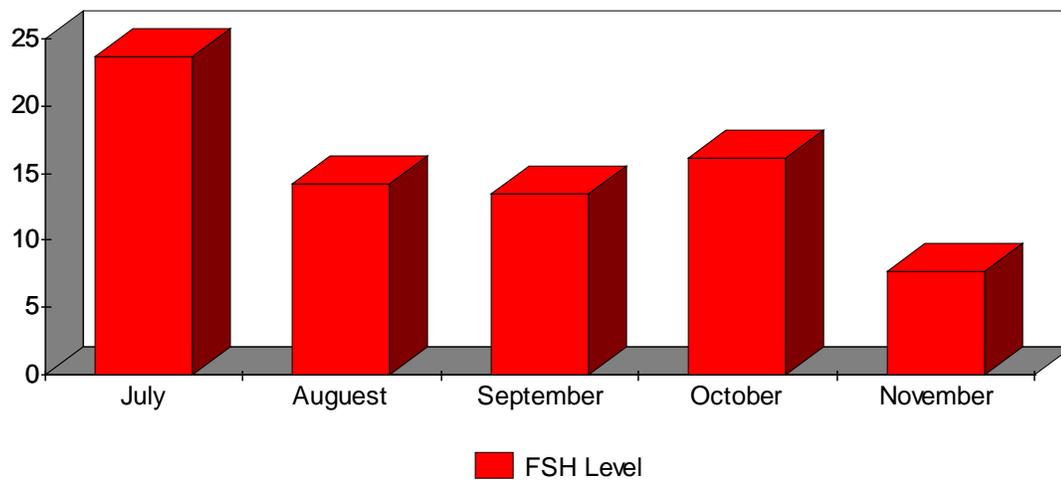
Should there be any significant changes that need to be made which would alter the research procedures that you have explained in your proposal, please consult with the IRB coordinator prior to making those changes.

Regards,

Jerome White
IRB Coordinator

Appendix B: FSH level changes overtime graph

	July	Auguest	September	October	November

■ FSH Level

Appendix C: Most common acupuncture points used in the study

Point function was reported and chosen base on Lyttelton &Clavey, (2007)

	Week 1	Week2	Week3	Week4
Tonify Qi	St 36, ren 4,6, du 20	St 36, ren 4,6, du 20	St36, Du 20	St 36, ren 4,6, du 20
Tonify Blood	St 36, Sp 6	St 36, Sp 6	St36	St 36, Sp 6
Tonify yin	Lu 7, kid 6, sp 6, kid 3	Lu 7, kid 6, sp 6, kid 3	Kid 6, kid 3	Lu 7, kid 6, sp 6, kid 3
Tonify yang	kid 3, kid 7	kid 3, kid 7	Kid 3, Kid 7	kid 3, kid 7
Move/reg qi	Sp 8, Li 4, Liv3	Sp 8, Li 4, Liv3	Ren 17, Ren 12	Sp 8, Li 4, Liv3
Move/reg Blood	Sp 10,			Sp 10,
Cool blood/3 jiaos	Li 11			
Reg. Ren	Lu 7, Kid 6	Lu 7, Kid 6		
Reg. Chong	Sp 4, Pc6	Sp 4, Pc6		
Reg. Dai				
Resolve phlegm/damp	Sp 9, St40		St 40, Sp 9	St 40, Sp 9
Induce ovulation		(E) ren 4, 3, 6, zi gong xue		
Calm shen	Du 20, yin tong, ren 17	Du 20, yin tong, ren 17	Du 20, yin tong, ren 17	Du 20, yin tong, ren 17

* Weeks indicate where patient was in her menstruation

Appendix D: Acupuncture point descriptions

Point location was reported according to Zheng, Xue, (1999).
Point function was reported and chosen base on Lyttelton & Clavey, (2007).

Point	Name	Location	Function
Ren 4	Guanyuan	On the anterior midline, 3 cun below the umbilicus	Tonify qi, yin, blood, yang. Locally increases blood circulation to the uterus
Ren 6	Qihai	On the anterior midline, 1.5 cun below umbilicus	Tonify Qi and yang. Locally increase blood circulation to the uterus
Ren 12	Zhongwang	On the anterior midline, 4 cun above the umbilicus	Regulate the function of bou lou
Ren 17	Tanzhong	On the anterior midline, at the level of 4th intercostal space between the nipples.	Reg. rebellious qi, calm shen
Du 20	Baihui	On midline of the head, 5 cun directly above the midpoint of the anterior hairline	Raises the clear yang
Yintang		Midway between the medial ends of the two eyebrows	Calm shen
Zi gong xue		3 cun lateral to Ren 3	Improve circulation to the ovaries
Li 4	Hegu	On the dorsum of the hand, between the first and second metacarpal bones, at midpoint of second metacarpal.	Regulate and move Qi
Li 11	Quchi	At the elbow, midway b/w Lu5 and the lateral epicondyle of the humerus	Clear heat from 3 jiaos
Liv3	Taichong	On dorsum of the foot, in the depression distal to the junction of the 1st and 2nd metatarsal bones	Regulate and move liver qi
Kid 3	Taixi	In the depression b/w medial malleolus and tendo-calcaneus, at the level of medial malleolus	Regulates and strengthens the kidneys
Kid 6	Zhaohai	In the depression below medical malleolus	Calm spirit, cools heat
Kid 7	Fuliu	2 cun above kid 3	Tonify kidney yang
LU 7	Lieque	Radial aspect of forearm, 1.5 cun above the transverse crease of wrist.	Opens and regulates the Ren
Sp 4	Gongsun	In the depression distal and inferior to the base of first metatarsal bone, and the junction of red and white skin	Regulates the chong channel
Sp6	Xiangu	3 cun above the medial mallelous	Strengthen Sp and transform damoness, spread liver qi and benefit the kidneys
Sp 8	DiJi	3 cun below Sp 9	Move Qi in the uterus
Sp 9	Yinlingquan	At the lower boarder of the medial condyle of the tibia, in the depression on the medial boarder of the tibia	Dispel damp stagnation and benefits the lower burner
Sp 10	Xuehai	On a flexed knee, it is located 2 cun above the mediosuperior boarder of patella	Moves blood and cools heat
Pc 6	Neiguan	2 cun above the wrist. b/w tendons of m. Palmaris longus and m. flexor carpi radialis	Calms heart
St 36	Zusanli	3 cun below St 35, one finger breath from the anterior crest of the tibia in m.tibialis anterior	Regulates qi and blood, strengthens weak and deficient condition
St 40	Fenglong	8 cun superior to the external malleolus, 2 finger breath from the anterior of the tibia	Transform phlegm and dampness and calms the spirits

Appendix E: Most common Chinese herbs used in the study

Herbal function was reported according to information from Maciocia, Kaptchuk, (1998), and Bensky, Gamble, Kaptchuk, (1986).

	Week 1	Week 2	Week 3	Week 4
Qi mover	Chai hu, chuan xiong, sha ren	Chai hu, chuan xiong, sha ren	Chai hu, chuam xiong, sha ren	Chai hu, chuang xiong, sha ren
Qi tonic	Bai shao, bai zhu, huang jing, dang shen	Bai shao, bai zhu, huang jing	bai shao, bai zhu, huang jing, dang shen	Bai shao, bai zhu
Blood mover	Chi shao, dang gui	Chi shao, dan shen, dang gui	Dang gui	Tao ren, hong hua, dan shen, dang gui
Blood tonic	Dang gui, dan shen, sang ji sheng	Dang gui,	Dang gui, gou qi zi	Dang gui, qui qi zi
Blood cooler	mu dan pi			Mu dan pi
Yin tonic	Qing hao, bie jiao, shu di huang, sheng di huang, shan zhu yu	Shu di huang, shan zhu yu, sheng di huang, nu zhen zi	shu di huang	Sheng di hunang, shan zhu yu, shu di huang
Yang tonic	Tu si zi, xu duan	xu duan, tu si zi	Xu duan, tu si zi,	Tu si zi
Damp/phlegm	Ban xiao, fu ling	Ban xiao, fu ling	ban xiao, fu ling	Ban xiao, fu ling
Calm shen	Fu shen, he huan pi	Fu shen		Fu shen

* Weeks indicate where patient was in her menstruation