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Diminished Ovarian Reserve, Clomid, and Traditional Chinese Medicine: A Case Study

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ABSTRACT

Background: Infertility caused by diminished ovarian reserve (DOR) can result from an endocrinological imbalance. A rise in follicle stimulating hormone (FSH) and decrease in antral follicle count (AFC) for women age ≤35 can lower pregnancy rates to <5%, and increase miscarriage rates to >75%. Chinese medicine may improve FSH and AFC levels in patients with DOR. It is common for women to seek adjunctive Traditional Chinese Medicine (TCM) treatment with biomedical clomid treatment.
Objective: This article reports the case of a female with DOR who had completed three multiple, serial clomid cycles from September to December 2005, and for whom clomid failed.
Design, Setting, and Patient: This is a case study of a 34-year-old patient with a 5-year history of infertility caused by DOR. She was treated in a private practice in Bellevue, WA.
Intervention: TCM treatment—including acupuncture and herbal therapy—lasted from from January 2007 to April 2007.
Main Outcome Measures: The main outcomes sought were improvements in this patient's reproductive hormone panel, including tests for FSH, estradiol, and AFC levels; in addition a pregnancy outcome was desired.
Results: After 4 months of TCM treatment, the patient returned to biomedical care. Pregnancy was not achieved during three more clomid cycles, although she had improvements her levels of FSH (from 14.5 mIU/mL to 8.7 mIU/mL) and AFC (from 10–12 to 16–18 total). After 3 more cycles with clomid, her FSH level increased to 16.8 mIU/mL and her AFC level was <10.
Conclusions: After three failed clomid cycles, a patient with DOR had improved FSH and AFC levels when she received TCM treatment. However, this patient was still unable to conceive although three more clomid cycles were attempted. More research is needed to discern demographically which patients benefit best from multiple, serial clomid interventions. In addition, it is important to investigate more-integrative treatments for patients with DOR, including assisted reproductive techniques, acupuncture, and Chinese herbs.

Key Words: Infertility, Diminished Ovarian Reserve, Acupuncture, Traditional Chinese Medicine

INTRODUCTION

The average female reproductive potential peaks at age 25 and then begins to decline. At first, it declines slowly through age 27, and then more quickly to age 35. After age 35, the decline becomes progressively steeper.[1] Reproductive endocrinologists determine female reproductive potential by assessing ovarian reserve in two primary ways: (1) blood chemistry value of follicle stimulating hormone (FSH) and (2) its relative ratio to estradiol (E2).[2,3] These values can be combined with antral follicle count (AFC), via transvaginal ultrasonography for a more-definitive assessment.[3] When

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blood samples are drawn on the third day of the menstrual cycle, FSH levels below 10 mIU/mL with E2 levels up to 75 pg/mL are considered to be normal.[1]

The importance of these hormonal values lies in their ability to manage the female reproductive system through a feedback mechanism. When hormone regulation occurs correctly, every cycle provides a 20%–25% chance of conception in optimal circumstances.[1] Challenges begin to occur when, for reasons that are not fully understood, the ovaries fail to respond to the FSH signal for follicular development. While this is an expected occurrence as women age, it can also arise in younger women, lower their likelihood of conceiving in each cycle from 20% to 5%, and increase the probability of pregnancy loss.[1,2] As a result, women with DOR often seek reproductive assistance to improve their chances of getting pregnant.

Female infertility is diagnosed in women under age 35 if no conception has occurred after 1 year, and in women 35 and over, when there is no conception after 6 months.[1] Women generally first seek the care of their gynecologists to assist conception before visiting fertility specialists. A common first-round intervention dispensed by gynecologists is ovulation-induction medication, such as clomid/clomiphene citrate.

Clomid is an ovulation-induction medication taken for 5 consecutive days, usually beginning on day 5 of the menstrual cycle.[4] Clomid is a selective estrogen-receptor modulator, and although the mechanism of action is not completely understood,[1] it works to blocks the E2 receptors in the hypothalamus, triggering a release of gonadotropin-releasing hormone (GnRH), which then signals the anterior pituitary to release FSH.[4] This increase in circulating FSH signals the ovaries to cause one or more follicles to mature.

Chinese medicine has been used to treat female infertility in China for more then 2000 years, and recent studies suggest that acupuncture improves assisted reproductive outcomes.[5,6] Chinese medicine does not have a DOR disease classification or category. However, more than 2000 years ago, a classical Chinese medicine text described the reproductive lifecycle in a way that mirrors the modern biomedical model closely. The *Huang di Nei Jing* (*The Yellow Emperor's Canon of Internal of Medicine*),[7] described a natural shift in female fertility in intervals of 7 years, which correlates closely with what is cited in current biomedical literature.

In Chapter 1 of the *Huang di Nei Jing*, two key concepts are identified regarding the reproductive lifecycle: (1) identification of the Kidneys as the governor of reproduction and (2) reproductive aging as observed in 7-year intervals. At age 28, fertility reaches its ''apex'' and begins its shift toward vacuity. This mirrors the biomedical statistical observation quite closely, as it is only 1 year after the subtle decline of ovarian reserve begins.[1] In Chinese medicine, the Kidney's role in governing reproduction is key to healthy fertility.[8–11] Kidney pathologies were the primary TCM diagnosis patterns among females undergoing *in vitro* fertilization (IVF).[12] Any etiologic factors the Kidney has to endure, such as repeated reproductive-medicine interventions, will deplete it and ultimately have a negative impact on reproductive outcomes.[11]

According to Chinese medical theory, multiple clomid cycles, can deplete the Kidney, Blood, and Yin, and affect the reproductive lifecycle adversely.[9,13]

Chinese medicine treatment strategies vary for patients with infertility. Lyttleton, based on the work of Xia Guicheng, described four distinct treatment protocols to administer in accordance with four distinct phases of the menstrual cycle.[9] These differ from the usual biomedical menstrual phases of menses, follicular, and luteal phases. According to Lyttleton, the phases are divided up as follows: (1) menses phase (cycle days or CD 1–4); (2) follicular phase (CD 5–11); (3) ovulation phase (CD 12–17), and (4) luteal phase (CD 18–onset of menses).[9] Treatment principles change according to the menses phase. Lewis agrees with this treatment strategy (R. Lewis, private communication, 2012). She also recommends the Stener-Victorin et al. protocol[14] in the follicular phase for patients who require strong tonification.

The objective of this article is to report the outcome of a single case of TCM treatment for DOR that may have been complicated by many consecutive clomid cycles.

CASE HISTORY

A nulliparous 34-year-old female presented in December 2006 with infertility caused by DOR. The patient was 5′8″ and 160 lbs. She reached menarche at age 13. She reported having regular 27–28-day cycles, and reported menstrual bleeding for 4 days of her cycle. This was a moderate menstrual flow that began with thin, fresh, red or pale red blood, and that tapered off on day 4 of her cycle. At that time, this blood became watery and pale brown. She denied having clotting, but reported that she had mild-to-moderate cramping that occurred up to 5 days prior to her menses and on the first 2 days of her cycle. She ovulated on CD 13 or 14, as confirmed by an ovulation-predictor kit. She also reported seeing some cervical fluid that appeared to be fertile in nature* and denied having any vaginal dryness or dyspareunia. Premenstrually, she noticed increased irritability, bloating, and breast tenderness occurring no more than 5 days prior to onset of her menses. She reported no history of smoking, and she confirmed that she drank no more than 7 (3–7) alcoholic beverages per week.

*At the time of ovulation, a woman can observe several changes in her body. The location of the cervix becomes higher (which can be palpated more deeply in the vaginal canal), the cervix becomes softer, the cervical os opens, and the vaginal discharge becomes more stretchy and clear, looking much like an uncooked egg white. This is called fertile, cervical fluid, which can indicate ovulation for most women. See: Brezina PR, Haberl E, Wallach E. At home testing: Optimizing management for the infertility physician. *Fertil Steril*. 2011;95(6):1867–1878.

This patient's biomedical history revealed no prior ovarian surgeries or family history of premature menopause. In the fall of 2005, the patient underwent three consecutive clomid cycles with intrauterine insemination (IUI) while under the care of a women's health nurse–practitioner (NP). No pregnancy resulted. At the time of her initial consultation, in late 2006, her highest recorded FSH reading was 14.5 mIU/mL, and her AFC count was 8–10 bilaterally. Each month, she took 100 mg of clomid and generally produced 1 primary follicle at ovulation. Her NP would then recommend a day for the IUI. She had no information on her endometrial thickness at the time of insemination. However, she reported that, during an ultrasound examination, her NP mentioned that her ovaries were small. Her fallopian tubes had not been evaluated for blockages nor was her uterus evaluated for abnormalities. A sperm analysis showed that her husband's count and motility were normal after processing. No information was available on any morphology testing.

This patient was soft-spoken, with a serious demeanor and a pale complexion. She became weepy and expressed hopelessness and frustration when discussing her fertility challenges. She stated that she found it very difficult to be around babies.

Other significant items that she reported were: low energy; moderate-to-high stress; heavy sleep with difficulty waking; gas and bloating after meals; sugar cravings; daily bowel movements that were occasionally loose or became urgent and/or crampy with stress; mild-to-moderate anxiety that manifested as chest palpitations, chest tightness and, shortness of breath; thirst; nocturia once nightly; frequent urination; no night sweats except when taking clomid; dull, ''achey'' headaches every 2 weeks; occasional dizziness; and a neutral core body temperature with cold hands and feet.

Her pulses, overall, were slow and deep. On her left side, the pulse was especially deep, soft, and weak in the *guan* and *chi* positions. On her right side, the pulse was soft and weak in the *chi* position. Her tongue was pale purple, swollen and wet.

Her TCM diagnoses were:

(1) Kidney Yang and Essence (*Jing*) deficiency, as evidenced by her low energy; frequent urination; nocturia; and weak, deep, soft pulses (according to Lyttleton, poor response to medications, small ovaries, and infertility also indicate this diagnosis[9])
(2) Liver/Heart Blood Deficiency, evidenced by pale menstrual blood, dryness, thirst, and palpitations
(3) Spleen Qi deficiency, evidenced by fatigue, gas/bloating after meals, soft (loose) stools
(4) Liver Qi stagnation, evidenced by frustration/irritability, breast tenderness, bloating, and premenstrual cramping.

TREATMENT

At this patient's initial consultation, a break from any reproductive interventions for 3 months was recommended; she agreed to this plan. A second biomedical opinion, including a full reproductive workup for her and her husband was also recommended, based on the failure to conceive after three attempts with clomid. Evaluation for male factors was also suggested to ensure that her partner's sperm morphology was normal. The patient declined to follow these last two recommendations.

Weekly acupuncture treatments and Chinese herbal therapy based on the cycle phases described by Lyttleton[9] were recommended. The needles used were 0.20×30 mm, Spring type (DBC, Korea) on body points, and 0.16×15 mm, D-type (Red Seirin, Japan) needles without guide tubes on the ears. Chinese herbal medicine (Kaiser Pharmaceutical Co., Ltd., Taiwan) was administered from January through April 2007. All point functions were determined according to *A Manual of Acupuncture*[15] and all herb functions were determined according to *Chinese Herbal Medicine: Formulas and Strategies, 2nd ed.,*[16] unless otherwise noted. When selecting points for treatment, great emphasis was placed on changes in pulse quality when acupuncture points were palpated. If the pulse improved when the point was palpated, it was selected for that treatment. All points were needled to elicit De Qi[17,18] with a lifting thrusting technique and manipulated with an even rotation technique.

Phase I: Menses Phase (CD 1–4)

During phase 1 of this patient's menstrual cycle, Blood is discharged. The treatment goals were to circulate Qi, nourish and move Blood, and tonify the Kidney.

Acupuncture treatment included:

- *Xuehai* SP 10—to move Blood and clear Heat
- Diji SP 8—to remove obstruction of Blood flow; *Xi*-Cleft of the Spleen channel
- *Shuidao* ST 28—to regulate menses
- *Siman* KI 14—to move Blood in the *Chong* channel
- *Neiguan* PC 6/Gongson SP 4—to open the *Chong* channel, using two confluent points of the *Chong* channel
- *Zusanli* ST 36—to tonify Qi
- *Qiuxu* GB 40—to circulate Qi.

The herbal formula was *Tao Hong Si Wu Tang* (Four Substance Decoction with Safflower and Peach Pit). She was given 40 g of the following premixed granular formula:

- *Tao Ren* 20% (*Persicae* spp. semen)
- *Hong Hua* 20% (*Carthami* spp. flos)
- *Dang Gui* 20% (*Angelica sinensis* radix)
- *Shu di Huang* 20% (*Rehmannia preparata* radix)
- *Chuan Xiong* 10% (*Chuanxiong* rhizoma)
- *Bai Shao* 10% (*Paeoniae alba* radix).

The dosage was 5 g twice daily, dissolved in warm water to be taken on CD 1–4 only. This formula was prescribed to ensure complete discharge of menstrual products, and to nourish and move the Blood.[9]

Phase II: Follicular Phase (CD 5–11)

During phase II of this patient's cycle, Yin and Blood become most abundant in the follicular phase. The treatment goals were to benefit the Kidney, nourish Yin and Blood, circulate Qi and Blood, and calm the *Shen*. Acupuncture was performed twice per week, alternating front and back treatments, to support follicle maturation and nourish Yin and Blood. Acupuncture was performed on her ear and manually on other parts of her body.

Back treatment. The Stener-Victorin protocol was used during back treatments, with no more than five auricular points and no more than two additional manual acupuncture points. The Stener-Victorin protocol decreases blood flow impedence and improves blood flow to the uterus and ovaries via electroacpuncture (EA).[14] Magarelli et al reported a series of Stener-Victorin protocol treatments prior to embryo transfer improved *in vitro* fertilization outcomes and may have have had an effect on cortisol and prolactin.[19] Both sets of EA points must be stimulated simultaneously to achieve the best effect.[19] This patient's back treatment involved EA, according to the the Stener-Victorin protocol,[14] using a Pantheon Research 4c, Electrostimulator (Venice, CA), at a continuous low intensity (10 Hz). The points used were: *Shenshu* BL 23 (Red) to *Ciliao* BL-32 (Black), and *Chengshan* BL 57 (Red) to *Sanyinjiao* SP 6 (Black).[14]

Ear treatment. This treatment involved Endocrine, Uterus, FSH, *Shenmen*, Liver, Kidney, and Heart points (no more than five were selected). The FSH point is located just posterior to the Endocrine point in the intratragic notch.[20] Manual acupuncture, with no more than two of the following points was also performed:

- *Shendao* GV 11—to regulate the Heart and calm the *Shen*
- *Jueyinshu* BL 14 (Pericardium *Shu*)—to calm the *Shen* and nourish the Heart
- *Ganshu* BL 18 (Liver *Shu*)—to circulate Qi and nourish the Liver
- *Pishu* BL 20 (Spleen *Shu*)—to tonify the Spleen and drain Damp
- *Xuanzhong* GB 39—to benefit the Essence and the marrow.

Front treatment. Six to eight body points, with no more than five ear points, were selected. Points were selected based on the patient's pulse and presentation on the day of treatment. Acupuncture of the ear included points involving Endocrine, Uterus, FSH, *Shenmen*, Liver, Kidney, or Heart areas as follows.

- Guanyuan CV 4 (Infant's Palace)—to address Yin, Essence, Qi, and Yang; regulate the Uterus; tonify the Kidney; and calm the *Shen*
- *Sanyinjiao* SP 6—to nourish Blood, circulate Qi, and calm the *Shen*
- *Qichong* ST 30—to promotes Kidney Essence, improves Middle Jiao function, and regulate Qi and Blood in the lower abdomen
- *Daju* ST 27—to tonify the Kidney and nourish Essence
- *Tituo* N-CA-4—Regulate Qi and Blood around the Uterus and Ovaries
- *Zi Gong* M-CA-18—to raise and regulates Qi around uterus and ovaries
- *Dahe* KI 12—to tonify the Kidney and nourish Essence
- *Huangshu*—KI 16—to influence *Chong*, and support Essence
- *Zusanli* St 36—to nourish the Blood and Qi
- *Taixi* KI 3—to tonify the Kidney and benefit the Essence
- *Dazhong* KI 4—to support the Kidney and lift the spirit
- *Zhaohai* KI 6—to nourish Yin, benefit the eyes, calm the *Shen*, cool the Blood, and regulate the Uterus.
- *Taichong* LV 3—to circulate Qi
- Jianshi PC 5—to calm the *Shen* and influence the *Bao* vessel[9]
- *Neiguan* PC 6—to calm the *Shen*, open the chest, harmonize the Stomach, and regulate the Blood
- *Gongson* SP 4—Combined with *Neiguan* PC 6 and *Chong Mai* confluent points
- *Lieque* LU 7 and *Zhaohai* KI 6—*Ren Mai* confluent points.

Herbal formula. The *Gui Shao di Huang Tang Jia* (*Angelica peonia rehmannia* Decoction with additions) was administered by combining the premixed granular formula *Liu Wei Di Huang Tang* (Six Ingredient Pill with *Rhemannia*) with single granular herbs. The premixed granular formula base included:

- Six Ingredient Pill with *Rhemannia*
- *Shu di Huang*, 32%
- *Shan Zhu Yu*, 16% (*Corni* spp. fructus)
- *Shan Yao*, 16% (*Dioscorea* spp. rhizoma)
- *Mu Dan Pi*, 12% (*Moutan* spp. cortex)
- *Ze Xie*, 12% (*Alismatis* spp. rhizoma)
- *Fu Ling*, 12% (*Poria* spp.).

Single granular herb additions included:

- *Dang Gui*, 7 g
- *Bai Shao*, 7 g
- *Tu Si Zi* (*Cuscutae* spp. semen), 5 g
- *Du Zhong* (*Eucommiae* spp. cortex), 5 g
- *Dan Shen* (*Salviae miltiorrhizae* radix), 5 g
- *Suan Zao Ren* (*Ziziphi spinosae* semen), 5 g
- *Xiang Fu* (*Cyperi* spp. rhizoma), 7 g
- *Fo Shou* (*Citri sarcodactylis* fructus), 7 g
- *Sha Ren* (*Amomi* spp. fructus), 7 g.

The dosage was 5 g, dissolved in warm water twice daily, and taken on CD 5–11. The *Angelica peonia rehmannia* Decoction consists of the Six Ingredient Pill with Rhemannia combined with *Dang Gui* and *Bai Shao*. This Decoction nourishes Yin and Blood. The formula was given to the patient with several additional herbs: *Du Zhong* and *Tu Si Zi* to support Yang; *Dan Shen* (which is cool) to circulate Qi and Blood in the Upper *Jiao*; *Suan Zao Ren* to nourish the Heart and calm the *Shen*; *Xiang Fu* and *Fo Shou* to circulate Qi in the Lower *Jiao* as well as directing the action of the herbs to the reproductive system.[21] *Sha Ren* was given to help her digest the heavy Yin and Blood tonics.

Phase III: Ovulation (CD 12–17)

Phase III of the cycle is the ovulatory phase. Yin transforms to Yang through the assistance of the Qi dynamic in the ovulation phase. Treatment goals during this phase were to circulate Qi and Blood, nourish the Heart, calm the *Shen*, promote ovulation, and tonify the Kidney.[22]

Acupuncture. Ear acupuncture points used included *Shenmen*, Endocrine, Thalamus, and the Uterus, as follows:

- *Zusanli* ST 36—to tonify Qi, which may promote ovulation indirectly by supporting the transition to Yang[8,10]
- *Hegu* LI 4/*Taichong* LR 3—to move Qi to promote release of eggs
- *Guanyuan* CV 4—to regulate the Uterus, tonify the Kidney, and calm the *Shen*
- *Neiguan* PC 6—to relax the cervix and calm the *Shen*
- *Taixi* KI 3—to tonify the Kidney, benefit the Essence, and regulate the Uterus
- *Guilai* ST 29—to influence the ovaries and vagina.

Herbal formula. *Pai Luan Tang* (Ovulation Decoction) and *Bai Zi Ren Wan* (Biota Seed Pill) formula was made from single herbs combined into one formula, including:

- *Bai Zi Ren* (*Platycladi* spp. semen), 5 g
- *Dan Shen*, 5 g
- *Dang Gui*, 5 g
- *Chi Shao* (*Paeoniae rubra* radix), 5 g
- *Xu Duan* (*Dipsaci* spp. radix), 5 g
- *Tu Si Zi* (*Cuscutae* spp. semen), 5 g
- *Sheng Di* (*Rhemannia* spp. radix), 5 g
- *Chuan Niu Xi* (*Cytathulae* spp. radix), 5 g
- *Hong Hua* (*Carthami* spp. flos), 2 g
- *Gou Teng* (*Uncariae raamulus* uncis), 5 g
- *He Huan Pi* (*Albiziae* spp. cortex), 6 g.

The dosage was 5 g, dissolved in warm water twice daily, taken on CD 12–16.[22] The formula, which was given to the patient is comprised of an Ovulation Decoction and a Biota Seed Pill). The formula promotes ovulation through the *Bao Mai*. The *Bao Mai* (*Bao* vessel) connects the Heart to the Uterus (*Bao Gong*). The Heart Qi, descending unimpeded, is required to promote ovulation and open the Uterus to allow sperm to enter. If the Heart Qi is obstructed because of Constraint or Vacuity, it cannot exert its influence via the *Bao Mai*, and ovulation may be disrupted.[8,9] *Bai Zi* Ren nourishes the Heart Blood to calm the *Shen*. *Dan Shen* and *He Huan Pi* circulate the Heart Qi to help promote ovulation. *Dang Gui* nourishes and moves Blood. *Chi Shao*, which is cool, and *Hong Hua*, which is warm, both move the Blood, while *Niu Xi* directs the actions downward. *Xu Duan* tonifies the Kidney and nourishes the Blood. *Gou Teng* clears Heat and subdues the Yang, because, during ovulation, Heat can accumulate and rise as with *Sheng Di*.

Phase IV: Luteal Phase (CD 18—Onset of Menses)

In Phase IV, Yang becomes most abundant. The treatment goals were to benefit the Kidney, support Kidney Yang by nourishing Qi and the Blood, raise Qi, circulate Liver Qi, and calm the *Shen*. This case required Yang support, through supplementation for the Qi and Blood.

Acupuncture. Six to eight points selected from the following:

- *Baihui* GV 20—to raise Yang/Qi and clears the mind
- *Sishenchong* M-HN-1, with *Baihui* GV 20—to calm the *Shen*
- *Zusanli* ST 36—to support Qi (and treat nausea with *Neiguan* PC 6)
- *Fuliu* KI 7—to tonify Kidney Yang and regulate sweating
- *Zhubin* KI 9—to clear the mind, nourish the Kidney, and open the chest
- *Ququan* LR 8—to nourish Liver Blood
- *Neiguan* PC 6—to calm the *Shen* and nourish the Blood
- *Juque* CV 14—to calm the *Shen*
- *Qiuxu* GB 40—to circulate Qi.

Herbal formula. *Yu Lin Zhu Jia Wei* (Fertility Pearls with additions and subtractions) was given to the patient during this phase. Ingredients included:

- *Dang Shen* (*Codonopsis* radix), 9 g
- *Bai Zhu* (*Atractyloides macrocephalae* rhizoma), 9 g
- *Fu Ling*, 12 g
- *Zhi Gan Cao* (*Glycyrrhiza* spp. radix), 3 g
- *Dang Gui*, 9 g
- *Chuan Xiong*, 6 g
- *Shu di Huang*, 7 g
- *Tu Si Zi*, 12 g

- *Du Zhong*, 12 g
- *Lu Jiao Jiao* (*Cervi colla cornus*), 12 g
- *Gui Ban* (*Plastrum testudinis*), 12 g
- *Dan Shen*, 6 g
- *Suan Zao Ren*, 6 g
- *Sha Ren*, 6 g.

The dosage was 5 g, dissolved in warm water twice daily, taken during CD 17–28.[9] Modified *Yu Lin Zhu* (Fertility Pearls) was formulated by combining single granular herbs. This formula is a modification of the *Ba Zhen Tang* (Eight Treasure Decoction), a classic formula used to tonify Qi and the Blood. The first seven herbs of the formula listed above are the ingredients of the Eight Treasure Decoction), with *Dang Shen* substituted for *Ren Shen* (ginseng; *Panax* spp. radix), and *Bai Shao* excluded. The following herbs were also added: *Tu Si Zi* and *Du Zhong* to tonify Kidney Yang, while *Lu Jiao Jiao* was used to nourish Kidney Yang, Essence, and Liver Blood. *Gui Ban* was used to prevent the Yang tonics from damaging the Yin while also nourishing the Essence. *Dan Shen* and *Suan Zao Ren* were used to address the Heart by moving and nourishing, respectively, and to calm the *Shen*. *Sha Ren* was used to assist digestion of the heavy tonics.

RESULTS

The treatment plan described above was performed for 3 months. Following this, the patient discontinued Chinese medical treatment and elected to resume biomedical treatment with a different gynecologist, who was located closer to her home. The new physician discouraged herbal treatment and was unsure about acupuncture's effectiveness.

On a follow-up phone call with the patient, she reported that her FSH was 8.7 mIU/mL in May 2007 and her AFC was 8–9 on each side. She was prescribed 100 mg of clomid, to be taken during CD 5–9. She was instructed to return for an ultrasound on CD 12. She developed 1 primary follicle that was 18.5 mm. Her endometrium was 8.9 mm and trilaminar. She received a human chorionic growth hormone (hCG) trigger shot and was instructed to return 36 hours later for an IUI. She received the IUI on CD14. No pregnancy resulted. This was repeated two more times. Cycle number 2 resulted in 1 primary follicle on CD 11, which was 17 mm, and her endometrium was 8.6 mm. No pregnancy resulted. Cycle number 3 resulted in no primary follicle and her endometrium was 7.2 mm. Again, no pregnancy resulted. Her FSH at the conclusion of these three clomid cycles was now 16.8 and her E2 was 57.7. Her AFC was now 3–4 bilaterally, or <10 total. She was no longer eligible for IVF with her own eggs, and her potential for conceiving naturally based on these measures was now less than 2%.[1] A year later, she reported via email, that she then pursued donor egg IVF. She conceived successfully and gave birth to a healthy baby girl.

DISCUSSION

It is theorized TCM treatment for 3 months may improve reproductive outcomes when further biomedical interventions are pursued later.[9,11] This is based on supporting the folliculogenesis cycle. Despite the negative outcome for this patient with clomid, she responded quite well to 3 months of TCM treatment: Her FSH was reduced and her AFC was increased. With the increase in her ovarian reserve, she was well-positioned to transition to biomedical *in vitro* fertilization (IVF). However, it is likely that the repeated clomid interventions following the acupuncture and herbal treatments put her past the acceptable parameters for IVF.

Despite respectful recommendations, the patient reported that she felt she was not giving clomid and her gynecologist enough of a chance to work. She reported that her new doctor was not concerned with pursuing three more rounds of clomid-based IUIs before referral to IVF. It is not uncommon for patients to continue with a doctor despite poor reproductive outcomes.[24] From a Chinese medical perspective, serial use of clomid may be problematic for a woman's reproductive health. Clomid consumes Yin and stagnates Qi.[9] Patients who are Yang Deficient tend to respond best to this medication, while patients who are Yin and/or Blood Deficient, or Qi Stagnant (as in the case of this patient) tend to respond quite poorly or have many side-effects.[9,11] Taking clomid for several consecutive months may deplete the Kidney further, damage the Yin, and engender Empty Fire. This was evident in this case by the increasingly poor follicular development response over time caused by repeated use of clomid and by the increased night sweats observed while this patient was on that medication. Favorable reproductive outcomes in patients with DOR—even with pharmaceuticals and reproductive technology—are substantially lower than other infertility diagnostic groups.[2,25–27]

TCM fertility specialists frequently treat patients who have undergone—or will soon undergo—many rounds of clomid. It is important to recommend a second opinion when a patient has already completed three cycles using this medication and when research shows clearly that many clomid interventions are not successful.[25–27] In addition, there is a challenge for acceptance of adjuvant Chinese herbal therapy with clomid, as Chinese herbs may improve clomid interventions.[28]

It is possible this patient would not have conceived regardless of the three additional clomid cycles after 3 months of TCM treatment. However, she did improve with respect to two important objective measures: FSH and follicle count. More research is needed to investigate the

effect acupuncture and Chinese herbs have on ovarian physiology.

CONCLUSIONS

Clomid may not be ideal for patients with DOR.[25–27] In this single case, after three failed clomid cycles, this patient with DOR had reduced FSH improved AFC after adjuvant TCM treatment. However, she was still unable to conceive when she underwent three more cycles with clomid. More research is needed to discern which patient population would benefit best from many serial clomid interventions. In addition, ideal treatments for patients with DOR must be investigated, including integrative treatment with assisted reproductive techniques, acupuncture, and Chinese herbs.

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DISCLOSURE STATEMENT

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