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Case Report: Acupuncture in Infertile Women of Advanced Reproductive Age with Low AMH

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Abstract

Female reproductive aging is a common cause of infertility in women in their late 30s and 40s [1] Because female fertility begins to decline in women of advanced reproductive age (≥ 35 years old), advanced reproductive age (ARA) is a risk factor for female infertility, pregnancy loss, fetal anomalies, stillbirth, and obstetric complications [2]. This article reviews on 10 clinical cases of Canadian women who are infertile due to advanced reproductive age with low AMH level (<1 ng/ml), and, who, after several failed IUI or IVF cycles, were treated with acupuncture for 3 to 6 months. All 10 women had spontaneous pregnancies and live births. Acupuncture is effective for patients of advanced reproductive aged with low AMH who did not respond to IUI or IVF protocol. Method: based on weekly treatments, the 12 course-treatment of acupuncture focussed on invigorating kidney qi and nourishing the spleen and stomach in order to increase the probability of the outcomes of pregnancy and live birth by regulating menstruation and ovulation, and improving egg quality.

Keywords: Advanced Reproductive Age; Low AMH; Acupuncture; Spontaneous Pregnancy

Low AMH

Anti-Müllerian Hormone (AMH) is a hormone produced by the granulosa cells in ovarian follicles. It indicates the presence of a woman's eggs. The more eggs a woman has the more granulosa cells she has and the higher her AMH. Lower AMH shows low egg supplying which is associated with infertility. According to the American College of Obstetricians and Gynecologists (ACOG) [3], the production of AMH is reflective of the ovarian reserve. A low AMH level (<0.5–1.1 ng/ml, Bologna criteria) points to a diminished ovarian reserve (DOR) or low egg count, which is linked to fertility. Consequently, low AMH can predict poor response in controlled ovarian stimulation [4]. According to traditional Chinese medicine (TCM), DOR is caused by four factors: the imbalance of qi, blood and body fluid; the dysfunction of the channels Chong and Ren; and the dysfunction of Zangfu/viscera such as kidney, spleen and stomach qi deficiency; and liver qi stagnation.

TCM Etiology and Pathogenesis

In traditional Chinese medicine, the book "The Inner Classic of the Yellow Emperor: Simple Question; The Universal Truth"

mentioned a physiological law called "Seven Women and Eight Men". It means that the rhythm of life of women is related to seven, while the rhythm of life of men is related to eight. "In general, the reproductive physiology of woman is such that at seven years of age, her kidneys' energy is strong. At fourteen years, Tian Gui, or fertility essence is mature, the Ren/conception and Chong/vital channels are flourishing, menstruation begins, and conception is possible. At twenty-one years, the kidney energy is strong and healthy, the wisdom teeth appear, and the body is vital and flourishing. At twenty-eight years, the bones and tendons are well-developed and the hair and secondary sex characteristics are complete. This is the height of female development. At thirty-five years the Yangming/ stomach and large intestine channels that govern the major facial muscles begin to deplete, the muscles begin to atrophy, facial wrinkles appear, and the hair begins to thin. At forty-two all three yang channels-Taiyang, Shaoyang and Yangming are exhausted, the face is wrinkled, and the hair begins to turn gray. At forty-nine years the Ren and Chong channel are completely empty, and the Tian Gui has dried up. Hence, the flow of the menses ceases and the woman is no longer able to conceive."

The Kidneys Govern Reproduction

Traditional Chinese medicine believes that infertility is caused by mutations in Chong and Ren, the dysfunction of viscera, and the inability to take innate essence (Jing) in the uterus. The kidneys are the storage place for the vital essence (Jing), a subtle substance responsible for the growth, development, reproduction and fertility. They are the source of yin and yang for all of the other organs. The kidneys are the source of prenatal qi, which is inherited from the parents and interpreted as a person's innate constitution. The kidneys govern the function and the control of the brain, Tiangui, Chong channel, Ren channel and uterus.

The Spleen is the Acquired Foundation

The spleen and the stomach are the root of postnatal qi in TCM. It is necessary to replenish the spleen and promote the transformation of the human body's subtle substances while invigorating the kidneys, so as to combine the innate and the acquired so that the innate and the acquired can nourish each other. However, the function of the spleen and stomach depends on the support and coordination of other organs. For the spleen to be healthy, it needs to be nourished by the kidney yang. If the kidney yang is insufficient, the Mingmen (vital gate) will fail, which also weakens the spleen yang.

The Liver is the Congenital Dependence of Women

The liver is the basis of the innate in women. The Chongmai originates in the uterus and passes through the liver. It is closely related to a woman's ability to conceive. The Chongmai communicates with the twelve meridians, which is the sea of twelve meridians. When the Taichong meridian is prosperous, menstruation is on time. This shows that the Chongmai is the foundation of menstruation.

Traditional Chinese medicine believes that the ability to conceive is most closely related to the health of the kidneys, spleen and liver. The kidneys are responsible for storing essence and are the foundation of reproduction. Therefore, deficiency of kidney qi is the foundation of infertility. The spleen is the foundation of acquired nature, which is responsible for digestion and absorption, which, in turn, transform nutrients into qi and blood. The liver stores blood and ensures the smooth flow of qi. If the liver qi stagnates, menstruation is disordered, and therefore it is difficult to conceive.

Acupuncture and Female Infertility

At present, most scholars believe that acupuncture increases the rate of pregnancy for the following reasons. Acupuncture has been proven to encourage the circulation of blood in the pelvic cavity and improve ovarian function [5]. Some studies have recommended that acupuncture can be beneficial in promoting follicle production

[6], enhancing uterine blood flow, [7,8] improving uterine lining thickness9, 10 and increasing endometrial receptivity during the implantation period [11,12] Acupuncture has also been counselled as a valuable alternative therapy for female infertility due to hormone disorders [13]. Acupuncture helps the woman's natural hormone cycle by influencing the hypothalamic pituitary gonadal axis (HPG axi--ovarian hormone feedback loops). Studies have also proven the positive effects of acupuncture on ovulation inductions [14-17].

Acupuncture Infertility Points

According to the theory of "Female Seven" physiological cycle in "The Inner Classic of the Yellow Emperor", acupuncture treatments focus on the kidneys, spleen, stomach, large intestine, and the Chong and Ren channels. Three groups of acupuncture points are needled bilaterally and alternately.

a. Group 1

St 25 (Tianshu), St36 (Zusanli) nourish stomach qi.

Li4 (Hegu), Liv3 (Taichong) calm liver yang, regulate qi and blood, unblock the meridians.

Ki3 (Taixi), Ki12 (Dahe) invigorate kidney qi.

 $\mbox{Sp6}$ (Sanyinjiao) , $\mbox{Sp9}$ (Yinlingquan) invigorate spleen and replenish qi.

Sp4 (Gongsun), Pc6(Neiguan) adjust Chongmai Qi and blood.

Rn 4 (Guanyuan), Rn 6(Qihai), Rn 12(Zhongwan)

EX-CA1 (Zigong) raises and regulates uterine Qi.

b. Group 2

Back shu points (Bl13, Bl18, Bl20, Bl21, Bl 23) regulates the qi and blood of five Zang.

Baliao (Bl31, Bl32, Bl33, Bl34) regulates the qi and blood of bladder channel and Baogong.

c. Group 3

Auricular points:

Zigong (TF2), Shenmen(TF4), Endocrine (CO18), Liver(CO12), Spleen(CO13), Kidney (CO10)

Frequency: 2 times a week, 12 times a course.

Manipulation

After disinfecting all points with a cotton ball dipped in alcohol, the order of inserting the puncture needles is from the lower limbs to the abdomen, starting on the left side and finishing on the right side. Disposable sterile needles, size 0.25x25mm, are used and are inserted perpendicularly in all points to a depth 10 to 15mm. A KWD-

808 I electro acupuncture instrument is connected at ipsilateral Ki12 and ZIGONG, Baliao (Bl31-34), and set to a continuous wave, the intensity of which is based on the patient's preference. Needles remain inserted for 30 minutes each session, and a TDP lamp is used on the belly during the session. For auricular points, the pressneedle SEIRIN Pyonex is used and the needle size is 0.2mm×0.3mm. Needles remain inserted for 24 to 72 hours.

During the treatment, all of the patients were told not to have cold drinks, raw food, or alcohol and to go to sleep before 11pm.

Discussion

Women begin life with a fixed number of eggs in their ovaries. The number of eggs decreases as women get older. A woman's peak reproductive years are between the late teens and late 20s. By age 30, the ability to get pregnant starts to decline. This decline becomes more rapid once she reaches her mid-30s. By 45, fertility has declined so much that getting pregnant naturally is unlikely for most women [18].

Ovarian aging will have begun before women notice any clinical changes to their menstrual cycles. Therefore, they are often unaware that they may be at greater risk of infertility. Ovarian function declines as women approach their later reproductive years until menopause. Consequently, increasing age is associated with lower fecundity and infertility. Women experience a decline in natural fertility that begins in the mid-30s, and they will often reach sterility many years before the complete cessation of menses [19].

In TCM, these observations were made in three major medical treatises. "The Inner Classic of the Yellow Emperor" (Huang Di Nei Jing) said: "women at thirty-five years old, the yangming/stomach and large intestine channels that govern the major facial muscles begin to deplete. At forty-two years old, all three yang channelstaiyang, shaoyang and yangming are exhausted, the entire face is wrinkled, and the hair begins to turn gray." During the Ming Dynasty, TCM Master Li Dongyuan's treatise "The Theory of Spleen and Stomach" said that "all diseases are caused by the decline of the spleen and stomach." Furthermore, the famous TCM doctor Zhang Xichun in the "Medical Records of Chinese and Western Medicines" said: "Both male and female fertility depends on the essence of kidney. Therefore, the kidney qi is the key to achieving a perfect pregnancy. Kidney essence is the basis of pregnancy. The exhaustion of Tiangui mainly dominates the rise and fall of reproductive function under the influence of kidney qi." As a result, the acupuncture protocol to treat women with DOR and low AMH is based on the Huang Di Nei Jing theory to focus on treating the qi in the spleen, stomach and kidney [20].

During the treatment of DOR, it is first necessary to protect the spleen qi and stomach qi while tonifying kidney qi. At the same time, the patient is asked to regulate their diet and adjust their

lifestyle by eliminating raw food, cold drinks, sugar and alcohol, going to sleep early, and doing regular exercise.

The method of acupuncture used in this article is based on the study of classic literatures and combined with clinical experience, and aims at the pathogenesis of DOR and its three basic etiologies: kidney essence deficiency, Chong-Ren imbalance, and spleen and stomach weakness. The principle of treatment is to invigorate the kidney essence, regulate Chong Ren channels, and tonify the spleen and stomach qi through specific abdomen channels like Ren, kidney, spleen, stomach channels points and the zangfu back shu points of the bladder channel, and through the holographic theory of auricular points. The different acupuncture points in the ear correspond to specific parts of the human body and internal organs such as the endocrine system, the uterus, liver, spleen, and kidneys. The acupuncture protocol used both body points and auricular points in order to replenish kidney essence, regulate Chong Ren and invigorate spleen and stomach qi.

Ren mai originates from Baogong (the uterus) and regulates menstruation and promotes women's reproductive function, hence the saying "the Baogong dominates". The three-foot yin channels intersect with the Ren Channel in the lower abdomen, and the Hand yin Meridian communicates with the Ren Channel through the Foot yin Meridian. Therefore, the Ren Channel has a regulating effect on the qi and blood of the Yin Channel. Rn6 (Guanyuan) belongs to the Ren vessel, which is where Yin and Yang are located. Rn 4(Qihai) and Rn12 (Zhongwan) are the points for invigorating the spleen and stomach, replenishing qi and consolidating the constitution. Bl23 (Shenshu) and Ki3 (Taixi) together cultivate kidney essence and replenish kidney qi. Ki12(Dahe) is the intersection of the Chong channel and the Kidney channel, where the qi and blood of the fivezang organs and the six-fu organs merge with the congenital qi, so that the circulation of qi and blood are fully filled.

St 36 (Zusanli) is the He point of the Stomach channel of Foot Yang Ming with more qi and blood. It regulates the spleen and stomach, strengthens the body and cultivates the qi and blood. St36 (Zusanli) and Sp6 (Sanyinjiao) condition Chong Ren channels. The back shu points of the bladder meridian, combined with Bl 23 (Shenshu), Bl20 (Pishu), Bl18 (Ganshu), and Bl21 (Weishu) points, nourish the spleen and kidney, soothe the liver and regulate qi, promote blood circulation and regulate menstruation. The combination of Rn12 (Zhongwan), St25 (Tianshu), St36 (Zusanli), Bl20 (Pishu), Bl21 (Weishu), and Sp6 (Sanyinjiao) are used to invigorate the spleen and stomach. Ki3 (Taixi) and Ki12 (Dahe) invigorate kidney qi.

Baliao is a group of four acupoints in the lumbosacral region of the bladder meridian where the qi and blood of the pelvic cavity converge, and is the main acupoint for the treatment of gynecological diseases. The Zigong (uterus) is an extraordinary acupuncture

point outside of the meridian. Needling at the Zigong point helps regulate menstruation and alleviate pain in the uterus. The Uterus is called Zigong or Baogong in Traditional Chinese Medicine (TCM). It literally translates to the 'palace of the infant' which is dominated by the kidneys, which in turn govern reproduction. Traditional Chinese medicine believes that if the kidney qi is prosperous, the Tian Gui, or fertility essence is mature. Then the two essences of Yin and Yang are united and planted in the uterus. The combined use of three groups of acupoints makes the kidney essence sufficient, strengthens the spleen and stomach, harmonizes the qi and blood, regulates menstruation, and ultimately restores ovarian function. As a result, implantation of the embryo in the uterus is easy and pregnancy is achieved.

Table 1: Summary of the 10 cases.

Auricular therapy was recorded in The Inner Classic of the Yellow Emperor (Huangdi Neijing). The ear is where the veins gather. It is closely related to the five internal organs and six internal organs. Each internal organ has a corresponding reaction zone (auricular point) in the auricle. Stimulating ear acupoints can regulate the physiological functions of the viscera of the whole body, and certain ear acupoints for the uterus, Shenmen, endocrine, liver, spleen, and kidney also coordinate the functions of the viscera.

In the 1950s, Dr. Paul Nogier, a French neurosurgeon, published the auricular map called the "Embryo Reflection" which theorized that the outer ear represents an inverted fetus within the womb and, thus, proposed the somatotopic correspondence of specific parts of the body to specific parts of the ear [20] (Table 1).

Cases	Date of Eva. dd/mm/yy	Age of giving birth	АМН	Failed IIU &IVF	LMP dd/mm/ yy	Date of deliver dd/mm/yy	Baby sex
Case 1	04-03-2014	44	0.25	2IUI	02-12-2014	08-09-2015	Boy
Case 2	04-05-2015	38	0.51	3IUI 2IVF	30-06-2016	10-03-2017	Girl
Case 3	03-04-2017	43	0.3	3IUI 4IVF	01-04-2018	31-12-2018	Girl
Case 4	23-11-2017	36	0.8	3IVF	10-03-2019	12-12-2019	Girl
Case 5	21-10-2018	37	0.16	4IUI	07-03-2019	27-12-2019	Boy
Case 6	14-03-2018	37	0.5	3IUI	15-02-2019	21-11-2019	Girl
Case 7	31-10-2018	38	0.6	2IVF	06-02-2019	09-01-2019	Boy
Case 8	26-04-2019	38	0.4	3IUI	16-05-2019	14-02-2020	Girl
Case 9	14-06-2019	36	0.62	2IUI	30-08-2019	04-06-2020	Boy
Case10	23-11-2019	37	0.47	2IUI	20-03-2020	25-12-2020	Girl

Typical Case (Case 5)

Quebecois woman, born on May 9, 1982; consultation date Oct. 21, 2018

a. Reason for Consultation

Secondary infertility; Diminished ovarian reserve (DOR)

b. History

G4P1 (1-2-1-1): 2 abortions, 1 miscarriage, 1 child of 4 years old (girl from a natural pregnancy)

She had failed 4 IUI already in 2018.

c. Menses

First menses: age 10; LMP: Oct.10, CD12; Heavy day: CD 2-3; Cycle: 24-26 days, regular; Period duration: 3-4 days; Period color: dark red; Clots: heavy clots at CD 1-2; Cramps: strong, before and during menstruation; PMS: irritable, sore, tender and swollen breasts, craves sugar.

d. General

She always feels tired in general. She always has cold feet and

hands, persistent chilliness! Sleeps well but goes to bed late around 12 pm. Digestion system: good, bowel movement every morning. She likes to eat fruit for breakfast, salads for lunch, cooked food for dinner. T: light red, white, teeth marks on the sides (TM); P: fine

e. Hormone Tests in Oct. 2018

AMH 0.16, FSH 24, LH 13, E2: 81

Ultrasound in Oct. 21, 2018: AFC: 4

f. TCM Opinion

Kidney and Spleen qi deficiency; Liver qi stagnation; Cold Baogong (uterus)

Acupuncture points (omitted)

I. 2018

- a. Oct. 21: CD 12, U/S: 2 follicles, max 15mm; acupoints: group 1+3
- b. Oct. 23: CD 14, U/S: 2 Follicles, Max 18 mm; IUI on Oct. 25, acupoints: group 2
- Oct. 25: Did IUI today, sperm count: 80 million cells per ml. acupoints: group 4

- d. Nov. 10: got a negative IUI result! LMP Nov., 9, CD2, heavy flow. acupoints: group 1+3
- e. Nov. 20: CD12, acupoints: group 2
- f. Nov. 29: CD 21, acupoints: group 1+3

II. 2019

- a. Jan. 3: LMP Dec. 31, 2019. She got it late after 5pm, CD 3, acupoints: group 1+3
- b. Jan. 8: CD8, acupoints: group 2
- c. Jan. 17: CD17: acupoints: group 1+3
- d. Jan. 24: CD 24, she will see the fertility doctor on March 6 for IVM. acupoints: group 2
- e. Feb. 1: LMP Jan. 25, cycle of 24 days, CD8, she has very cold feet! acupoints: group 1+3
- f. Feb.8: CD15, she saw signs of ovulation of cervical mucus 2 days ago. acupoints: group 2
- g. Feb. 14: CD 21, acupoints: group1+3
- h. Note on May 4: she texted me to update the news. LMP March7. She got pregnant naturally after 4 months of acupuncture treatments. 8 weeks already!
- i. 8) Jun 7: pregnant 13 weeks, Symptoms: very tired and heart burn. T: red, white; P: slippery. Acupoints: Group 4
- j. 9) Jul.19: pregnant of 18 weeks. Down syndrome: normal. Acupoints: Groupe 4
- k. 10) Sep. 12: pregnant of 26.5 weeks. Sex: boy. Due date: Dec 27, 2019. She gained some weight. Current is 160lbs! Fatigue and LBP. Acupoints: Groupe 4
- Nov. 13: pregnant 35 weeks, weight: 168ibs. She is very tired, LBP. Acupoints: Groupe 4
- m. 12) Dec.13: pregnant 39 weeks. According to the midwife's check-up today, she has a big baby, the baby position is very high. Her cervix is still long, no dilation at all. Acupoints: SP6, LI4, St36, Liv3.
- Note on Jan. 7, 2020: emergency C-section due to distressed breathing of the baby. Baby Sammy was born at 2:35 pm (Figure 1).



Figure 1.

Abbreviations

AFC- Antral Follicle Count; AMH- Antimüllerian Hormone; DOR- Diminished Ovarian Reserve; FSH- Follicle-Stimulating Hormone; HPG- Axis Hypothalamic-Pituitary-Gonadal Axis; IUI- Intrauterine Insemination; LBP- Lower Back Pain; PMS-Premenstrual Syndrome; TCM- Traditional Chinese Medicine

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