

Acupuncture protocol in the process of In Vitro Fertilization (IVF) —An integrated approach

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Abstract: An analysis of current acupuncture and IVF research points out their inconsistent outcomes. Previous trials about acupuncture and IVF do not reflect the reality of acupuncture practice and essence. They employed a simplified acupuncture to meet the demands of randomized controlled trials (RCT), acupuncture has become handicapped. More well-designed trials about acupuncture and IVF are needed in the future to get a clear picture. Through my 10 years of clinical practice with about 3000 IVF patients, I have developed my own acupuncture protocol considering women's cycle, hormone characteristics in TCM and individual TCM patterns. The feedback from my patients is satisfactory.

Key Words: Acupuncture protocol; Infertility; IVF; Embryo transfer; Clinical trials.

I. Brief summary of the present situation of acupuncture and IVF researches

Acupuncture is an ancient therapy, which can be traced back at least 2500 years. It is based on experience and is often regarded as an art. In the last 60 years China has carried out widely scaled researches within the field of acupuncture, aiming at finding out what acupuncture is, how it works and why it works. During the past 30 years, Western researchers have also been working on the same issues. Researchers have brought forth some knowledge about acupuncture working mechanisms. For example, acupuncture may work on neuron transmitter system such as β - endorphins. However, until now, no clear mechanisms have been discovered and the "black box" stays unopened.

Since Paulus's (1) research showed that acupuncture could increase IVF (in vitro fertilization) outcomes (42% vs. 26%). By then, the great interest for acupuncture in the fertility field has been aroused. More and more acupuncturists use acupuncture treating IVF patients worldwide, and the same time more research has been carried out. There are 9 randomized controlled trials (RCT)(1-9) on the application of acupuncture in connection with embryo transfer (ET) during IVF treatment. All of the trials used more or less the same acupuncture protocol as Paulus, et al. did in their research, by administering acupuncture 25 min. before and after ET. Westergaard et al. treated one more time three days after ET (2); Smith et al. treated one more time before the aspiration (4). All of the acuapunctures in the research used in less than 4 sessions. The research outcomes were inconsistent: some showed that acupuncture works, and others showed that it doesn't work. A systematic review and meta-analysis (Manheimer et al. 10) and a Cochrane review (Cheong et al. 11) have shown a beneficial effect of acupuncture in connection with Embryo transfer. However, more recent researchers have put these two reviews in question (So et al, 8; Andersen, et al. 9). So, does acupuncture work in the IVF outcome?

The acupuncture efficacy mechanism is to activate the body's own ability to achieve balance and heal itself. This

requires a certain number of acupuncture sessions in order to accumulate the stimulation and reach the desired effect. A few acupuncture sessions may have a little effect. If we study the effect of a few sessions, a large amount of samples need to be recruited. Using the results of the study by Anderson et al. (9) to calculate sample size, any future high-quality and sufficiently powered clinical trial examining the value of acupuncture in IVF will need to recruit 2300 women in each arm to have an 80% power to detect a 4% difference in the clinical pregnancy rate at a double-sided alpha of 0.05 (El-Toukhy, 12). The prospect of such study being conducted is unrealistic (12). Was the acupuncture and IVF research so far suitable?

In my opinion, to be able to carry on a professional acupuncture treatment, there are three basic demands: a. individual combination of points; b. precise points location; c. Deqi (Deqi is a needling sensation, which can be felt by both therapists and patients.).

RCT research (single or double blind) rules out interactions between therapists and patients (13). The importance of establishing a positive practitioner-patient relationship is the basis for proceeding with treatment including both verbal and non-verbal communication (13). The individualizing of treatment is usually seen as a core approach within TCM. Getting patients involved into treatment, for example by changing their lifestyle, will increase therapeutic effects (13). The use of a standardized treatment, either one-treatment fitting all (as acupuncture and IVF research commonly does.), or even one treatment, fixed to a patient over time was not supported model to the acupuncturists in Macpherson et al.'s trial (13).

In my opinion, those researches about acupuncture and IVF don't reflect the reality of acupuncture practice and acupuncture essence. They used a simplified acupuncture. To meet the demands of a RCT, acupuncture has become handicapped.

In both Anderson et al.'s and So et al.'s research, placebo needles were being used. Both of their results showed that acupuncture did not improve IVF outcomes (8, 9). So et al.'s results showed even that Placebo group had better results than the acupuncture group (8). Is

placebo acupuncture suitable in acupuncture and IVF trial? Manheimer (10) in his exclusive analysis has examined the theoretical and methodological rationales for the use of sham or placebo acupuncture controls in all acupuncture and IVF RCTs' trials and argues that sham acupuncture or placebo acupuncture may unnecessarily complicated the RCT evidence base, because the outcome is pregnancy rate which is entirely objective and unlikely to be affected by a patient's expectations of a benefit of acupuncture. It seems unlikely that an IVF patients' knowledge of whether she was receiving adjuvant acupuncture would affect her ability to become pregnant from IVF. Therefore, using sham or placebo acupuncture to control for expectation/placebo effect seems unnecessary in this context. Even if adjuvant acupuncture were to increase IVF success rates only through a psychosomatic effect mechanism such as by reducing stress, this stress-reduction effect would be integral to the working mechanism by which adjuvant acupuncture increases IVF pregnancy rates. Therefore, it seems inappropriate to control for and separate out any such stress-reduction effect by using a sham control. Because of the risk that the sham is not an inert placebo but rather an active treatment that may affect the pregnancy outcome, using sham acupuncture as the control may unnecessarily confuse rather than clarify the interpretation of the effects of IVF adjuvant acupuncture. Using both theoretical concerns and epidemiologic evidence, researchers should carefully weigh the benefits and drawbacks of using sham acupuncture to blind patients in adjuvant acupuncture for IVF trials, and should question, rather than automatically accept, whether "placebo effects" are an important risk of bias in this context (10).

So, more well designed acupuncture and IVF trials that take into account of individual and professional combinations of points and proper stimulus doses in the future may contribute to reach a clearer picture.

II. Acupuncture Protocol in the process of

2. Three principles to be considered while using acupuncture in connection with IVF

1) Considering woman's cycle

Cycle day	1-14	15-28
Basic body temperature	Low	High
Endometrium	Proliferative phase, Follicles phase	Secretion phase, Luteal phase
TCM	Yin phase	Yang phase
Basic pattern	Blood deficiency	Blood stagnation

2) Considering hormones' characteristics

Hormones and their characteristics in TCM (my own opinion):

Medicine	Functions	Side effects	Effect on energy
Synarela, uprefact, Zoladex	Down regulation	Hot flush, moody, dry mucosa	Yin depleting
Gonal-F, Puregon Menopur	Follicle stimulating	Headache, abdominal distension, overstimulation	Liver Qi stagnation, Liver yang rising
Pregnyl	Inducing ovulation	Headache, embolism	Extreme yang rising
Pergotime Tamoxifen Clomifen	Follicles stimulating during insemination	Headache, nausea, breast tension, feeling warm, moody, distension	Liver Qi stagnation, Liver yang rising

IVF treatment

How is clinical practice worldwide? Acupuncture assisting IVF is blooming despite of the unclear research results!

Every year there are about 15000 IVF (in vitro fertilization) treatments in Denmark and many patients use acupuncture to support their IVF treatments. I have been treating about 3000 IVF patients in the last 10 years and I have created my own acupuncture protocol. The feedback from my patients is satisfactory. Here I would like to share my experience with fellow TCM fertility specialist.

One most common IVF protocol is the long protocol, in which the down regulation drugs like Synarela start at the day 21 of the cycle continuing for 14 days, and then FSH (Follicle Stimulating Hormone) such as Gonal-F begins while the down regulation continues with decreased doses. Normally FSH is administrated for about 8 to 12 days, followed by ovulation-inducing hormone such as Pregnyl, 36 hours later the aspiration takes place. Two to three days after the aspiration, the embryos are transferred into the uterus (ET). After ET, progesterone such as Crinone is administrated vaginally. 14 days later, a blood HCG test will show if the woman is pregnant or not.

Here I will briefly introduce my acupuncture protocol in the process of the long protocol of IVF treatment.

1. The functions of acupuncture in the process of IVF

- Inhibit uterus contraction and improve blood circulation in the uterus and increase B-endorphin level, which is beneficial for conception (14, 15, 16).
- Stress is a very common phenomenon in connection with IVF (17, 18, 19), and women's emotions are like a rollercoaster. Acupuncture is good at reducing stress level (17, 19, 20).
- Improve ovarian function to produce follicles of better quality.
- Decrease side effects of hormones such as headache, tiredness and discomfort.

Bromocriptine P-pills	Decrease prolactine Depress endometrium and eliminate water cysts	Headache, nausea Depression, water accumulation	Liver Qi stagnation Liver Qi stagnation, Accumulation of dampness due to Spleen deficiency
Estrogens (Estradiol, Estrofem)	For frozen egg or donor egg treatment	Depression, water accumulation	Liver Qi stagnation Accumulation of damp phlegm
Metformin Prednisone	PCOS Prevention of abortion	Poor appetite, loose stools If < 7.5mg daily for a short time, few side effects	Spleen Qi deficiency. If >7.5mg daily for a long term, depleting yin and Qi
Progesterone (Crinone)	Assisting implantation	Rashes and itching, tiredness, dizzy, breast distension, water retention, headache, leukorrhagia, discomfort during intercourse and spot bleeding	Warm uterus

3) Considering the individual TCM patterns:

Common patterns: a. Cold uterus; b. Liver Qi stagnation; c. Blood stasis; d. Accumulation of damp phlegm; e. Kidney jing, yang, and/or yin deficiency; F. Qi and blood deficiency

3. Acupuncture protocol in the process of long protocol IVF treatment

Down regulation	Nourish yin	Yingtang, SP9, LI4, LR3, LI6, LU7, SP6 or BL18, BL20, BL23, SP9, KI3 (1)
Cycle day 1-3	No acupuncture	If painful menstruation or headache (2)
Cycle day 4-7	Tonify Qi and blood	DU20, RN4, RN3, ST36, SP6
Follicle stimulation period from cycle day 8 to aspiration (3)	Continue to support Qi and Blood, regulate LR Qi, and suppress LR Yang	DU 20, ST29, LI4, LR3, SP36, SP10, SP8, SP6 (4)
On the day of ET	Standard	Half hour before ET: DU20, ST29, PC6, SP8, LR3, plus ear points: Shenmen, Endocrine and Uterus; After ET: LI4, SP6, SP10, ST36 (5)

* Explanation for each red mark:

- (1) No acupuncture on the lower abdomen: Maybe she is pregnant under the down regulation (which happens quite often in my clinic) or one purpose of the down regulation is to make the uterus lining thinner and acupuncture above the uterus may have the opposite effect.
- (2) Additional points
 - a. Painful menstruation: BL32, PC6, SP6
 - b. Strong headache and migraine: Taiyang, GB20, LI4, LR3, SJ5, GB41, ST8
- (3) Theoretically, menstruation comes 28 days after previous cycle and FSH starts day 8 of the cycle after the down regulation has been administrated for 14 days. However in practice, women's cycle is often delayed during the down regulation so the group should be used while FSH is being administrated.
- (4) If PCOS women or women that produced a lot of follicles in their previous IVF treatment: remove ST29, and plus KI12; if there were poor or few follicles in their previous IVF: KI3, KI6 / KI7 or BL23, BL32, KI3 and ST29/Zigong (with electrical acupuncture).
- (5) If you are not in the fertility clinic treating patients (recommended), you can give acupuncture once on all the points including pints before and after ET in your own clinic; if before embryos transfer (ET), use TDP above the lower abdomen; if after ET, no TDP above the lower abdomen.

4. Treatment frequency

How often should acupuncture be administered? Normally I start acupuncture around the down regulation, once a week until FSH is administrated and then twice a week until ET. For women over 40 years old, have tried more than 3 attempts of IVF and/or produced poor quality follicle in their previous IVFs, I will start acupuncture session at least two to three months before their IVF treatment. While you treat IVF patients, you can chose the points from the acupuncture protocol plus some few points based on their individual pattern. For instance, the patient comes at day 5 of her cycle, and her basic pattern is Kidney Qi deficiency. You chose points like DU20, RN3, RN4, SP36, and SP6 from the table (cycle day 4-7) and KI 3 for Kidney Qi.

5. Plan after Embryo transfer

	Acupuncture stops	Acupuncture continues
IVF treatment	< 3times	> 3 times
Woman's age	< 40 years old	> 40 years old
Early abortion	< 2 times	> 2 times
General health conditions	Good	Poor

If acupuncture treatments need to be continued, normally I will use Back-Shu points like BL18, BL20 and BL23 to strengthen Yang, because in the second phase of the cycle Progesterone is the dominating hormone and has yang energy.

III. A Case study

Linda was a 32 years old woman. She came to my clinic on 30th August 2011. The cause of her infertility was PCOS. She has never been pregnant. Her menarche was at 11 years of age. Her menstrual cycle was irregular and about 30 to 50 days long. Her menses were red, scanty, no pain or clots. Her last menstruation was on 24th August 2011. She has taken P-pills from 19 to 29 years of age. General symptoms: poor sleep, headache, irritable bowel movement, palpitations, depression, worrying, asthma, and hay fever. Her tongue coating was greasy and pulse was irregular and slow. She did not drink coffee, alcohol or smoke. She had only eaten very few sweets and done little exercise. It was her first IVF treatment. She started down regulation on 15th August 2011 and got her menstruation on 24th August 2011.

TCM diagnosis: spleen and heart qi deficiency and liver qi stagnation.

Treatment principles: strengthen spleen and heart qi and regulate liver qi.

Treatment:

30th August: cycle day 7, FSH (Gonal-F) 150 IE from 29/8, DU20, Taiyang, SP6, LR3, LU7, KI6, HT7, RN3, ST36;

3rd September: cycle day 11, No more headache after last treatment, generally felt better and was happier. Remove Taiyang, LU7, KI6 and RN3, and add LI4, ST29, SP8 and SP10;

5th September: cycle day 13, scanning showed that she had 8 follicles and Gonal-F was continued.

6th September: cycle day 14, acupuncture points: DU20, ST29, ST36, LI4, LR3, SP10, SP8, SP6.

8th September: cycle day 16, she was going to get her aspiration on 9th September. The same points were used as on cycle day 14.

11th September: cycle day 19, she came to my clinic before she went to her fertility clinic for ET. The same points as on cycle day 14 plus PC6 and ear points (Shenmen, Endocrine, Uterus) were used. She became pregnant and gave birth to a beautiful and healthy boy.

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