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A Retrospective Study of Improving the Pregnancy Rate of *In-Vitro* Fertilization with Acupuncture Only Tapping at Fixed Points

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Abstract

Background: In 2007, Japan restricted the number of embryos that could be transferred during *in-vitro* fertilization.

Objectives: Researchers have sought to improve the pregnancy rate per embryo transfer cycle.

Subjects: Subjects were 35 of patients who underwent single thawed blastocyst transfer at this Hospital from January 2016 to March 2017 and who underwent 3 or more acupuncture sessions to improve their pregnancy rate.

Design: 50 transfer cycles of subjects were compared to 315 cycles of all other patients without acupuncture who underwent single blastocyst transfer during the same period, and the pregnancy rate per embryo transfer cycle of the 2 groups was compared retrospectively.

Setting: Acupuncture was performed by the current author, and embryos were transferred using the same technique. The date of the start of acupuncture was left to the patient's discretion; in principle, patients underwent 1 session per week. Six sessions constituted 1 round of acupuncture. After 1 round of acupuncture, patients were encouraged to undergo an additional 1-2 sessions during the embryo transfer cycle. Acupuncture was performed in which needles were inserted slightly by only tapping into place at 31 fixed acupoints.

Results: Over 50 transfer cycles, subjects had a biochemical pregnancy rate per transfer cycle of 62.0% and a clinical pregnancy rate of 52.0%. A biochemical pregnancy rate per transfer cycle increased 1.35 times and a clinical pregnancy rate increased 1.42 times by current acupuncture.

Conclusion: Results suggested that slight insertion of acupuncture needles at fixed points markedly improved the pregnancy rate of *in-vitro* fertilization.

Keywords: Pregnancy rate; Acupuncture; Assisted reproductive technologies; Infertility; *In-vitro* fertilization

Introduction

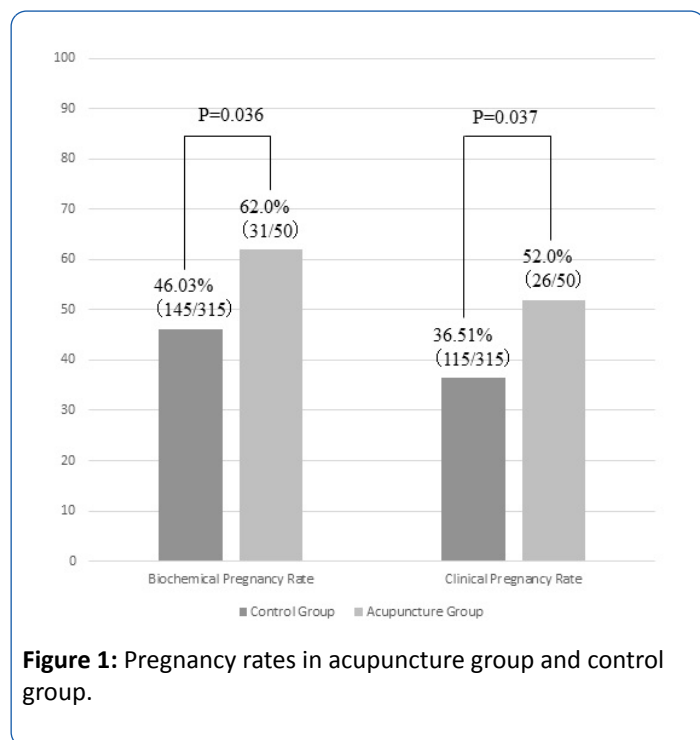
Nowadays, many women are marrying and becoming pregnant later in life. As a result, the number of infertile couples is increasing and the demand for *in-vitro* fertilization is increasing. In 2007, Japan restricted the number of embryos that could be transferred during *in-vitro* fertilization. Since then, researchers have sought to improve the pregnancy rate per embryo transfer cycle. Over the past few years, studies overseas have reported cases where acupuncture facilitated *in-vitro* fertilization [1-8], but a standardized approach has yet to be developed. China is considered to be the birthplace of acupuncture, and the acupuncture points that are selected to treat a certain condition in Chinese texts have changed with the times. In Japan, the acupuncture points that are selected vary considerably depending on the acupuncturist. The current study retrospectively examined whether acupuncture performed at this Hospital improved the pregnancy rate of *in-vitro* fertilization.

Subjects and Methods

One group of 35 subjects underwent 3 or more acupuncture sessions at this Hospital from January 2016 to March 2017 to improve the pregnancy rate of 50 cycles of single blastocyst transfer (denoted here as the acupuncture group). A second group of subjects did not undergo acupuncture during the same period but they did undergo 315 cycles of single blastocyst transfer (denoted here as the control group). The pregnancy rates of the 2 groups were retrospectively compared. Acupuncture was performed by the current author on patients who wished to undergo the treatment and from whom informed consent could be obtained. Embryo transfer was performed in the same manner by physicians at this Hospital (Department of Infertility, Green Bell Clinic).

Acupuncture procedure

Fifty-one needles were placed at 31 fixed points, as shown in **Figure 1**, in all of the patients who underwent acupuncture. Acupuncture was done using disposable needles (2-gauge, dia. 0.18 × length 40 mm, Seirin Corporation) with a guide tube. Each needle was inserted slightly by only tapping the portion protruded from the guide tube without penetrating deep into tissue. Acupuncture points were located while patients were in the supine position, and needles were left in place for 15 min. The date of the start of acupuncture was left to the patient's discretion; in principle, patients underwent 1 session per week. Six sessions constituted 1 round of acupuncture. After 1 round of acupuncture, patients were encouraged to undergo an additional 1-2 sessions during the blastocyst transfer cycle.



response to a GnRH agonist (buserelin acetate) nasal spray. An attempt was made to fertilize the harvested oocyte via insemination or intracytoplasmic sperm injection, and the fertilized ovum was cultured to generate a blastocyst that was rapidly frozen through vitrification.

In all patients, the embryo was transferred during a hormone replacement cycle. Estrogen (E) was administered via a patch. Endometrial thickness was measured using ultrasonography and E levels in the blood were measured. When the endometrium was 8 mm or thicker and the level of E in the blood was 200 pg/ml or higher, administration of progesterone (P) as a vaginal suppository began. On day 6 of P administration, a thawed blastocyst was transferred to a site 7-8 mm from the fundus of the uterus. A rest period was not provided after transfer.

This study was conducted in compliance with the Helsinki Declaration. All patients provided consent to the current treatment procedures, and obtained data were kept secure at this facility in a form in which patients could not be identified individually.

Results

As shown in **Figure 1**, the acupuncture group had a biochemical pregnancy rate (a positive result on a pregnancy test) of 62.0% (31/50) and a clinical pregnancy rate (a fetal heart beat detected with ultrasound) of 52.0% (26/50) per blastocyst transfer cycle. The control group had a biochemical pregnancy rate of 46.03% (145/315) and a clinical pregnancy rate of 36.51% (115/315). In the acupuncture group, the biochemical pregnancy rate increased by 1.35-fold, i.e. by 15.97%, and the clinical pregnancy rate increased by 1.42-fold, i.e. 15.49%. A ratio test with a significance level of 0.05 indicated that the acupuncture group had a significantly higher biochemical pregnancy rate and a significantly higher clinical pregnancy rate in comparison to the control group (P=0.036, P=0.037).

In-vitro fertilization procedure

Follicular development was stimulated with FSH or HMG. Spontaneous ovulation was inhibited by administering a GnRH antagonist (cetorelix acetate) in a dose of 0.25 mg in the time a dominant follicle grew with a dia. of 18 mm or greater, and oocyte maturation was stimulated by inducing a flare in

As shown in **Table 1**, fifty-one needles were placed at 31 fixed points in all of the patients who underwent acupuncture. Acupuncture points that were selected in the current study included the points which were significantly effective for treatment of menstrual cramps and premenstrual syndrome in addition to the 6-9 acupuncture points that were selected in other previous studies of acupuncture for upgrading pregnancy rates.

Table 1: Pattern of acupuncture points selected in the current study.

Large Intestine Meridian	LI4 (Hegu)			
Heart Meridian	HT7 (Shenmen)			
Gallbladder Meridian	GB34 (Yanglingquan)			
Pericardium Meridian	PC6 (Neiguan)	PC7 (Daling)		
Kidney Meridian	KI3 (Taixi)	KI7 (Fuliu)		
Liver Meridian	LR3 (Taichong)	LR6 (Zhongdu)	LR14 (Qimen)	

Stomach Meridian	ST25 (Tianshu)	ST27 (Daju)	ST36 (Zusanli)	ST40 (Fenglong)	
Spleen Meridian	SP6 (Sanyinjiao)	SP8 (Diji)	SP9 (Yinlingquan)	SP10 (Xuehai)	SP12 (Chongmen)
Gover Vessel Meridian	GV20 (Baihui)	GV24 (Shenting)			
Conception Vessel Meridian	CV3 (Zhongji)	CV4 (Guanyuan)	CV6 (Qihai)	CV9 (Shuifen)	CV12 (Zhongwan)
	CV13 (Shangwan)	CV14 (Jiuque)	CV15 (Jiuwei)	CV17 (Tanzhong)	
Extra Meridian acupoint	Zigong				

As shown in **Table 2**, the average age of the acupuncture group by blastocyst transfer cycle was 36.22 ± 3.59 years. Fourteen percent of cycles were undergone by patients age 40 or older. In contrast, the average age of the control group was 35.04 ± 4.88 years. Nineteen-point-six-eight percent of cycles were undergone by patients age 40 or older. An unpaired t-test with a significance level of 0.05 revealed no significant differences in the age distributions of the 2 groups ($P=0.12$).

Table 2: Characteristics of control group and acupuncture group.

Parameters	Acupuncture Group	Control Group
Age per transfer cycle	36.22 ± 3.59	35.04 ± 4.88
Percent Rate over 40 years old	14	19.68

As shown in **Table 3**, patients in the acupuncture group with a clinical pregnancy underwent an average of 6.42 acupuncture sessions. Patients who tested negative on a pregnancy test underwent an average of 6.74 sessions. During transfer, the endometrium was an average of 11.25-mm thick in patients with a clinical pregnancy and an average of 11.19 mm thick in patients who tested negative on a pregnancy test.

Table 3: Acupuncture conditions and Embryo transfer conditions of Clinical pregnancy group or Non-pregnancy group.

Parameters	Clinical Pregnancy Case	Non Pregnancy Case
Average numbers of Acupuncture (times)	6.42	6.74
Width of Endometrium (mm)	11.25	11.19
Average distance from uterine fundus to transfer point (mm)	7.82	8.35

The distance from the transfer site to the fundus of the uterus was an average of 7.82 mm in patients with a clinical pregnancy and an average of 8.35 mm in patients who tested negative on a pregnancy test. An unpaired t-test with a significance level of 0.05 revealed no significant differences between the 2 groups in terms of the number of acupuncture sessions undergone, endometrial thickness, or the distance from the transfer site to the fundus of the uterus ($P=0.37, 0.46, 0.12$).

Discussion

The current study noted an increase in the clinical pregnancy rate of 1.42-fold, which is similar to increases of 1.24-1.62-fold reported in previous studies [1-4]. Control groups in previous studies have had a clinical pregnancy rate of 23.0-26.3% [1-4], while the control group in the current study had a higher clinical pregnancy rate of 36.51%. In those studies, up to 3 early cleaving embryos on day 2-3 of development were transferred, while a single blastocyst was transferred in the current study, thus accounting for the higher clinical pregnancy rate. Nonetheless, the clinical pregnancy rate increased to a similar extent even though the control group had a higher clinical pregnancy rate than that reported in previous studies. This is presumably the result of differences in which acupuncture points were selected and where those points were operated on the body.

There are many acupuncturists who insist on needling sensation to make acupuncture effective. However, needling sensation is generally easy to be considered painful, and many patients wish to avoid such a sensation.

Acupuncture in the current study was performed by only tapping the portion protruded from the guide tube at fixed points, so the treatment can be performed in a short amount of time. Very thin needles are inserted slightly without inducing needling sensation, so there is no pain during insertion and patients are more amenable to the treatment.

One round of acupuncture consisted of 6 sessions and patients were encouraged to undergo an additional 1-2 sessions during the blastocyst transfer cycle. The rationale for doing this was based on studies done by the current author involving use of acupuncture to treat headaches, neck/shoulder stiffness, dizziness, lower back pain, menstrual cramps, and premenstrual syndrome. Undergoing an average of 5.53 sessions every other week was 81.48-94.61% effective, and in patients who responded to treatment, the average time until symptoms recurred was 156 days (about 5.2 months); in patients whose symptoms recurred, those symptoms were alleviated by an average of 1.47 additional sessions [9-13]. The rationale for assessing pregnancy rates in subsequent transfer cycles after the conclusion of 3 sessions is because the aforementioned symptoms begin to be alleviated by an average of 3.23 sessions [11]. Previous studies did not examine the sustained effects of acupuncture. Acupuncture was performed on the date of a blastocyst transfer, just before, or just after, but the current study examined the sustained effects of acupuncture.

The current author previously selected acupuncture points for treatment of menstrual cramps that were 89.47% effective [8] and points for treatment of premenstrual syndrome (e.g. irritability or depression before menses) that were 93.3% effective [13,14]. Acupuncture points that were selected in the current study included the points in those studies in addition to the 6-9 acupuncture points that were selected in other previous studies of acupuncture for upgrading pregnancy rates. When acupuncture points used to treat menstrual cramps were selected for treatment of men, semen quality improved [15]. Thus, many of the acupuncture points that were selected presumably affect the genitals. In light of the mindset of patients undergoing fertility treatment (and especially expensive treatment like *in-vitro* fertilization), mental improvement is linked to physical improvement. Incorporation of this ancient Chinese concept of mind-body unity in the selection of acupuncture points presumably improved the mental and physical state of patients and it improved the pregnancy rate. The effectiveness of treatment changes as a result of which acupuncture points are selected. Adding extra meridian points "Zigong" during the treatment of menstrual cramps improved the effectiveness of treatment from 75.47% to 89.47% according to one study [12]. In the future, which acupuncture points are selected and how those points are operated on the body need to be determined in order for acupuncture to have the most benefit.

Conclusion

Results suggested that acupuncture only tapping at fixed points markedly improved the pregnancy rate of *in-vitro* fertilization.

Declaration of Interests

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Acknowledgments

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