Electroacupuncture Reduces Uterine Artery Blood Flow Impedance in Infertile Women

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SUMMARY

Objective: To evaluate the effects of electroacupuncture (EA) on pregnancy rate and uterine artery blood flow impedance in patients undergoing *in vitro* fertilization (IVF).

Materials and Methods: This prospective, randomized trial was carried out in the IVF center of China Medical University Hospital in Taiwan, from February 1, 2004 to January 30, 2005. A total of 44 patients were enrolled in the study. Of these, 30 were allocated to acupuncture, and 14 were allocated to no acupuncture. EA was performed four times, twice a week for 2 weeks, from day 2 of the study to the day before oocyte retrieval. After patients felt the needle reaction, the needles were attached to an electrical stimulator for 30 minutes. Clinical pregnancy and pulsatility index (PI) of right and left uterine arteries before and after EA were measured.

Results: There was no significant difference in pregnancy rate between the two groups (acupuncture group, 30%; non-acupuncture group, 28.6%). The mean PI of both uterine arteries was significantly reduced after EA (left uterine artery, 2.3 to 2.0; right uterine artery, 2.4 to 2.2). There was no significant change in PI in the group with no acupuncture (left uterine artery, 2.5 to 2.3; right uterine artery, 2.4 to 2.3).

Conclusion: EA could be useful for reducing uterine artery blood flow impedance, but did not increase the pregnancy rate in patients undergoing IVF. [*Taiwan J Obstet Gynecol* 2009;48(2):148–151]

Key Words: blood flow impedance, electroacupuncture, *in vitro* fertilization, pregnancy rate, uterine artery

Introduction

Approximately 9% of women of reproductive age suffer from infertility. *In vitro* fertilization with embryo transfer (IVF-ET) is a common treatment for infertile couples. However, the overall success rate of *in vitro* fertilization (IVF) remains less than 30%. Because of repeated disappointments after IVF, or for financial reasons, some couples seek alternative means of achieving a successful pregnancy. Acupuncture is one of the most popular alternative therapies. Acupuncture involves inserting needles at specific points on a meridian that represent various organs and ailments. The specific points are selected based on examination and/or the condition to be treated. Studies have shown encouraging results for acupuncture treatment of nausea and vomiting [1], postoperative pain [2], addiction [3], and general pain syndromes [4]. Acupuncture has also been used to treat various gynecologic and obstetric problems, such as amenorrhea, morning sickness, and problems during labor and delivery [5].

There have been a few recent studies concerning the use of acupuncture in reproductive medicine. Two studies showed that acupuncture might have a beneficial effect on women with polycystic ovary syndrome and anovulation [6,7]. Chen [8] showed that electroacupuncture (EA) could normalize dysfunction of the hypothalamic pituitary–ovarian axis by altering the expression of some genes in the brain. Stener-Victorin et al [9] found that EA could reduce blood flow impedance in the uterine arteries of infertile women. Two prospective randomized trials recently showed that acupuncture administered on the days of embryo transfer

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Accepted: March 10, 2009

(ET) resulted in significant improvements in reproductive outcome in infertile women [10,11].

In the current study, women undergoing IVF-ET were randomly allocated to one of two groups: a control (non-acupuncture) group or an experimental (acupuncture) group. The control group received no acupuncture, while the experimental group received EA. The acupuncture points were selected according to the innervation of the uterus and ovary. According to traditional Chinese medicine theory, these points are associated with relaxation of the uterus. Our study evaluated the effects of acupuncture on reproductive outcome in infertile women by comparing the pregnancy rates and the changes in uterine artery pulsatility index (PI) during IVF cycles between the two groups.

Materials and Methods

This study was a prospective randomized trial. It was carried out in the IVF center of the China Medical University Hospital in Taiwan, from February 1, 2004 to January 30, 2005. During that period, women undergoing IVF who were interested in our study were invited to participate. The only criterion was that couples had to consent to be randomly assigned to one of the two groups. The assignment was independent of infertility diagnosis and number of previous cycles. Patients were excluded from the study if they were not able to achieve ET or they no longer wished to participate for any reason. A total of 56 couples participated in the study during the 12-month trial period. They were randomly assigned to one of the two groups by selection of a sealed envelope on day 1 of the study. Written informed consent was obtained from all patients. During the study period, 12 patients in the control group were excluded from the study: four of them failed ovarian stimulation and the other eight patients declined to participate further after randomization.

All patients underwent ovarian stimulation on day 2 or 3 of the menstrual cycle. Younger patients (< 35 years) commenced with 150 IU of recombinant follicle stimulating hormone (rFSH) (Gonal-F; Serono, Rome, Italy) daily, while older patients (≥ 35 years) commenced with 225 IU of rFSH daily, and a gonadotropin-releasing hormone antagonist, cetrorelix (Cetrotide; Serono), was also administered on day 8. Follicle size and number were monitored by ultrasound and serum levels of estradiol (E_2). Follicle-stimulating hormone and luteinizing hormone were also measured. If the day-8 E_2 level was < 100 pg/mL, then the daily gonadotropin dose was increased to 225 IU of rFSH for younger patients and 300 IU of rFSH for older patients. Criteria for cancellation included a low E_2 level on menstrual day 8 (< 50 pg/mL) and poor follicle growth during control ovarian hyperstimulation. Gonadotropin and cetrorelix administration continued until two or more follicles measured > 18 mm, then 5,000 IU of human chorionic gonadotropin (hCG; Serono) was administered. Oocytes were retrieved transvaginally 34–36 hours later. Oocyte culture, insemination, ET, and cryopreservation were performed normally. Transvaginal ET was performed 72 hours after oocyte retrieval. A maximum of four embryos were transferred into each patient. The luteal phase was supported with hCG (2,500 IU/day) on days 1, 4 and 7 post-ET, and 400 mg of progesterone (Utrogestan; Besins, Brussels, Belgium) from day 1 post-ET. Clinical pregnancy was defined as elevated serum β-hCG 12 days after ET and visualization of a gestational sac by ultrasound.

The acupuncture points were selected according to the concepts of traditional Chinese medicine and the innervation of the uterus and ovary. EA was administered four times, twice a week for 2 weeks, from day 2 to the day before oocyte retrieval. Sterile disposable stainless steel needles were inserted intramuscularly to a depth of 10–20 mm. The needles were twirled by hand to evoke a needle reaction; this often resulted in soreness, numbness, and distension around the point. These sensations sometimes radiated out from the point of insertion. The needles were then attached to an electrical stimulator (Trio 300; Ito Co., Ltd., Japan) at a low frequency of 10 Hz for 30 minutes. We used six pairs of acupuncture points (LR3, SP6, ST28, EX-CA1, RN6, RN4), and two needles were located bilaterally in all women undergoing EA. The patients in the control group received the same treatment as the experimental group, except for the acupuncture. The PI valve of the right and left uterine arteries were measured by transvaginal sonography on day 2 (before acupuncture) and on the day before oocyte retrieval (after the complete course of acupuncture treatment).

The Wilcoxon two-sample test was used to test for possible imbalances between the groups in terms of patient's age, endometrial thickness, mean number of oocytes retrieved, causes of infertility, and PI value of both uterine arteries on day 2. The intra-group impedance of both uterine arteries was compared using the Wilcoxon signed rank sum test. Chi-squared tests were used to compare the pregnancy rates. All statistical analyses were carried out using SAS (SAS Institute Inc., Cary, NC, USA). A p value < 0.05 was considered to be statistically significant.

Results

A total of 44 patients participated in the study. Thirty patients received acupuncture and 14 did not. Twelve

patients in the control group dropped out, of which four failed ovarian stimulation and eight no longer wished to continue after randomization.

Demographic characteristics were compared between the two groups. There were no significant differences in the following factors: patient's age, number of oocytes retrieved, number of transferred embryos, endometrial thickness, cause of infertility, or PI value of both uterine arteries on day 2 (Table 1).

Clinical pregnancy was documented in nine out of 30 patients in the acupuncture group and four out of 14 patients in the control group. The pregnancy rate was not significantly different between the two groups (30% in acupuncture group *vs.* 28.6% in non-acupuncture group; $p = 0.71$). The mean PI of both uterine arteries was significantly reduced after EA (left uterine artery, from 2.3 to 2.0, $p = 0.002$; right uterine artery, from 2.4 to 2.2, $p = 0.01$; Table 2).There was no significant change in PI in the group without acupuncture (left uterine artery, from 2.5 to 2.3, $p = 0.27$; right uterine artery, from 2.4 to 2.3, $p = 0.44$).

Discussion

The prospective randomized studies by Paulus et al [10] and Westergaard et al [11] suggested that acupuncture on the day of embryo transfer could significantly improve the reproductive outcomes in women undergoing IVF or intracytoplasmic sperm injection for infertility. However, studies by Stener-Victorin et al [12] and Humaidan et al [13] using EA on the day of oocyte retrieval did not confirm this positive effect on reproductive outcome. The results from our study also failed to show a significant increase in the pregnancy rate following the use of EA during ovarian stimulation and before oocyte retrieval. The discrepancy between these could be accounted for by the use of a different acupuncture protocol. However, the available results suggest that the influence of acupuncture on pregnancy outcome is transient.

Stener-Victorin et al [6] demonstrated that EA had a positive impact on endocrinologic parameters and ovulation in women with polycystic ovary syndrome. Other authors in China have also reported positive results for EA in some anovulatory patients [7,8]. Acupuncture is believed to affect the central stimulation of β-endorphin secretion [14], resulting in the promotion of gonadotropin-releasing hormone release. Gonadotropin-releasing hormone has a positive impact on pituitary gonadotropin secretion, ovarian follicular growth, and ovulation [15]. In our study, the number of follicles produced by patients in the acupuncture group was slightly, but not significantly, increased. However, every patient in the EA group responded to ovarian

Table 1. Descriptive data for acupuncture and control groups*

	Acupuncture group ($n = 30$)	Control group ($n = 14$)	Statistics
Age (yr)	35.5 ± 4.5	34.0 ± 5.2	NS
Endometrial thickness (cm)	1.0 ± 0.3	1.0 ± 0.3	NS
Number of oocytes retrieved	8.5 ± 5.4	7.7 ± 3.1	NS
Number of ETs	3.5 ± 0.9	3.7 ± 0.6	NS
Endometriosis infertility	20.0	21.4	NS
Male factor infertility	40.0	42.9	NS
Tubal factor infertility	30.0	28.6	NS
Unexplained infertility	10.0	7.1	NS
PI of right uterine artery on day 2	2.4 ± 0.7	2.3 ± 0.6	NS
PI of left uterine artery on day 2	2.3 ± 0.6	2.4 ± 0.8	NS

**Data are presented as mean ± standard deviation or percentage. NS = non-significant difference; ET = embryo transfer; PI = pulsatility index.*

Table 2. Pulsatility indices of uterine arteries on day 2 and before oocyte retrieval*

	Day 2 (before EA)	Before oocyte retrieval (after EA)	*p*
Acupuncture group			
Right uterine artery PI	2.4 ± 0.7	2.2 ± 0.6	0.01
Left uterine artery PI	2.3 ± 0.6	2.0 ± 0.6	0.002
Control group			
Right uterine artery PI	2.4 ± 0.6	2.3 ± 0.5	0.44
Left uterine artery PI	2.5 ± 0.8	2.3 ± 0.4	0.27

**Data are presented as mean ± standard deviation. EA = electroacupuncture; PI = pulsatility index.*

stimulation, while four patients in the non-acupuncture group failed to respond. This suggests that acupuncture could act as a useful adjuvant to ovarian stimulation. Further research is needed to evaluate the role of acupuncture in ovarian stimulation.

Successful IVF and ET require optimal endometrial receptivity at the time of implantation. The endometrial circulation or blood flow impedance in the uterine arteries, which is measured as the PI, is considered to be useful for assessing endometrial receptivity. Steer et al [16] found that a PI value >3.0 at the time of ET was associated with a low pregnancy rate. Stener-Victorin et al [9] demonstrated a reduction in PI in the uterine arteries following a series of acupuncture treatments. They suggested that the most likely cause was decreased tonic activity in the sympathetic vasoconstrictor fibers to the uterus and an involvement of the central mechanism, with general inhibition of the sympathetic outflow after acupuncture. In the current study, we found that the PI value of both uterine arteries decreased significantly in the experimental group, but no significant change was found in the control group. These results confirm and extend the findings of Stener-Victorin et al [9].

Preeclampsia is thought to be a circulatory maladaptation disease that is characterized by defective trophoblastic invasion of the maternal spiral arteries [17]. Previous studies have shown that about 45% of pregnancies with increased uterine artery impedance subsequently develop preeclampsia or intrauterine growth restriction [18]. The findings of the current study and those of Stener-Victorin [9] showed that acupuncture could reduce the uterine artery impedance. In addition, Zeisler et al [19] found a positive influence of acupuncture treatment on umbilical artery waveforms. Acupuncture treatment using specific acupoints could, therefore, provide an alterative method of preventing preeclampsia or intrauterine growth restriction in high-risk women. Further studies are needed to confirm these findings and to investigate the safety of acupuncture in pregnant women.

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