

Adjuvant acupuncture reduces first trimester pregnancy loss after IVF

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ABSTRACT

Background: The objective of this study was to determine the effects of acupuncture treatment as an adjunctive therapy on the outcome of *in vitro* fertilization (IVF)/Intracytoplasmic Sperm Injection (ICSI). **Material/Methods:** We conducted a retrospective study of 238 patients who underwent conventional IVF/ICSI alone or in conjunction with acupuncture over a course of 2 years. Patients in the two treatment groups were matched in terms of age and diagnosis. Acupuncture was administered in two sessions 5 to 7 days prior to and on the day of embryo transfer. **Results:** There were no differences between the two groups in terms of fertilization rate, pregnancy or implantation rates, and endometrial thickness. The number of oocytes retrieved ($P < 0.005$) and the number of first trimester miscarriages were significantly lower in the group receiving acupuncture ($P < 0.001$). **Conclusions:** Acupuncture reduces miscarriage rates in patients undergoing IVF/ICSI possibly secondary to stress relief.

Keywords: Acupuncture; IVF/ICSI; Pregnancy Rates; Implantation Rate; Miscarriage

1. INTRODUCTION

Acupuncture, an ancient Chinese treatment, is based on the energy flow of Qi. Disease results when this energy flow is disrupted, and can subsequently be treated via stimulation of specific points on the body that balance this energy flow [1]. In recent studies, the use of acupuncture in conjunction with *in vitro* fertilization (IVF) treatments has produced mixed results with both positive and no effects. In relation to female infertility, acupuncture is believed to stimulate β -endorphin secretion which in turn stimulates blood flow to the uterus and ovaries [2]. The principle mechanisms by which acupuncture could

improve the outcome of IVF are thought to be: modulation of neuroendocrine factors; increased blood flow to the uterus and ovaries; cytokine modulation; and reduction of stress and anxiety [3].

In a randomized controlled study Paulus *et al.* [4] reported a higher pregnancy rate in women who received acupuncture both before and after embryo transfer was reported. This study was limited due to lack of a placebo control group [4,5]. In a retrospective study by Magarelli *et al.* [6] higher pregnancy rates (51% vs 36%, $P < 0.05$) as well as lower miscarriage rates (8% vs 20%, $P < 0.05$) among poor responder women who received acupuncture was reported. In a subsequent study by the same investigators significantly higher pregnancy rates for good prognosis patients receiving acupuncture (53% vs 38%, $P < 0.01$) was reported [7]. However, in a study conducted by Wang *et al.* [8] where acupuncture treatments were only performed during the follicular and luteal phase but not on the day of embryo transfer no difference in pregnancy rates was found. The aim of this study was to determine the effects of acupuncture treatment delivered by a single acupuncturist as an adjunctive therapy on the outcome of IVF/ICSI and the resultant pregnancies in two groups of women matched for age and diagnosis.

2. MATERIALS AND METHODS

This study was a retrospective analysis using data collected at Pacific Fertility Center over a two year course. Data was obtained from 127 patients having IVF/ICSI in conjunction with acupuncture, and another 111 patients undergoing IVF/ICSI alone. Being a retrospective chart analysis the study was considered as IRB exempt. Patients in the study were derived from the practices of two physicians working in the same center and using the same embryology laboratory with one physician referring all their patients for acupuncture and the other physician not referring their patients for acupuncture. Both physicians are board certified reproductive endocrinolo-

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gists using the same stimulation protocols and medications for controlled ovarian hyperstimulation. The stimulation protocol consisted of oral contraceptive suppression for one month followed by Leuprolide acetate for down regulation. For controlled ovarian hyperstimulation a combination of recombinant FSH and HMG preparation (1:1 or 2:1 ratio) was used. Luteal support was provided with progesterone in oil (50 mg/ml IM, daily) and vaginal suppository (50 mg daily). A single acupuncturist administered the treatment. A minimum of two acupuncture treatments were given 5 to 7 days prior to and on the day of embryo transfer. The acupuncture protocol consisted of three groups of acupuncture points, each group promoting fertility in a different way. These groups were Eight Extraordinary Vessel points, Twelve Meridian acupuncture points, and Auricular points. Additionally, each session incorporated acu-points selected to treat specific presenting symptoms related to side effects of the fertility medications.

The first group of points inserted pertains to the deep lying Extraordinary Vessels. The combination of Pericardium Six and Spleen Four opens the Chong Mai, the Sea of Blood, which promotes blood flow to the uterus. The combination points Lung 7 and Kidney 6 open the Ren Mai, the Receiving Vessel, tonifying all aspects of reproduction and fertility. The second group of points is related to the meridians located more superficially on the body. Stomach 36, Spleen 6, Kidney 3, Ren 4 (conception vessel 4), Stomach 28, Liver 3 and Large Intestine 4 all work together to activate and strengthen Qi and Blood.

The data were then analyzed documenting seven variables including the clinical outcome, as well as age, diagnosis, endometrial thickness, number of oocytes retrieved, percent fertilization, and implantation rates. The implantation rate was calculated by dividing the number of gestational sacs on the ultrasound by the number of embryos transferred. All pregnancies were followed for the first trimester. Data was analyzed using the Sigma Stat software. The Chi-square and student's t-test were used to compare the various end points in the two study groups.

3. RESULTS

Table 1 demonstrates the demographics of the two study groups. As shown there were no differences in terms of age or infertility diagnosis or percentage of patients undergoing Intracytoplasmic Sperm Injection (ICSI) between the two groups. Outcome data are shown in **Table 2**. There were no significant differences between the groups in terms of endometrial thickness, percent fertilization, or pregnancy rates. The number of oocytes retrieved in the control group was significantly higher

Table 1. Diagnosis and age of patients in acupuncture and control groups.

	Control (n = 111)	Acupuncture (n = 127)	P
Average Age	36.61 ± 0.41	36.83 ± 0.51	NS
Ovulatory Dysfunction	8.3%	11%	NS
Male Factor	33%	38.5%	NS
Tubal Disease	13%	9.7%	NS
Unexplained	16.2%	20%	NS
Age Factor	8.3%	5.3%	NS
Endometriosis	21%	15.8%	NS

Table 2. End points analyzed in acupuncture and control groups.

	Control (n = 111)	Acupuncture (n = 127)	P
Endometrial Thickness (mm)	8.73 ± 0.21	8.29 ± 0.19	NS
Mean Number of Oocytes Retrieved	13.55 ± 0.88	10.57 ± 0.60	0.005
Percent Fertilization	66.36% ± 2.09%	68.97% ± 2.29%	NS
Implantation Rate	34.74% ± 3.29%	31.12% ± 3.28%	NS
Pregnancy Rate	45.45% ± 0.04%	39.37% ± 0.04%	NS
Miscarriage Rate	40% ± 0.07%	31.8% ± 0.07%	0.001

than acupuncture group ($P < 0.005$). First trimester miscarriage rates were significantly lower ($P < 0.001$) in the acupuncture group as compared with the control group. The 95% confidence interval for the difference between the two means (miscarriage) was determined to be -0.280 to $+0.117$ making it plausible that μ_1 and μ_2 are nearly equal and the null hypothesis can be accepted.

4. DISCUSSION

In this study comparing two well-matched groups undergoing IVF/ICSI alone or in conjunction with acupuncture no differences in terms of endometrial thickness, fertilization, or pregnancy rates was observed. However, the rates of first trimester miscarriage rates were significantly lower in the acupuncture group.

Patients undergoing IVF are often times under great emotional stress, and it has been found that stress can reduce fertility [9], and increase miscarriages [10]. Acupuncture can help eliminate mental stress [11,12] even in the setting of patients undergoing IVF [13]. In our study subjects receiving acupuncture reported feeling relaxed after the treatment sessions, possibly indicating reduced stress in this group. The reduction in stress induced by acupuncture has been associated with higher β -

endorphin secretion [14]. At the time of embryo transfer uterine contraction frequency is increased [15], and acupuncture has been shown to reduce uterine contractions [16] and thereby increase pregnancy rates [17]. The reduction of uterine contractions might be another potential mechanism for reduction of miscarriage rates found in our study. In a systematic online review and meta-analysis of seven trials involving 1366 women undergoing IVF and IVF in conjunction with acupuncture treatments on day of embryo transfer [18] an increase in clinical pregnancy (odds ratio 1.65, 95% confidence interval 1.27 to 2.14; number needed to treat (NNT) 10 (7 to 17); seven trials), ongoing pregnancy (1.87, 1.40 to 2.49; NNT 9 (6 to 15); five trials), and live birth (1.91, 1.39 to 2.64; NNT 9 (6 to 17); four trials) was reported. While the miscarriage rates were not specified, live birth rates were determined to be higher in the acupuncture group. Stener *et al.* [19] also reported a higher take home baby rate per embryo transfer in the acupuncture group (41% versus 19.4%, $P < 0.05$). The miscarriage rate in this study was determined to be non-significantly lower in the acupuncture group, (10.7% vs 31.6%). Magarelli *et al.* [20] found statistically lower ectopic pregnancy rates in the acupuncture group ($P \leq 0.05$) with no differences in implantation and fertilization rates or number of oocytes retrieved. Stener-Victorin *et al.* [19] also showed a significantly higher implantation rate per embryo transfer (27.2% vs 16.3%, $P < 0.05$) in the acupuncture group. The reason for the lower number of oocytes retrieved in the acupuncture group in our study is unknown. If acupuncture increases blood flow to the ovary we would have expected to retrieve higher number of oocytes in the acupuncture group. The reported differences in outcomes in the various acupuncture studies are related to heterogeneity of the patients studied, the timing and manner of acupuncture administered. To control for these variables multi-center randomized prospective trials using the same protocols will be needed to address the beneficial or lack of effect of acupuncture as an adjunct to IVF/ICSI. The effects of acupuncture on uterine blood flow, contractions and correlation with stress level will need to be assessed in such trials.

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