

## Acupuncture Treatment For Infertile Women Undergoing Intracytoplasmic Sperm injection

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"Aurum Nostrum Non Est Aurum Vulgi"

### ABSTRACT

**Background** Little information exists regarding the use of acupuncture in combination with allopathic treatment of infertility.

**Objective** To describe the use of acupuncture to stimulate follicle development in women undergoing in vitro fertilization.

**Design, Setting, and Patients** Prospective case series of 6 women receiving intracytoplasmic sperm injection and acupuncture along with agents for ovarian stimulation.

**Main Outcome Measures** Number of follicles retrieved, conception, and pregnancy past the 1st trimester before and after acupuncture treatment.

**Results** No pregnancies occurred in the non-acupuncture cycles. Three women produced more follicles with acupuncture treatment (mean, 11.3 vs 3.9 prior to acupuncture;  $P=.005$ ). All 3 women conceived, but only 1 pregnancy lasted past the 1st trimester.

**Conclusion** Acupuncture may be a useful adjunct to gonadotropin therapy to produce follicles in women undergoing in vitro fertilization.

### KEY WORDS

Female Infertility, Intracytoplasmic Sperm Injection, In Vitro Fertilization, Acupuncture

### INTRODUCTION

Infertility is an area of women's health that has sparked much consumer interest in acupuncture. However, there is little published information concerning the combination of acupuncture with allopathic infertility technology.

We present results from 6 women treated with acupuncture to enhance follicle development during in vitro fertilization with intracytoplasmic sperm injection (ICSI) cycles. Our patients all had difficulty with follicle production despite maximum gonadotropin therapy. They were referred for acupuncture as a last resort. We compare results for the acupuncture cycle with results previous to acupuncture.

### MATERIALS AND METHODS

The methods used for ovarian hyperstimulation have been described.<sup>1</sup> Briefly, ovarian hyperstimulation was achieved using a long-acting gonadotropin-releasing hormone agonist (Lupron, TAP Pharmaceuticals Inc, Deerfield, Ill) administered either in the mid-luteal phase or following a minimum of 2 weeks of oral contraceptive treatment. After biochemical evidence of pituitary suppression (serum estradiol <40 pg/mL),

subcutaneous follicle-stimulating hormone was given twice daily (3-6 amps/d). Follicular response was monitored with serial pelvic ultrasonography and serum estradiol measurements. When at least 2 follicles were >17 mm, 7500 IU of human chorionic gonadotropin was given intramuscularly, and transvaginal ultrasound-directed oocyte retrieval was scheduled 36 hours later. Oocytes were identified and then rinsed free of follicular fluid, blood, and debris in TALP-Hepes plus 10% serum substitute supplement (SSS) before being placed in 0.9 mL of bicarbonate-buffered human tubal fluid (HTF) medium plus 10% SSS.2 Spermatozoa were prepared using a discontinuous Percoll gradient. Oocytes for injection were denuded of cumulus cells using hyaluronidase followed by mechanical removal and then assessment for maturity. Metaphase II oocytes were injected with a single immobilized sperm.

Following ICSI, oocytes were cultured in 0.9 mL of HTF plus 10% SSS in organ culture dishes and housed in individually gassed chambers at 37°C with 5% CO<sub>2</sub>, 5% O<sub>2</sub>, and 90% N<sub>2</sub>. At 15-18 hours following insemination, oocytes were assessed for pronuclei as evidence of fertilization. On the morning of day 3, cleaving embryos were transferred to 50- $\mu$ L drops of S2 (Scandinavian IVF Sciences, Gothenburg, Sweden) under oil. Embryos of similar quality were grouped together. Embryos cultured beyond day 5 were transferred to fresh medium.

Luteal support consisted of intravaginal progesterone (300 mg/d) beginning on the day following embryo transfer in combination with 1500 IU of hCG intramuscularly given 5 days after oocyte retrieval. Embryo transfer was performed on day 5 or 6 of extended culture using a Soft-Pass catheter (Cook Ob-Gyn, Bloomington, Ind).

The women began acupuncture treatment at the same time that they began follicle-stimulating hormone injections. They had 3 or 4 twice-weekly treatments, on days 1-3, 4-6, 7-9 and in some cases 9-11, with the final treatment on the day of or prior to egg retrieval.

Acupuncture treatments were aimed at stimulating Ming Men (BL 23, GV 4), Chong Mo, and Ren Mo. Points BL 23 and GV 4 were used at all treatments, whereas the Chong Mo (SP 4, MH 6) and Jenn Mo (KI 6, LU 7) Master and Couple points were alternated. Additional points were added on an individual basis, including LR 3, CV 4, 6, SP 30, BL 18, 20, 60, and 62.

Main outcome measures included the number of follicles retrieved, the incidence of pregnancy, and pregnancy lasting past the 1st trimester. Statistical analyses were calculated using SPSS version 10 (SPSS Inc, Chicago, Ill).

## RESULTS

Results are shown in Table 1. None of the women achieved pregnancy during the non-acupuncture cycles. Three of the women (patients 1-3) clearly recruited more follicles with acupuncture than prior to acupuncture. For the 3 who responded, the mean number of follicles with acupuncture was 11.3 vs 3.9 prior to acupuncture ( $P=.005$ ). All 3 achieved chemical pregnancy, but only 1 continued the pregnancy past the 1st trimester.

Patient 4 recruited fewer follicles during the acupuncture cycle than during previous cycles. Patients 5 and 6 recruited more follicles with acupuncture, but still recruited few follicles ( $P=.13$ ). Patient 6 did achieve a chemical pregnancy, whereas patient 5 had the retrieval cancelled due to too few follicles.

On average, significantly more follicles were recruited with acupuncture than without ( $P=.02$ ). Data on estrogen levels and endometrial lining thickness were not routinely collected in all cycles. For the 4 women (patients 1, 3, 4, and 5) who had estradiol levels measured during both acupuncture and non-acupuncture cycles, mean estradiol levels were higher during the acupuncture cycles than the non-acupuncture cycles (mean [SD], 1471 [480] pg/mL for acupuncture vs 731 [505] pg/mL for non-acupuncture), but this finding did not reach statistical significance ( $P=.08$ ). Three women (patients 1, 3, and 6) had endometrial lining measurements recorded for both acupuncture and non-acupuncture cycles. The difference in average endometrial lining thickness, measured on the day of follicle retrieval, did not approach statistical significance (acupuncture, 10.4 [2.2] mm vs non-acupuncture, 12.1 [1.1] mm,  $P=.33$ ).

None of the 6 women reported any adverse reaction to the acupuncture treatments. There were no adverse

reactions from the follicle retrievals or embryo transfers during either acupuncture or non-acupuncture cycles.

Table 1. Outcomes for Acupuncture vs Non-Acupuncture Cycles Among 6 Women Undergoing ICSI\*

Patient No.	Age, y	Non-Acupuncture Cycles		AcupunctureCycles		Outcome
		Follicles Mean No.	Cycles No.	Follicles Mean No.	Cycles No.	
1	29	4.7	3	8	1	IUP
2	34	2	1	10	2	SAB twice
3	36	3	2	14	1	SAB
4	37	8	1	6	1	No pregnancy
5	38	1	1	4	1	Cycle canceled
6	41	2	1	6	1	SAB
Mean (SD)		3.7 (1.0)		8.4 (1.3)		

\*ICSI indicates intracytoplasmic sperm injection; IUP, intrauterine pregnancy; and SAB, early spontaneous abortion. P=.02 for overall acupuncture follicles vs non-acupuncture follicles.

## DISCUSSION

Our findings suggest that acupuncture may be a useful adjuvant to gonadotropin therapy among women undergoing ICSI. In this context, acupuncture increased the number of follicles produced and appeared to also increase the estradiol level, but did not appear to affect endometrial lining thickness. However, none of the women in this report had difficulty with achieving adequate endometrial lining.

Although there is significant consumer interest in using alternative and complementary therapies for infertility, there is little research that addresses the combination of techniques. Stener-Victorin et al<sup>3</sup> published a report of using acupuncture to decrease the uterine pulsatility index among women with a history of poor uterine lining response to in vitro fertilization. They demonstrated a significant decrease in uterine pulsatility index, which was maintained for 2 weeks, by using 4 set acupuncture points with electric stimulation. Gerhard and Postneek<sup>4</sup> published results of infertile women treated with acupuncture vs similar women treated hormonally, and showed a similar pregnancy rate among the 2 groups. Siterman et al<sup>5</sup> showed improvement in sperm quality among subfertile men treated with acupuncture.

The mechanisms responsible for the systemic actions of acupuncture have been debated but not yet clearly defined. Traditional Chinese Medicine (TCM) speaks to increasing and harmonizing Qi within the reproductive organs.<sup>6</sup> Scientific analysis of acupuncture used in the context of pain syndromes has shown acupuncture to raise the level of endogenous opiates<sup>7</sup> and to decrease the level of sympathetic nerve stimulation<sup>8</sup> at the painful area. The decrease in sympathetic stimulation may be 1 of the factors that results in an increased level of blood flow to the area.<sup>7,8</sup> In the context of infertility, acupuncture may be helpful by increasing blood supply to the reproductive organs, or may simply increase relaxation or reduce subjective stress surrounding the infertility diagnosis and treatment.

## Study Limitations

These cases have an obvious bias. The group was selected from those who responded poorly to gonadotropin therapy. The patients served as their own historical controls, but there was no similar group that simply had another ICSI attempt without acupuncture to compare before and after results. The acupuncture treatments were not standardized. Even though similar points were chosen for all women, points based on the individual TCM diagnosis were also used.

## CONCLUSION

The cases do present evidence that a structured clinical trial of acupuncture to assist in follicle development for women undergoing in vitro fertilization and/or ICSI would be of interest. Many women undergoing infertility treatment seek alternative care; knowing the interaction of these 2 systems would be most useful.

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