Reproductive Medicine: Research Projects in Acupuncture

Elisabet Stener-Victorin

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Summary
Two studies are briefly reported in which electroacupuncture is found to be beneficial in aspects of infertility treatment. They are the first in a series planned to investigate acupuncture in this area of gynaecology.

1. A high impedance in the blood flow of the uterine arteries has been shown to reduce the pregnancy rate of in-vitro fertilisation treatment. So ten healthy, but infertile, women with a high uterine artery pulsatility index were treated with electroacupuncture twice a week over a period of four weeks. There was a significant reduction (p<0.0001) in pulsatility index that was maintained for a further two weeks.

2. Twenty-four women with polycystic ovary syndrome were treated with electroacupuncture over a period of three months. Ovulation patterns were observed by daily recording of basal body temperature over nine months, including three months before treatment and three after. The main outcome was that electroacupuncture induced regular ovulation in more than a third of the women. The women were found to fall into two categories; a group in whom regular ovulation was induced following electroacupuncture who were less androgenic and had less metabolic disturbance, and a group who were more affected by the syndrome and who did not respond to treatment.

Key words
Acupuncture, Electroacupuncture, Gynaecology, Infertility treatment, Ovulation, Polycystic ovary syndrome, Reproductive medicine.

General Introduction
The use of acupuncture in the area of reproductive medicine is still an unknown and poorly investigated application. A few studies have indicated that acupuncture may have an effect on hormonal disturbances, e.g. anovulation and therefore also infertility (1-3). Recently we have reported that repeated electro-acupuncture (EA) treatments in women with infertility due to a high impedance of the arterial blood flow in the uterus resulted in an increased blood flow (4,5). The effect of EA on anovulation and high uterine arterial blood flow impedance were attributed to decreased activity in a hyperactive sympathetic nervous system (1,3,4). Repeated EA treatments by stimulation of muscle afferents (Aδ and possibly C-fibres) may result in a central sympathetic inhibition, probably mediated via the β-endorphin system. In addition to central sympathetic inhibition, stimulation of muscle afferents can inhibit sympathetic outflow at the spinal levels (6-8). The details of the underlying mechanisms are, however, still largely unknown.

The aim of this series of studies is to elucidate whether acupuncture is a valuable alternative or complement to standard pharmacological treatments in reproductive medicine. Three studies have been completed, namely:
1. The effect of EA on blood flow impedance in the uterine arteries of infertile women (4).
2. The effect of EA on anovulation in women with polycystic ovary syndrome.

In a fourth, ongoing study, the attempt is to see if EA could improve the rates of implantation and pregnancy in infertile women undergoing IVF/ET treatment. Furthermore, in an attempt to elucidate the acupuncture mechanisms behind ovulation induction, we have begun experimental EA studies on rats. The first two studies are presented below:

Reduction of Blood Flow Impedance in the Uterine Arteries of Infertile Women with Electroacupuncture

Introduction
Optimal endometrial receptivity at the time of implantation is important in the IVF/ET cycle. Increased impedance in the blood flow in the uterine arteries [pulsatility index (PI)=3.0] has been found to reduce the pregnancy rate in IVF/ET treatment.

There is support for the theory that EA has cardiovascular effects, probably mediated by central opioid activity via the β-endorphin system from the hypothalamus. In addition, vasodilation may be caused by stimulation of the sensory nerve fibres
that inhibit sympathetic outflow at the spinal level, or by antidromic nerve impulses which release substance-P and calcitonin gene-related peptide from peripheral nerve terminals.

This prospective, non-randomised study was designed to assess if EA could induce a high impedance in the uterine arterial blood flow (4).

**Method**

Ten infertile but otherwise healthy women with a mean PI of 3.0 in the uterine arteries were treated with EA. After inclusion in the study and throughout the entire study period, the women were downregulated with a gonadotropin releasing hormone (GnRH) analogue to exclude any fluctuating endogenous hormonal effects on the PI. The baseline PI was measured when estradiol in serum was 0.1 nmol/l; thereafter the women received eight EA treatments: two a week for 4 weeks.

Acupuncture points were selected in somatic segments according to the innervation of the uterus: bilateral BL.23 and 28 points were electrically stimulated at 100 Hz and bilateral SP.6 and BL.57 were electrically stimulated at 2 Hz. Each treatment lasted for 30 min with a total of 8 treatments over 4 weeks. The PI was measured again soon after the eighth EA treatment, and once more 10-14 days after the last EA treatment. Skin temperatures on the forehead and in the lumbar sacral area were measured during the first, fifth and eighth EA treatments.

**Results**

Compared to the mean baseline PI, the mean PI was significantly reduced both soon after the last EA treatment (p<0.0001) and 10-14 days later (p=0.0001), at which time six women had a mean PI<2.6. Skin temperature on the forehead increased significantly during the EA treatments.

**Conclusion**

The present study showed a decrease in the PI to an optimal level in the uterine arteries following EA. The most likely cause is a decreased tonic activity in the sympathetic vasoconstrictor fibres to the uterus. Since the skin temperature on the forehead increases, a central mechanism involving hypothalamic and brainstem systems may be responsible.

**Introduction**

This prospective, non-randomised study was designed to evaluate if and to what extent EA could induce regular ovulation and hormonal parameters in women with polycystic ovary syndrome. EA may influence anovulation by regulating the hypothalamic-pituitary-ovarian axis by affecting the concentrations of endogenous opioids in the central nervous system. In addition to central sympathetic inhibition, stimulation of muscle afferents could inhibit sympathetic outflow at the spinal level.

**Method**

Twenty-four women with polycystic ovary syndrome, aged between 24 and 40 years (mean 32 years) were included in the study. The diagnosis was based on the presence of oligo-amenorrhea and ultrasonographic images of the ovaries. Needles at bilateral BL.23 and 28, and SP.6 and 9 points were electrically stimulated at 2 Hz continuously, and needles at unilateral PC.6 and TE.5, and GV.20 were manually stimulated five times during each 30 min treatment. The acupuncture was given twice a week for 2 weeks and then once a week: altogether 10-14 treatments. The study period was defined as extending from 3 months before the first acupuncture treatment to 3 months after the last, in total 8-9 months.

The menstrual and ovulation patterns were confirmed by recording the vaginal bleeding and by daily measurement of basal body temperature throughout the entire study period. Women were considered to have experienced a good effect if the basal body temperature disclosed repeated ovulations (or pregnancy) during the treatment period or in the following 3 months. In women who experienced no effect the ovulation pattern did not differ before, during or after the EA period.

**Results**

Of 24 women, 9 (38%) experienced a good effect and displayed a mean of 0.66 ovulations per woman per month in the time during and after the EA period compared to a mean of 0.15 ovulations per woman per month before the EA period (p=0.004). Fifteen women (62%) experienced no effect, and the number of ovulations did not change in this group.

Before EA, the group of women with good effect had a significantly lower body mass index (p<0.001), waist and hip circumference ratio (p=0.0058), insulin (p=0.0054), testosterone (p=0.0036), testosterone/sex hormone binding globulin (SHBG) ratio (p=0.011) and a significantly higher serum SHBG (p=0.040) than did the group of women who had experienced no effect.

When analysing all the women in the study together and comparing the blood samples taken before starting EA with samples taken 3 months after completion of the EA, a significant increase in serum prolactin levels (p=0.022) and a significant decrease in LH/FSH ratios (p=0.042), serum testosterone levels (p=0.016) and in plasma β-endorphin (p=0.013) was found.

**Conclusion**

Electroacupuncture induced regular ovulation in more than a third of the women with polycystic ovary syndrome. Women who had experienced a good effect following electroacupuncture were less...
androgenic and had less pronounced metabolic disturbance compared to those who had had no effect. In addition to this, those with good effect had lower neuropeptide levels than did the women with no effect, indicating a less active sympathetic nervous system. This suggests that electroacupuncture may be a suitable alternative to pharmacological induction of ovulation in those women with polycystic ovary syndrome who are less androgenic and less metabolically affected.

Elisabet Stener-Victorin RPT
Department of Obstetrics and Gynecology
Kvinnokliniken, Sahlgrenska University Hospital
SE-413 45 Göteborg, Sweden
Email: elisabet.stener-victorin@medstud.gu.se

References

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