

ACUPUNCTURE AND ASSISTED CONCEPTION

About infertility and assisted conception

Currently, about 17% couples in industrialised countries seek medical advice for infertility (Cahill 2002). The definition of infertility is usually the failure to conceive after 1 year of unprotected intercourse (European Society 1996). Infertility can be primary, in women who have never conceived, or secondary, in women who have previously conceived. In the UK, about 10–20% of infertility cases are unexplained (Isaksson 2004). The rest are the result of ovulatory failure (27%), tubal damage (14%), endometriosis (5%), low sperm count or quality (19%), or other causes (5%) (Effective Health Care 1992).

In developed countries, 95% of couples attempting to conceive are successful after 2 years (Brosens 2004). However, the chances of becoming pregnant vary with the cause and duration of infertility, the woman's age, the woman's previous pregnancy history, and the availability of different treatment options (Templeton 1998, Collins 1995). For the first 2–3 years of unexplained infertility, cumulative conception rates are 27–46% but decrease with increasing age of the woman and duration of infertility (Collins 1995).

The aims of infertility treatment in conventional medicine are to achieve the delivery of one healthy baby, and to reduce the distress associated with infertility, with minimal adverse effects. Interventions include intrauterine insemination plus controlled ovarian stimulation, in vitro fertilisation, intracytoplasmic sperm injection, gonadotrophin releasing hormone agonists, clomifene and tamoxifen, laparoscopic ovarian drilling, tubal flushing and laparoscopic ablation of endometrial deposits, depending on the cause of the infertility (Al-Inany 2004).

References

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How acupuncture can help

Most clinical trials to date suggest that acupuncture may be useful in the embryo transfer stage of in vitro fertilisation, and results in an increased pregnancy rate and a greater number of live births (Cheong 2008, Manheimer 2008, Kong 2009, Chen 2009, Smith 2006, Westergaard 2006), though there have been exceptions (Domar 2009) (see Table overleaf). In one recent large trial the pregnancy rate in the acupuncture group was lower than that of the control (So 2009), thus affecting the results of subsequent reviews (Cheong 2010). This trial used an inappropriately active control treatment, a sort of acupressure, thus casting doubt on the validity of the findings.

Acupuncture may help in the treatment of infertility by:

- regulating fertility hormones - stress and other factors can disrupt the function of the hypothalamic pituitary-ovarian axis (HPOA). Acupuncture promotes the release of beta-endorphin in the brain, which regulates gonadotrophin releasing hormone from the hypothalamus, follicle stimulating hormone from the pituitary gland, and oestrogen and progesterone levels from the ovary (Anderson 2007).
- increasing blood flow to the reproductive organs (Ho 2009, Anderson 2007), which can improve the thickness of the endometrial lining, so increasing the chances of embryo implantation.
- increasing egg production (Jin 2009) and improving oocyte quality (Chen 2009), which could increase the chance of fertilisation.
- enhancing luteal function (Huang 2009)
- regulating follicle stimulation hormone-receptor expression (Jin 2009).
- normalising cortisol and prolactin levels on IVF medication days (Magarelli 2008); reducing stress (Anderson 2007)
- promoting embryo implantation (Liu 2008).

About traditional acupuncture

Acupuncture is a tried and tested system of traditional medicine, which has been used in China and other eastern cultures for thousands of years to restore, promote and maintain good health. Its benefits are now widely acknowledged all over the world, and in the past decade traditional acupuncture has begun to feature more prominently in mainstream healthcare in the UK. In conjunction with needling, the practitioner may use techniques such as moxibustion, cupping, massage or electro-acupuncture. They may also suggest dietary or lifestyle changes.

Traditional acupuncture takes a holistic approach to health and regards illness as a sign that the body is out of balance. The exact pattern and degree of imbalance is unique to each individual. The traditional acupuncturist's skill lies in identifying the precise nature of the underlying disharmony and selecting the most effective treatment. The choice of acupuncture points will be specific to each patient's needs. Traditional acupuncture can also be used as a preventive measure to strengthen the constitution and promote general wellbeing.

An increasing weight of evidence from Western scientific research (see overleaf) is demonstrating the effectiveness of acupuncture for treating a wide variety of conditions. From a biomedical viewpoint, acupuncture is believed to stimulate the nervous system, influencing the production of the body's communication substances - hormones and neurotransmitters. The resulting biochemical changes activate the body's self-regulating homeostatic systems, stimulating its natural healing abilities and promoting physical and emotional wellbeing.

About the British Acupuncture Council

With over 3000 members, the British Acupuncture Council (BAcC) is the UK's largest professional body for traditional acupuncturists. Membership of the BAcC guarantees excellence in training, safe practice and professional conduct. To find a qualified traditional acupuncturist, contact the BAcC on 020 8735 0400 or visit www.acupuncture.org.uk

ACUPUNCTURE AND ASSISTED CONCEPTION

The evidence

| Research | Conclusions |
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| Reviews | |
| <p>Cheong Y et al. Acupuncture and herbal medicine in in vitro fertilisation: a review of the evidence for clinical practice. <i>Hum Fertil</i> 2010 Jan 7. [Epub ahead of print]</p> | <p>A systematic review and meta-analysis that looked at the effectiveness of acupuncture and Chinese herbal medicine in the treatment of male and female subfertility by assisted reproductive technologies (ART). It included 14 randomised controlled trials involving a total of 2,670 participants of acupuncture and/or Chinese herbal medicine in ART. The outcome measures were: live birth rate, ongoing pregnancy rate, clinical pregnancy rate, the incidence of ovarian hyperstimulation syndrome and multiple pregnancy, miscarriage rate and adverse effects arising from treatment. Adjunctive acupuncture improved live birth and pregnancy rates but the superiority over control groups was not statistically significant. Hence the reviewers concluded that there was no evidence of benefit in the use of acupuncture during assisted conception.</p> |
| <p>Cheong YC, Hung Yu Ng E, Ledger WL. Acupuncture and assisted conception. <i>Cochrane Database of Systematic Reviews</i> 2008, Issue 4. Art. No.: CD006920. DOI: 10.1002/14651858.CD006920.pub 2.</p> | <p>A systematic review that looked at the effectiveness of acupuncture in the outcomes of assisted reproductive treatment (ART). A total of 13 randomised controlled trials were included of acupuncture for couples who were undergoing ART comparing acupuncture treatment alone or acupuncture with concurrent ART versus no treatment, placebo or sham acupuncture plus ART for the treatment of primary and secondary infertility. These found evidence of benefit when acupuncture is performed on the day of embryo transfer on the live birth rate (OR 1.86, 95%CI 1.29 to 2.77), but not when it is performed two to three days after embryo transfer (OR 1.79, 95%CI 0.93 to 3.44). There was no evidence of benefit on pregnancy outcomes when acupuncture was performed around the time of oocyte retrieval. The reviewers concluded that acupuncture performed on the day of embryo transfer shows a beneficial effect on the live birth rate.</p> |
| <p>Manheimer E et al. Effects of acupuncture on rates of pregnancy and live birth among women undergoing in vitro fertilisation: systematic review and meta-analysis. <i>BMJ</i> 2008;336(7643):545-9.</p> | <p>A systematic review that evaluated whether acupuncture improves rates of pregnancy and live birth when used as an adjuvant treatment to embryo transfer in women undergoing in vitro fertilisation. It included a total of 7 randomised controlled trials with 1,366 women. Trials with sham acupuncture and no adjuvant treatment as controls were pooled for the primary analysis. Complementing the embryo transfer process with acupuncture was associated with significant and clinically relevant improvements in clinical pregnancy (OR 1.65, 95%CI 1.27 to 2.14; number needed to treat [NNT] 10, 95%CI 7 to 17), ongoing pregnancy (1.87, 1.40 to 2.49; NNT 9 (6 to 15); five trials), and live birth (1.91, 95%CI 1.39 to 2.64; NNT 9, 95%CI 6 to 17). The reviewers concluded that current preliminary evidence suggests that</p> |

acupuncture given with embryo transfer improves rates of pregnancy and live birth among women undergoing in vitro fertilisation.

Anderson et al. In vitro fertilization and acupuncture: clinical efficacy and mechanistic basis. *Altern. Ther. Health Med.* 2007;13(3):38-48

An overview of the use of acupuncture as an adjunct therapy for in vitro fertilization (IVF). There is limited but supportive evidence suggesting that acupuncture may improve the success rate of IVF and the quality of life of patients undergoing IVF and that it is a safe adjunct therapy. Most studies reviewed had design limitations, and the acupuncture interventions employed often were not consistent with traditional Chinese medical principles. The reviewed literature suggested 4 possible mechanisms by which acupuncture could improve the outcome of IVF: modulating neuroendocrinological factors; increasing blood flow to the uterus and ovaries; modulating cytokines; and reducing stress, anxiety, and depression. They concluded that more high-quality randomized, controlled trials were required.

Clinical studies

Ho M et al. Electroacupuncture Reduces Uterine Artery Blood Flow Impedance in Infertile Women. *Taiwanese Journal of Obstetrics and Gynecology* 2009;48:148-51.

A randomised controlled trial that evaluated the effects of electroacupuncture on pregnancy rate and uterine artery blood flow impedance in patients undergoing in vitro fertilization (IVF). A total of 44 patients were enrolled in the study. Acupuncture was performed four times, twice a week for 2 weeks, from day 2 of the study to the day before oocyte retrieval. Clinical pregnancy and pulsatility index (PI) of right and left uterine arteries before and after treatment were measured. 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 acupuncture (left uterine artery 2.3 to 2.0; right uterine artery 2.4 to 2.2), but not in the no acupuncture group (left uterine artery 2.5 to 2.3; right uterine artery 2.4 to 2.3). The researchers concluded that electroacupuncture could be useful for reducing uterine artery blood flow impedance, but did not increase the pregnancy rate in patients undergoing IVF.

Kong S, Hughes A. Acupuncture as an adjunct to in vitro fertilization: A randomized trial. *Medical Acupuncture* 2009;21:179-82.

A randomised controlled trial that compared three acupuncture methods to evaluate which method is most effective for IVF. A total of 52 IVF patients were randomly assigned to receive traditional Chinese acupuncture plus electroacupuncture, acupuncture alone (control), or electroacupuncture alone (second control). Comparisons of IVF effectiveness rates were made for each method. All three acupuncture methods increased the success rate for IVF, and there was a marked increase with the combination treatment (81.8% success, which is twice the US average for IVF alone; $p < 0.01$). The success rates for the control groups were 64.3% with acupuncture and 62.5% with electroacupuncture ($p > 0.05$). The researchers concluded that their results suggest the combination of acupuncture and electroacupuncture is a promising new technique for the treatment of infertility with a higher IVF success rate than that of either treatment alone.

Chen J et al. Effects of

A randomised controlled trial to observe the effect of

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| <p>electroacupuncture on in vitro fertilization-embryo transfer (IVF-ET) of patients with poor ovarian response.[Chinese] <i>Zhongguo Zhenjiu</i> 2009;29:775-9.</p> | <p>electroacupuncture therapy on oocyte quality and pregnancy outcome of 60 patients with poor ovarian response or decreased reserve in the course of in vitro fertilization (IVF). The levels of serum estradiol, fertilization rate, oocyte maturation rate, good quality embryos rate, and implantation rate in the acupuncture group were superior to those in the control group on the day of human Chorionic Gonadotropin (hCG) injection (all $p < 0.05$). Also, the levels of stem cell factor in follicular fluid and serum in the acupuncture group were significantly higher than those in the control group (both $p < 0.05$). The researchers concluded that electroacupuncture therapy has a good clinical effect for IVF patients with poor ovarian reserve, and can improve oocyte quality and pregnancy outcome.</p> |
| <p>Domar AD et al. The impact of acupuncture on in vitro fertilization outcome. <i>Fertil Steril</i> 2009;91:723-6.</p> | <p>A randomised controlled trial to assess the efficacy of acupuncture on pregnancy rates in 150 women undergoing IVF. The women were allocated to acupuncture before and after embryo transfer, while the control group lay quietly. All the women then completed questionnaires on anxiety and optimism. There were no significant differences in pregnancy rates between the two groups, but the acupuncture patients reported significantly less anxiety post-transfer and reported feeling more optimistic about their cycle and enjoyed their sessions more than the control subjects. The researchers concluded that the use of acupuncture in patients undergoing IVF was not associated with an increase in pregnancy rates but did help women feel more relaxed and more optimistic.</p> |
| <p>So EWS et al. A randomized double blind comparison of real and placebo acupuncture in IVF treatment. <i>Human Reproduction</i> 2009; 24: 341-8.</p> | <p>A randomised controlled trial that compared real acupuncture with sham acupuncture before and after embryo transfer in 370 patients undergoing IVF treatment. The sham treatment used pressure at the same locations as used for real acupuncture, in effect a comparison of acupuncture and acupressure, not a placebo. The clinical pregnancy rate was significantly higher in the sham acupuncture group than the real acupuncture group (55.1 versus 43.8%, respectively, $p = 0.038$). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and sub-endometrial vascularity, serum cortisol concentrations and anxiety levels were observed in both groups. The researchers concluded that placebo acupuncture was associated with a significantly higher overall pregnancy rate than real acupuncture, but that placebo acupuncture may not be inert.</p> |
| <p>Smith C et al. Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer. <i>Fertil Steril</i>. 2006; 85(5):1352-8.</p> | <p>A randomised controlled trial of 228 women receiving 3 sessions (one either side of embryo transfer and one earlier in the process) of acupuncture or non-invasive sham needling. The clinical pregnancy rates were 31% for acupuncture, 23% control. Pregnancy rates at 18 weeks were 28% and 18% respectively. The differences were not statistically significant but would be clinically significant. Authors conclusions: there was no significant difference in the pregnancy rate between groups; however, a smaller treatment effect can not be excluded</p> |
| <p>Westergaard LG et al. Acupuncture on the day of embryo transfer significantly</p> | <p>A randomised controlled trial that evaluated the effect of acupuncture on reproductive outcome in 273 women</p> |

improves the reproductive outcome in infertile women: a prospective, randomized trial. *Fertil Steril* 2006;85:1341-6.

undergoing IVF/intracytoplasmic sperm injection (ICSI). One group of patients received acupuncture on the day of embryo transfer, another group on embryo transfer day and again 2 days later (i.e. closer to implantation day), and both groups were compared with a control group that did not receive acupuncture. Clinical and ongoing pregnancy rates were significantly higher in the first acupuncture group compared with controls (39% vs. 26% and 36% vs. 22%, respectively). The clinical and ongoing pregnancy rates in the second acupuncture group (36% and 26%, respectively) were higher than in controls, but the difference did not reach statistical difference. The researchers concluded that acupuncture on the day of embryo transfer significantly improves the reproductive outcome of IVF/ICSI, compared with no acupuncture, but repeating acupuncture two days later provides no additional beneficial effect.

Physiology studies (human and animal)

Huang HDJ, Zhang MM. Effects of acupuncture on the luteal function of rats with dysfunctional embryo implantation. *Zhongguo zhen jiu* 2009;29:910-3.

A study in rats that looked at the influence of acupuncture on the luteal function of rats with dysfunctional embryo implantation. Levels of luteinizing hormone (LH) and progesterone (P) in serum, and the expression of vascular endothelial growth factor (VEGF) in the ovary, and the mRNA expression of VEGF and luteinizing hormone receptor (LHR) in the ovary were significantly higher in the acupuncture group than the non-acupuncture group ($P < 0.05$). Thus, acupuncture may enhance the luteal function of rats with dysfunctional embryo implantation and improve embryo implantation.

Jin CL et al. Increased Oocyte Production after Acupuncture Treatment during Superovulation Process in Mice. *Journal of Reproduction and Contraception* 2009;20:35-44.

A study to investigate whether acupuncture treatment during superovulation process improves ovarian response and increases egg production. Female mice were divided into a control group, anaesthesia group and acupuncture group, then injected intraperitoneally with pregnant mare's serum gonadotropin (PMSG), followed by human chorionic gonadotropin (hCG) injection 56 hours later. Acupuncture treatment statistically increased the number of ovulated eggs. All matured follicles ruptured and converted into corpus lutea in the acupuncture group, but not in the other groups. Expression of follicle stimulation hormone-receptor (FSH-R) in the ovary was decreased in the acupuncture group compared with those of the two others. The results suggest that acupuncture during superovulation process improves ovarian response, so increasing egg production, which may be associated with regulated FSH-R expression.

Magarelli PC et al. Changes in serum cortisol and prolactin associated with acupuncture during controlled ovarian hyperstimulation in women undergoing in vitro fertilization-embryo transfer treatment. *Fertil Steril* 2008; 92(6):1870-9.

A study that looked at whether changes in serum cortisol and prolactin are affected by acupuncture in IVF patients. In all, 67 infertile women undergoing IVF were grouped as controls (IVF with no acupuncture) and treated (IVF with acupuncture) according to acupuncture protocols derived from randomized controlled trials. Cortisol levels in the acupuncture group were significantly higher on IVF medication days 7, 8, 9, 11, 12, and 13 compared with controls. Prolactin levels in the acupuncture group were significantly higher on IVF medication days 5, 6, 7, and 8 compared with controls. The researchers concluded that

there appears to be a beneficial regulation of cortisol and prolactin with acupuncture during the medication phase of the IVF treatment.

Liu XY et al. Preliminary study on the mechanisms of acupuncture in promoting embryo implantation in rats [Article in Chinese] *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007;27:633-6.

A study to observe the influence of acupuncture on embryo implantation in a rat model of embryo implantation dysfunction. Rats were randomly allocated into a control group, a model group and an acupuncture group. The pregnancy rate and average number of blastocysts were significantly higher in the acupuncture group than those in the control group ($p < 0.01$). The serum levels of progesterone and prolactin, as well as the protein and mRNA expression levels of progesterone and prolactin receptors in the endometrial tissue of the implantation site, were significantly lower in the model group than in the other two groups ($p < 0.05$).

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