

Short Briefing Paper 1

Female Infertility

The evidence for the effectiveness of
ACUPUNCTURE



British
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The logo for the British Acupuncture Council consists of the text 'British Acupuncture Council' stacked vertically in a black, sans-serif font. Below the text is a stylized, teal-colored wave or swoosh graphic.

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This short briefing paper is as comprehensive as the main series of papers in assembling the relevant literature but it does not describe the procedures used nor provide the same degree of critical examination of the material

INFERTILITY AND ACUPUNCTURE: evidence for effectiveness

A. Anovulation/amenorrhoea/oligomenorrhoea

1. Controlled trials

Author <i>/conditions</i>	Type of control	Number	Outcomes (acupuncture group value given first)
Gerhard & Postneek 1992 /various hormonal disorders; all amenorrhoea or oligomenorrhoea	Retrospective matched pairs: vs best medical treatment	90	PR: similar in each group (ns). Fewer miscarriages, no side effects
Ji et al 1999 /ovulation induction for infertility/amen/oligomen	Unkown: vs clomiphene, HCG, stilboestral, progesterone	98	OR: 79 v 83% (ns) PR: 69 v 40% (*)
Zhao & Jin 2001 /ovulation induction for pubertal oligomenorrhoea.	RCT: vs oestrogen vs acup + oestrogen	60 (3 groups)	OR: 60 v 25 v 70%
Jin 2002 /ovulation induction for pubertal dysfunctional uterine bleeding	Unknown: vs clomiphene	22	OR: 87 v 70%
Yang et al 2005 /ovulation induction for hormonal infertility	RCT: vs clomiphene	240	PR: 65 v 45% (*)

OR = ovulation rate PR = pregnancy rate

(*) indicates statistical significance (where given)

(ns) not significant

2. Uncontrolled trials

Author /condition	No.	Acupuncture treatment	OR %	PR %	Outcome – more details
Gerhard & Postneek 1988 / <i>oligomenorrhoea & luteal body insufficiency</i>	27	Auricular points, semi-formulaic		Similar to medication	Fewer side effects and abortions; best results if +ve gestagen test/normal hormones/hyper-androgen
Yu et al 1989 / <i>anovulation, mostly PCOS</i>	11	TCM formula, electroacup, 3 days in 1 cycle	46	33	Increases in LH and FSH in those ovulating
Mo et al 1993 / <i>diverse causes of anovulation, most with amenorrhoea</i>	34	TCM formula, 3 per week for 3 months	18% no improvement at all, 47% some, 35% cycling or pregnant [after 3 cycles]		Hormone levels and follicular development better
Li 1995 / <i>diverse infertility</i>	100	TCM formula, 10 per cycle up to 5 cycles		79 [1-2 cycles]	97% pregnant after 5 cycles
Cai 1997 / <i>ovulation induction for ovarian hyper-stimulation syndrome</i>	10	TCM semi-formula, 1-3 per day for 1 cycle	90		Ovarian hyper-stimulation better
Stener-Victorin 2000 / <i>PCOS & amen/oligomen</i>	24	TCM/medical formula, 14 in 3 months	37.5 [after 3 cycles]		Can predict best responders from hormones & body mass index
Luo & Sa 2001 / <i>anovulatory infertility</i>	11	TCM formula, 1-3 per day for 10-12 days	82	36	
Zhang et al 2004 / <i>ovulation induction, most amen/oligomen</i>	35	TCM semi-formula, 6 per course for up to 4 courses	89 [after 4 courses]		
Peng & Zhao 2004 / <i>PCOS, bleeding, amen, anovulation</i>	106	TCM semi-formula, one cycle		39	
Xu 2004 / <i>ovulation induction for PCOS</i>	15	Electro-acup, 6 sessions	41 (0% pre-treatment)		Increases in progesterone and endometrial thickness

Summary of anovulation/amenorrhoea/oligomenorrhoea papers

These studies are largely of stand-alone acupuncture used for ovulation induction. Most patients were either not cycling at all or erratically so. Polycystic ovaries or dysfunctional uterine bleeding featured in a substantial number of the trials but others covered a range of different causes of infertility.

The five controlled trials included only two randomised ones (RCTs). Four of the controlled trials were Chinese and for three of them only very brief details are available. All the controlled studies compared acupuncture with standard Western drug treatment. Only one was large, a recent Chinese RCT showing a 20% advantage in pregnancy rate for acupuncture over clomiphene. The other Chinese studies also found similar significant advantages in either pregnancy or ovulation rates. By contrast the one Western trial showed no overall difference in pregnancy rates (though those with irregular menstruation did better with acupuncture) but there was a distinct advantage in reduced miscarriages and no side-effects.

The ten uncontrolled trials were again largely Chinese (7/10) and mostly rather small (only two had more than 100 subjects ; the rest fewer than 40). None used entirely individualised treatment protocols even though they were mostly TCM-based. The outcomes covered a wide range of values for ovulation rate (35-90%) and pregnancy rate (35-80%). Also noted were fewer complications and normalised hormonal profiles.

B. Acupuncture adjunctive to Assisted Reproductive Therapy

Author /type of ART	Study type /nature of control	No.	Pregnancy Rate %	Ongoing PR or live births
Stener-Victorin et al 1996 /IVF	Uncontrolled	10	<i>Normal uterine blood flow restored in 75% of women</i>	
Balk et al 2003 /IVF	Uncontrolled	10	PR not increased by acupuncture <i>[No change in uterine blood flow]</i>	
Emmons & Patton 2000 /ICSI	N=1 /patients are own controls	6	<i>Follicles recruited for IVF: 8 v 4; 3 pregnancies, only 1 maintained</i>	
Paulus et al 2002 /ICSI, IVF	RCT; vs no acupuncture	80+80	42.5 v 26.3 (*)	<i>[No differences in oestradiol, endometrial thickness, uterine blood flow]</i>
Zhang et al 2003 /ICSI, IVF	RCT; vs sham acup vs no acupuncture	70+70+70	44 v 27 v 24. Acu v sham or v no acu (*)	<i>[Less uterine contraction after embryo transfer with acupuncture]</i>
Magarelli et al 2004 /good prognosis IVF patients	Retrospective case control; vs no acupuncture	53+61	51 v 36 (*)	23 % higher (*) <i>[Miscarriages and tubal pregnancies much fewer with acupuncture (*)]</i>
Magarelli & Cridennda 2004 / IVF poor responders	Retrospective case control; vs no acupuncture	53+94	53 v 38 (*) [after statistical adjustment]	
Quintero et al 2004 /IVF	RCT crossover (in 2 nd cycle if 1 st not successful); vs Sham acup	17	70 v 30 (*)	40 v 25 (ns) <i>[Less gonadotropin needed to stimulate follicle growth]</i>
Dieterle et al 2006 /ICSI, IVF	RCT; vs sham acup	119+109	34 v 16 (*)	28 v 14 (*)
Smith et al 2006 /IVF	RCT; vs sham acup	228 (2 groups)	31 v 23 (ns)	28 v 18 (ns)
Westergaard et al 2006 / ICSI, IVF	RCT; 2 acup arms - either 2 or 3 treatments vs no acup	95+91+87	39 v 36 v 26 Acup 1 (*) Acup 2 (ns)	36 v 26 v 22 Acup 1 (*) Acup 2 (ns)
Johnson 2006 /IVF	Case control; vs no acupuncture	22 + ?	58 v 45 (ns)	

Acupuncture group results given first

(*) statistically significant

(ns) not significant

Summary of papers on assisted reproductive therapy

Quite unlike the stand-alone acupuncture studies these were a) nearly all controlled (10/12), and b) nearly all Western (11/12).

Of the ten controlled trials five were prospective RCTs, one a RCT crossover, one a n=1 and three case controlled. The case controls all compared acupuncture to no acupuncture. The RCTs compared acupuncture either to sham, to no acupuncture or to both. The numbers of participants were consistently higher than in the stand-alone studies: 150-270 for the RCTs; 40-150 in the case controls.

Apart from the n=1 study, which was too small to establish such statistics, there was considerable agreement in the results: the acupuncture groups show an increase in pregnancy rates of about 15% over the control. For the sham controls the difference is only about one percentage point lower than the comparison with no acupuncture. Not all of the results were statistically significant, even though apparently clinically significant.

The range of values for clinical pregnancy rate was 31-70% for acupuncture, 16-45% for the control. Some studies followed up beyond 12 weeks to measure what they call ongoing pregnancy: 26-40% with acupuncture, 14-25% in the control

Two uncontrolled studies were both very small and both focused on uterine artery flow: one found an effect and one did not.

C. Other infertility research

PHYSIOLOGY

- Various studies have found that acupuncture can affect hormone levels: oestrogens, progesterone, LH, FSH, GnRH, cortisol, prolactin. Particular attention has been paid to its regulatory effect via β -endorphin on the hypothalamus-pituitary-ovarian-adrenal axis.
- Various possible routes have been suggested as to how acupuncture may help PCOS patients: corticotrophin releasing hormone, nerve growth factor, endothelin, ovarian blood flow, β -endorphin and the HPOA axis, ovarian β 2-adrenoceptors, neurotrophin receptor, sympathetic nervous system

HEALTH STATUS OF IVF PATIENTS

A survey using the SF36 questionnaire and also diagnosis according to TCM pattern showed that women undergoing IVF had poorer health than average in several respects. Kidney Yang deficiency was the commonest TCM pattern. Qi or Blood Stasis were associated with poorer mental health

CAM USE BY INFERTILITY PATIENTS

A survey of 400 couples showed a high use of CAM, especially amongst females and in private clinics. This was despite some scepticism about its efficacy.

D. Reviews

Chang et al (02) [Cornell University, USA]

Describes in physiological terms how acupuncture may affect fertility

Reviews MEDLINE trials up to 2002:

- "there is sufficient evidence of acupuncture's value to expand its use into conventional medicine and treatment of female infertility"
- further studies, especially RCTs, needed to definitely establish its clinical value

Stener-Victorin et al (02) [Goteborg University, Sweden]

- Written to answer a sceptical paper in the same journal (Human Reproduction)
- Talks generally about the physiological mechanisms behind acupuncture's effects
- For reproductive medicine it takes three areas as examples
 - Uterine artery flow – interesting, but needs RCT follow-up
 - Anaesthetic for oocyte aspiration – works very well, they use it routinely
 - Hormonal disturbances, e.g. PCOS, anovulation: need better studies, RCTs especially, to establish the effect, but does appear that acupuncture may have a beneficial effect – there is both clinical and experimental evidence. Hence acupuncture may be a suitable alternative or complement to drugs for inducing ovulation, and with no negative side effects

White (03) [Peninsular Med School, UK]

- Reviews controlled trials in MEDLINE, EMBASE, COCHRANE
- Finds 3 suitable trials of acupuncture for infertility (Stener-Victorin et al, 1999; Gerhard & Postneek; Paulus): they have positive results but methodological weaknesses
- The evidence is positive but not conclusive – however, the known physiological mechanisms of acupuncture, via β -endorphin and hence gonadal hormones, would support its effectiveness. He concludes that it is promising for infertility

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