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**Acupuncture prior to and at embryo transfer in an assisted conception unit--
a case series.**

[Johnson D.](#)

Chobham Acupuncture Clinic, Chobham, Surrey. info@acupuncture-chobham.co.uk

Over a period of three years, acupuncture was offered to patients entering assisted reproduction therapy. Acupuncture sessions were given at varying, but usually weekly, intervals during the in vitro fertilisation (IVF) cycle, and immediately before and after embryo transfer. Twenty two patients (average age 36.2 years) were treated over a total of 26 IVF cycles and 15 pregnancies were achieved, as determined by presence of foetal heartbeat on ultrasound at four weeks post embryo transfer. This was a success rate of 57.7% compared with 45.3% for patients in the IVF unit not treated with acupuncture ($P > 0.05$). Relaxing effects were noted following acupuncture and it is speculated that this may have contributed to the increase in pregnancy rate for the acupuncture group.

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Acupuncture prior to and at embryo transfer in an assisted conception unit – a case series

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Abstract

Over a period of three years, acupuncture was offered to patients entering assisted reproduction therapy. Acupuncture sessions were given at varying, but usually weekly, intervals during the in vitro fertilisation (IVF) cycle, and immediately before and after embryo transfer. Twenty two patients (average age 36.2 years) were treated over a total of 26 IVF cycles and 15 pregnancies were achieved, as determined by presence of foetal heartbeat on ultrasound at four weeks post embryo transfer. This was a success rate of 57.7% compared with 45.3% for patients in the IVF unit not treated with acupuncture ($P>0.05$). Relaxing effects were noted following acupuncture and it is speculated that this may have contributed to the increase in pregnancy rate for the acupuncture group.

Keywords

Acupuncture, assisted reproduction, in vitro fertilisation (IVF).

David Johnson
 medical acupuncturist
 Chobham Acupuncture
 Clinic
 Chobham, Surrey
 info@acupuncture-
 chobham.co.uk

Introduction

In 2002 Paulus and colleagues in Germany published the result of a randomised controlled trial on pregnancy rates after embryo transfer with and without acupuncture during assisted reproduction therapy.¹ They reported an improved success rate in the acupuncture group ($P=0.03$). Also, Stener-Victorin and colleagues in Sweden reported a higher pregnancy rate ($P<0.05$) when using electroacupuncture for analgesia during oocyte aspiration prior to in vitro fertilisation (IVF).² However, this finding was not confirmed in their subsequent investigations.^{3,4}

My intention on starting this series in 2002 was to use acupuncture during IVF treatment at the Woking Nuffield Hospital (Surrey, England) to try and improve the IVF results in the same way as Paulus and colleagues, keeping closely to their acupuncture points and needling technique at the time of embryo transfer, and aiming to audit any change in the pregnancy rate.

The standard IVF cycle used at Woking starts with down regulation using a gonadotrophin releasing hormone (GnRH) analogue (buserelin) which makes the ovaries inactive and thins the endometrium. The

ovaries are then stimulated for 10–12 days with daily follicle-stimulating hormone/human menopausal gonadotrophin (FSH/hMG) injections. This produces multiple follicles. The development of the follicles is monitored with ultrasound scans on alternate days, measuring their number and size as well as the thickness of the endometrium. When the follicles appear sufficiently mature, a single injection of human chorionic gonadotrophin (HCG) causes a luteinising hormone (LH) surge which initiates a growth spurt in the development of eggs (not all follicles develop into eggs). Egg collection takes place 36 hours after that injection. Stener-Victorin and colleagues gave the electroacupuncture at this stage, during and for 30 minutes prior to oocyte aspiration. The oocytes are then externally fertilised and two to three days later the embryos are transferred into the endometrium. Paulus and colleagues gave manual acupuncture for 25 minutes before, and again for 25 minutes after embryo transfer.

I was concerned that waiting to undergo acupuncture as a new experience on the day of embryo transfer might increase the stress of the IVF programme for some patients.² An introductory

acupuncture session using sedating points should reduce this. Stener-Victorin and colleagues had previously demonstrated that uterine artery blood flow improved in infertile women following electroacupuncture given over a period of four weeks (eight treatments).⁵ They used the points GV20 and bilateral TE5, LI4, ST29 and ST36. The improvement lasted for at least a further two weeks and is expected to have the effect of making the endometrium more receptive to a transferred embryo. I reasoned that the greatest possibilities for benefit would be offered by having an introductory acupuncture session for those who had never had acupuncture before, followed for all patients by acupuncture treatments during the IVF cycle, and culminating in the acupuncture protocol at embryo transfer used by Paulus and colleagues. This would allow familiarisation to needling, promote relaxation and improve pelvic blood flow. This paper is an evaluative report of the initial results from an ongoing clinical series taking this approach to acupuncture during IVF that I have been carrying out in conjunction with the Woking Nuffield Assisted Conception Unit.

Methods

All patients were self-referred for acupuncture. Initially the service was offered via leaflets left in the waiting room of the IVF unit, and subsequently news of it was spread via word of mouth or internet discussion with other patients. The services of the IVF and acupuncture clinics have to be paid for by patients, as no National Health Service (NHS) funding is available. Any patient entering an IVF

cycle at the Assisted Conception Unit of the Woking Nuffield Hospital was eligible for acupuncture during that cycle, and nobody was excluded for any reason from starting a course of acupuncture. Age, cause of infertility, past IVF history or previous acupuncture experience were not considered cause for exclusion, nor did failure to conceive following the use of acupuncture in one IVF cycle exclude a patient from further attempts as part of this series. All patients given acupuncture during an IVF cycle were included in the series reported here provided they completed the required sessions.

The acupuncture was not given at the conception unit, but at a private clinic in Chobham or the outpatient department of the Nuffield Hospital. For patients who were new to acupuncture, the introductory session, preferably early in the IVF cycle, involved taking the history and explaining acupuncture and its relevance to IVF, followed by 10 minutes of needling at GV20 and bilateral LI4 and LR3. All patients were then given treatments during the IVF cycle, building up to the full Paulus protocol at the time of embryo transfer. Initially consent was verbal, but written consent was obtained on the day of embryo transfer for the final two sessions of acupuncture which were more directly associated with the hospital surgical procedure.

The number and frequency of sessions depended on patient preference and the time available prior to embryo transfer. However, I aimed to give the first full session at the beginning of the IVF cycle with the next session a week later, then another treatment one or occasionally two days prior to egg collection, and the final two sessions on the day of embryo transfer.

Acupuncture treatment schedule to accompany in vitro fertilisation

Introductory session: GV20 and bilateral LI4 and LR3, for 10 minutes.

First full session: GV20 and bilateral LR3, SP6, ST36, PC6 and LI4, for 20 minutes.

Second full session: The same points as the first, but with the addition of ear points (Chinese nomenclature) left *Shenmen* and *Neifenmi*, right *Zhigong* and *Naodian*, for 20 minutes.

Third full session: The same body and ear points as

on the second, plus ST29, again for 20 minutes. The points used at this third session are repeated at any additional booster sessions.

On the day of embryo transfer, two 25 minute sessions, one immediately prior to and one after embryo transfer, using the following points:

Prior to transfer: GV20 and bilateral LR3, SP8, PC6 and ST29 with ear points left *Shenmen* and *Neifenmi*, and right *Zhigong* and *Naodian*.

Post transfer: Bilateral SP6, SP10, ST36 and LI4 with the ear points reversed: left *Zhigong* and *Naodian*, and right *Shenmen* and *Neifenmi*.

To be included in this series, a patient new to acupuncture must have had a short (10min) introductory acupuncture session, and all patients must have had at least one full (20min) treatment session during the IVF cycle, plus the two Paulus protocol sessions on the day of embryo transfer. The escalation of treatments is shown in the Box.

The needles used were *Qi* Japanese style (Harmony Medical, London UK) 0.26x30mm for all the body points, and CC type (AcuMedic, London UK) 0.20x7mm for ear points, all with guide tubes. Insertion depths are 10-20mm on the body and 1-2mm on the ears. The body needles were rotated by hand, frequently but irregularly (approximately three or four groups of rotation per needle every five minutes, with short breaks) but the ear points were not stimulated. Needling sensation (*de qi*) was obtained at some points, but not all. On the day of embryo transfer I used the Paulus protocol exactly, giving a single stimulation manually at 10 minutes to the body needles but not the ear needles. All egg collections at the Woking Nuffield are done under general anaesthesia, so no acupuncture was used at that time.

This is an early report of results from the first participants in an ongoing series, so it is not possible to give the outcome in terms of live births because not all pregnancies were completed at the time of writing. All patients completing an IVF cycle at the Woking unit had a pregnancy test two weeks after embryo transfer and those with a positive test had an ultrasound scan at four weeks to look for foetal heart beat as evidence of pregnancy. Foetal heart beat was used as the formal outcome of the IVF treatment for this report.

Although this is a report of a case series without a randomised control group, the results were compared with the overall outcomes from the Woking Assisted Conception Unit for the first full year of the series (2003). Statistics from this and other UK units are published by the Human Fertilisation and Embryology Authority (HFEA).⁶ Analysis was carried out using Fisher's exact test on GraphPad Prism software.

Results

This case series covers the period from the start of the service in 2002 to mid 2005. After I had obtained agreement in 2002 from the gynaecologists at the

Woking Assisted Conception Unit to use acupuncture on their patients, all IVF patients at the unit who requested acupuncture were entered in the series. Two patients (in three IVF cycles), both in 2002, had to be excluded because they did not complete the required sessions; neither of them achieved pregnancy. The first patient was being treated for backache at the acupuncture clinic and received the introductory session followed by treatment on the day of embryo transfer, but with no build-up sessions. The second patient had no acupuncture session before the day of embryo transfer. She had also been seeing a Chinese acupuncturist who did not approve of the use of 'expulsion' points, so LI4, SP6 and ear *Zhigong* were not used. She returned the following year during a second IVF cycle, but again did not have an acupuncture session before the day of embryo transfer. There were no other exclusions. The details of all other patients are recorded in Table 1.

All patients not reported in Table 1 as having an introductory session had had previous acupuncture. Some patients had additional needling for other problems. A common side effect of the IVF drug therapy is headache, so several had acupuncture treatment for this. Patient number 3 had two extra sessions using LI4, LR3 and GV20, with GB30 for backache, and GB20 and EX2 (*Taiyang*) for headache. Patient number 7 had one session that included GB20, 21 and EX2 (*Taiyang*) to treat headaches. Patient number 13 had two extra sessions (LI4, LR3, GV20, PC6 and *Shenmen* in both ears) for relaxation and one for treatment of migraines (GB20 and GB21 added). Patient 14 had an extra two sessions (LI4, LR3, GB21, SP6 and ST29) for treatment of migraines and endometriosis prior to starting her IVF cycle, and patient number 25 had LI20 and EX1 (*Yintang*) added for hay fever at her first session.

In the 22 included patients, 26 embryo transfers were carried out, four patients receiving two cycles of IVF with acupuncture (Table 1). The summary of the findings is given in Table 2: the average age was 36.2 years, and the mean number of previous IVF cycles was 1.6. All women except one had two embryos implanted: patient 9, the oldest in the group at 43, had three implanted. Three patients (one for two IVF cycles) were treated with embryos frozen from a previous cycle. Out of the 26 IVF cycles treated

Table 1 Details of patients treated with acupuncture in this series

	Age (years)	Previous IVF cycles / successes	Cause of infertility	Acupuncture sessions prior to embryo transfer day	Positive pregnancy test at 2 weeks	Ultrasound scan (4 weeks)
1	33.3	2 / 0	Tubal blockage	Introduction + 1	Yes	Twin
2	36.8	0	Unknown	2	Yes	Single
3	36.8	1 / 0	Ovulation failure	Introduction + 1	Yes	Single
4	38.7	1 / 0	Tubal blockage	Introduction + 4	Yes	Single
5	36.4	2 / 0	Unknown	Introduction + 3	Yes	Single
6	36.3	3 / 0	Unknown	Introduction + 2	No	
7*	32.3	2 / 0	Male problem	Introduction + 4	Yes	Single
8*	36.6	2 / 0	Unknown	Introduction + 3	Yes	No pregnancy
9	43.2	2 / 0	Male problem	2	No	
10	33.8	0	Ovulation failure	3	Yes	Single
11	35.8	0	Unknown	Introduction + 3	Yes	Single
12	36.0	0	Tubal blockage	3	No	
13*	36.9	3 / 0	Unknown	3	No	
14	34.5	0	Endometriosis	Introduction + 3	Yes	Twin
15	38.8	3 / 0	Unknown	Introduction + 3	No	
16	40.1	0	Endometriosis	Introduction + 5	Yes	Single
17	33.0	2 / 0	Unknown	Introduction + 4	No	
18	31.5	0	Ovulation failure	3	Yes	Twin
19	42.3	1 / 0	Tubal blockage	3	No	
20	37.0	1 / 0	Male problem	Introduction + 3	Yes	Single
21*	35.3	6 / 0	Tubal blockage	Introduction + 4	No	
22	34.2	0	Polycystic ovaries	Introduction + 4	No	
23	33.1	2 / 1	Polycystic ovaries	2	Yes	Single
24	35.7	7 / 0	Tubal blockage	4	No	
25	37.8	0	Unknown	3	Yes	Twin
26	34.4	1 / 0	Polycystic ovaries	3	Yes	Single

* indicated patients in whom two frozen embryos were used

8 and 13 are the same patient

21 and 24 are the same patient

22 and 26 are the same patient

Table 2 Summary of results of case series of acupuncture with IVF, compared with figures for non-acupuncture patients in Woking Assisted Conception Unit (2003 data)

Details	Acupuncture group (2002–mid 2005)	Non-acupuncture group (2003 only)
Number of patients	26	265
Mean age (years)	36.2	36.3
Age range (years)	31-43	25-45
Mean number of previous IVF cycles	1.6	Not recorded
Mean number of transferred embryos	2.0	2.0
Number of pregnancies	15	120
Pregnancy rate	57.7%	45.3%

with acupuncture 15 patients achieved pregnancies, a success rate of 57.7%. Four pregnancies were twin (15.4%). To date, 14 babies have been born (three sets of twins and eight singletons) and the one remaining pregnancy is progressing satisfactorily. One pregnancy (patient 16) miscarried at eight weeks, patient 20 developed severe ovarian hyperstimulation with ascites and miscarried at six weeks, and patient 26 had a missed abortion at 10 weeks.

The published results of the Woking Assisted Conception Unit for 2003 show that, excluding those patients in the acupuncture study, 265 embryo transfers were carried out on women aged 25-45 with an average age of 36.3 years (see Table 2). The mean number of transferred embryos was 2.0. Pregnancies were achieved in 120 (45.3%) women and 115 resulted in live births. The incidence of twins was 17.5%.

There is thus a higher success rate in the acupuncture group compared with women in the unit not having acupuncture, but the improvement does not reach statistical significance ($P>0.05$).

Discussion

There is substantial difference in the IVF success rates of different units.⁶ A league table published in 2005 for assisted conception units in the UK showed a variation from 10% to 58% in live birth rate after embryo transfer. The national average for all ages was 26.4% in 2003, whereas the Woking Nuffield achieved 42.8% that year, coming second in the 2005 league table. The figures are very age-dependent: the UK national figures for women under age 35 years are 27.6%; 35-37, 22.3%; 38-39, 18.3%; and 40-42, 10%.

Paulus and colleagues randomly assigned 160 women undergoing embryo transfer into two equal groups: 80 with and 80 without acupuncture.¹ They

used the presence of a foetal sac on ultrasound scan at six weeks after embryo transfer as their outcome, rather than live birth as in the UK tables. The Woking unit similarly records ultrasound evidence, but of foetal heart beat at four weeks. This was used as the outcome for this study, though pregnancy outcome is also reported when available. As shown in Table 3, Paulus and colleagues reported pregnancy rates of 42.5% in the acupuncture group and 26.3% in controls, a statistically significant difference ($P=0.03$).

The pregnancy rate of the control group in Paulus's study was much lower than in the Woking unit (even in Paulus et al's acupuncture group the pregnancy rate remained lower than that of the Woking control group) offering comparatively greater scope for improvement. Paulus and colleagues were also treating a younger age-group (average 32 years) than in this series (average 36 years). Thus an interpretation of the results in this case series might be that there is a genuine effect of acupuncture on pregnancy rate, but that it failed to reach statistical significance because the sample size was too small, bearing in mind the high baseline pregnancy rate.

There appear to be at least three possible mechanisms by which acupuncture could influence pregnancy rate. First, Chinese tradition suggests that there might be a direct response from stimulation of points such as SP6 (*Sanyinjiao*) and certain lower abdominal points, which could influence ovarian and uterine function.⁷ This is now thought to work via modulation of hypothalamic-pituitary-ovarian axis function producing normalisation in secretion of hormones, notably GnRH and LH.⁸ However, this is probably not a mechanism of significance during IVF treatment in view of the drug-induced suppression and stimulation of the ovaries during the IVF process.

Secondly, there is evidence that acupuncture

Table 3 Summary of results of a previously published study for comparison

Details from Paulus et al (2002) ¹	Acupuncture group	Control group
Number of patients	80	80
Mean age (years)	32.1	32.8
Age range (combined)	----- 21-43 years -----	
Mean number of previous IVF cycles	2.0	2.1
Mean number of embryos transferred	2.1	2.2
Number of pregnancies	34	21
Pregnancy rate	42.5%	26.3%

increases blood flow to the ovarian and uterine arteries, thus thickening the endometrium and making it more receptive to the transferred embryo.⁵ This appears to be a response to a reduction in sympathetic nervous tone induced by the acupuncture.⁹ My series of needling sessions during the IVF cycle is designed to encourage this.

Thirdly, the calming and anti-anxiety effects of acupuncture are likely to be of real importance. Stress and anxiety are seen as significant factors in failure to achieve pregnancy. Acupuncture is well known to have a relaxing effect,¹⁰ and during this study several patients who had experienced previous IVF cycles commented on how much more relaxed they were in the acupuncture-supported cycle. They also claimed to have experienced fewer side effects from the drugs. The relaxation was confirmed by the gynaecologist performing the embryo transfer as applying generally to patients in the acupuncture group, although this was not formally recorded.

It has taken almost three years to collect this small group of patients, so a multicentre trial might offer more rapid results. Unfortunately the wide variation in base success rates between centres makes this difficult to standardise. It would be useful also to be able to standardise the number and timing of sessions in the time before embryo transfer and establish the optimum formula. To date, this has not been possible because the patients have been variable in their attendance for acupuncture and in the time available before embryo transfer (from a few days to about six weeks) and some have wanted additional symptoms to be treated (eg backache, headache, hay fever, etc).

Conclusion

The evidence that acupuncture provides real benefit during IVF treatment is far from clear but, despite the lack of statistical significance, the results of this study offer encouragement to persevere in further trials. In particular, the anti-anxiety and relaxing effects of acupuncture in relation to achieving a

successful pregnancy are likely to be of importance, and need more careful evaluation.

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