

Combining TCM and IVF to Improve Clinical Outcomes

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Use of Acupuncture Before and After Embryo Transfer

Dalton-Brewer N et al, Hum Fert 2010 Vol 12 No 4 212 - 255
Human Fertility (abstracts from UK Fertility Societies Conference 2009)

This report describes outcomes for all patients who attended The London Bridge Fertility, Gynaecology and Genetics Centre in London over a 2 year period, and who had acupuncture. In the acupuncture group positive pregnancy rates/ET were 44.6% comparing favourably with the non-acupuncture historic control group. When they analysed outcomes in different age groups they discovered that acupuncture intervention was particularly effective in woman in the 35 - 39 and the over 40 group.



Abstract

Use of Acupuncture Before and After Embryo Transfer

Nick Dalton-Brewer, David Gillott, Nataly Atalla, Mohamed Menabawey, Pauline Wright, & Alan Thornhill
The London Bridge Fertility, Gynaecology and Genetics Centre, London, UK

All IVF cases in which acupuncture was administered before and after embryo transfer at a large private infertility centre were reviewed for a 2 year period. All patients were treated by the same practitioner (NDB) using Traditional Chinese Acupuncture (TCA). Patients received acupuncture to the protocol developed by Paulus, W.E., Zhang, M., Strehler, E., El-Danasouri, I., & Sterzik, K. (2002). Influence of acupuncture on the pregnancy rate in patients who undergo assisted reproduction therapy. *Fertility & Sterility*, 77, 721–724: Liver 3, Spleen 8, Stomach 29, Pericardium 6, GV 20 were manually stimulated five times over a 40-min period, at Bridge, approximately 10–20 minutes prior to embryo transfer. Embryo transfer was carried out under ultrasound guidance as per routine at Bridge. Ten minutes following embryo transfer acupoints Spleen 6, Stomach 36, Spleen 10, Large Intestine 4 were manually stimulated five times over a 40-min period before discharging the patient. Ear points 34, 55 and 58 were used in both treatments and not stimulated.

A total of 71 patients underwent 74 cycles involving acupuncture before and after embryo transfer.

Overall, positive pregnancy rates/ET were 44.6% comparing favourably with the non-acupuncture historic control group.

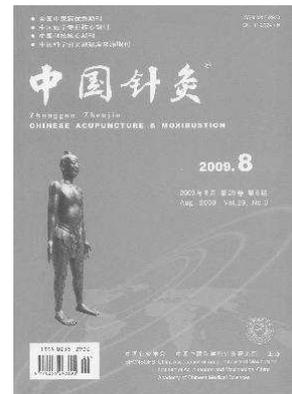
When analysed by maternal age at time of treatment, biochemical pregnancy results for acupuncture treated women were as follows: <35 years–52%; 35–39 years – 45%; 40–45 years – 35%.

Results for women aged 35–39 years and those over 40 years were markedly better than controls suggesting that acupuncture intervention of this type may be more effective in older women. No side effects or complications were experienced by women receiving acupuncture. Acupuncture is a safe, adjunct therapy in IVF and in other randomised clinical trials has been shown to significantly improve outcomes when used at the IVF centre before and after embryo transfer. Our preliminary data are encouraging and suggest that a trial involving older women may be effective.

Effect of Acupuncture on the Pregnancy Rate in Embryo Transfer and Mechanisms: A randomized and controlled study

Zhang M et al, Chin Acup and Moxabustion 2003, Jan 23 (1): 3 - 5
Chinese Acupuncture and Moxabustion

210 IVF patients were randomly placed in groups that received real acupuncture or placebo or no treatment on the day of embryo transfer. The pregnancy rate was significantly higher in the group who received real acupuncture. Additionally this trial showed that the women who received real acupuncture had fewer uterine contractions after the transfer.



Abstract

Objective To observe the effect of acupuncture on the pregnancy rate in assisted reproduction therapy such as in-vitro-fertilisation (IVF) and intracytoplasmic spermatozoen injection (ICSI), and mechanisms.

Methods: 210 cases undergoing IVF or ICSI were divided randomly into three groups: acupuncture treatment group, placebo group and control group. The acupuncture treatment group and the placebo group were treated respectively with body acupuncture and placebo acupuncture before and after embryo transfer, and in the control group embryos were transferred without any supportive therapy. Contraction frequency of the uterine junctional zone and the pregnancy rate were observed.

Results: The contraction frequency before embryo transfer was not significantly different among the three groups, but after embryo transfer in the acupuncture treatment group was lower than that in the placebo group and the control group, respectively. The pregnancy rate was 44.3% (31/70) in the acupuncture treatment group, and 27.1% (19/70) in the placebo group and 24.3% (17/70) in the control group. The pregnancy rate in the acupuncture treatment group was significantly higher than that in the placebo acupuncture group and the control group (P0.05).

Conclusion: Acupuncture is a powerful tool for improving pregnancy rate after assisted reproduction therapy.

A Randomized Double Blind Comparison of Real and Placebo Acupuncture in IVF Treatment.

So et al, Hum Reprod. 2009 Feb;24(2):341-8.

Human Reproduction



Researchers in Hong Kong found no significant difference between the effects of placebo and regular acupuncture in clinical or ongoing pregnancy rates however on initial hCG testing the placebo group had more positive tests.

Both placebo and regular acupuncture significantly reduced vascularity of the uterus, reduced stress hormones and anxiety levels. These findings lead the researchers to suggest that placebo acupuncture is in fact not inert. Placebo acupuncture needles prick the skin at the acupuncture point but do not penetrate the skin. Many Japanese acupuncturists (who routinely use minimal stimulation of acupuncture points) would argue strongly that this is not an inert placebo procedure but a therapeutic one.

Unfortunately there was no control group in this trial which received no acupuncture.

Abstract

Background: Acupuncture has been used during IVF treatment as it may improve outcome, however, there are concerns about the true efficacy of this approach. This randomized double blind study aimed to compare real acupuncture with placebo acupuncture in patients undergoing IVF treatment.

Methods: On the day of embryo transfer (ET), 370 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received 25 min of real or placebo acupuncture before and after ET. The endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were evaluated before and after real and placebo acupuncture.

Results: The overall pregnancy rate was significantly higher in the placebo acupuncture group than that in the real acupuncture group (55.1 versus 43.8%, respectively, $P = 0.038$; Common odds ratio 1.578 95% confidence interval 1.047–2.378). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were observed following both real and placebo acupuncture, although there were no significant differences in the changes in all these indices between the two groups.

Conclusions: Placebo acupuncture was associated with a significantly higher overall pregnancy rate when compared with real acupuncture. Placebo acupuncture may not be inert.

The Relationship Between Perceived Stress, Acupuncture, and Pregnancy Rates Among IVF patients: Pilot Study

Balk J et al, Compl Therapies in Clinical Practice 2010,16,154–157
Complementary Therapies in Clinical Practice

These researchers at a university IVF clinic in Pittsburgh were interested to investigate the relationship between acupuncture, stress and pregnancy rates. The patients who received acupuncture on the day of embryo of transfer had a pregnancy rate of 55.6% compared with the control group pregnancy rate of 35.5%.



Abstract

The aim of this paper was to determine the effect of acupuncture on perceived stress levels in women on the day of embryo transfer (ET), and to determine if perceived stress levels at embryo transfer correlated with pregnancy rates. The study was an observational, prospective, cohort study based at the University IVF center.

Patient(s): 57 infertile patients undergoing IVF or IVF/ICSI.

Interventions(s): Patients were undergoing Embryo Transfer with or without acupuncture as part of their standard clinical care.

Main outcome measure(s): Perceive Stress Scale scores, pregnancy rates.

Result(s): women who received this acupuncture regimen achieved pregnancy 64.7%, whereas those without acupuncture achieved pregnancy 42.5%. When stratified by donor recipient status, only non-donor recipients potentially had an improvement with acupuncture (35.5% without acupuncture vs. 55.6% with acupuncture). Those who received this acupuncture regimen had lower stress scores both pre-ET and post-ET compared to those who did not. Those with decreased perceived stress scores compared to baseline had higher pregnancy rates than those who did not demonstrate this decrease, regardless of acupuncture status.

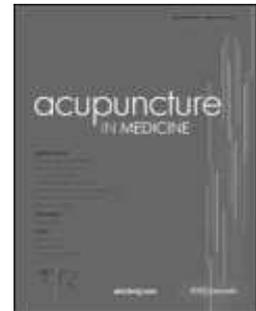
Conclusions(s): The acupuncture regimen was associated with less stress both before and after embryo transfer, and it possibly improved pregnancy rates. Lower perceived stress at the time of embryo transfer may play a role in an improved pregnancy rate.

Effect of Acupuncture on Assisted Reproduction Treatment Outcomes

Madaschi C et al, Acupunct Med 2010;28:180-184

Acupuncture in Medicine (BMJ)

This trial conducted in Brazil looked at the effect of acupuncture administered before and after embryo transfer on a large group of women undergoing IVF (208 women in both the acupuncture and the control group). They found an increase in implantation rates, and a significant increase in pregnancy rates where there was no known issue with egg or sperm quality in the acupuncture group. However analysis of all cases together showed no impact of acupuncture on pregnancy rates.



Abstract

Background: Acupuncture has recently been used as a complementary technique in the management of infertility. It has physiological and psychological effects and may be considered an alternative for stress reduction in women undergoing infertility treatments.

Objective: To examine the hypothesis that acupuncture treatment may increase the pregnancy rate in patients undergoing intracytoplasmic sperm injection cycles.

Methods: Patients enrolled in the study were stratified according to age and randomised to either a control group (n=208) or acupuncture group, (n=208). The pregnancy, implantation and abortion rates of the two groups were compared.

Results: No influence of acupuncture treatment on clinical outcomes was seen; however, when cycles in which the causes of infertility were exclusively tubal-uterine or idiopathic were evaluated separately, a positive influence of acupuncture on pregnancy (OR=5.15, 95% CI 1.03 to 34.5; p=0.048) was noted. Moreover, trends toward an increase in implantation were seen when acupuncture was performed (regression coefficient: 0.645; p=0.092).

Conclusion: The results suggest that acupuncture treatment had no influence when performed immediately before and immediately after embryo transfer, on clinical outcomes overall. In a subgroup analysis, when the embryo was not affected by an ovarian or seminal influence, a benefit was noted.

Acupuncture on the Day of Embryo Transfer: A Randomized Controlled Trial of 635 Patients

Andersen D et al, Reproductive BioMedicine Online, 2010, 21, 3, 366-372
Reproductive BioMedicine Online

This trial conducted in Denmark found no difference in pregnancy rates in IVF patients given acupuncture on the day of embryo transfer with a real acupuncture needle or a placebo one which just pricked the point rather than penetrated it. As with other trials mentioned above there is an understanding now that such a placebo is not inert and trials such as this one, need a control group of women who have no acupuncture.



Abstract

This prospective, randomized, controlled and double-blinded trial studied whether acupuncture in relation to embryo transfer could increase the ongoing pregnancy rates and live birth rates in women undergoing assisted reproductive therapy. A total of 635 patients undergoing IVF or intracytoplasmic sperm injection (ICSI) were included.

In 314 patients, embryo transfer was accompanied by acupuncture according to the principles of traditional Chinese medicine. In the control group, 321 patients received placebo acupuncture using a validated placebo needle. In the acupuncture group and the placebo group, the ongoing pregnancy rates were 27% (95% CI 22–32) and 32% (95% CI 27–37), respectively.

Live birth rates were 25% (95% CI 20–30) in the acupuncture group and 30% (95% CI 25–30) in the placebo group. The differences were not statistically significant. These results suggest that acupuncture administered in relation to embryo transfer has no effect on the outcome of IVF and ICSI.

Pilot Study: Acupuncture May Improve Results of IVF

Jancin B, 2010, Elsevier News

Elsevier Global Medical News

This trial was presented at the Annual Society for Reproductive Medicine meeting by Dr Omedei from Italy, and was reported by Elsevier and ObGyn News. It has not yet been published in a journal. They found that women who had acupuncture at the time of embryo transfer, had a 45% pregnancy rate (determined by ultrasound) compared with women in the control group (no acupuncture) who had a pregnancy rate of 28%. The acupuncture-treated women reported a sense of well being while the controls generally reported feeling emotionally stressed and fatigued.



Abstract

ASRM presentation reported in Elsevier Medical News

In a prospective randomized trial involving 168 consecutive women undergoing IVF, the clinical pregnancy rate documented by ultrasound 6 weeks post procedure was 45% in the 44 women assigned to acupuncture, compared with 28% in 124 controls.

Influence of Acupuncture on the Outcomes of In-vitro Fertilisation when Embryo Implantation has Failed: a Prospective Randomised Controlled Clinical Trial.

Isoyama Manca di Villahermosa D et al, *Acupunct Med.* 2013 Mar 19. [Epub ahead of print]
Acupuncture in Medicine (BMJ)

A group of researchers in Brazil gave acupuncture and moxibustion to patients who had not had success with 2 failed IVF cycles. Treatment was administered during the stimulation phase of the 3rd IVF cycle and after embryo transfer. Significantly more women in the acupuncture group conceived compared to the control groups.



Abstract

Objective: To evaluate the effectiveness of acupuncture and moxibustion as an adjuvant treatment in women undergoing in vitro fertilisation (IVF) when embryo implantation has failed.

Methods: A prospective, randomised controlled clinical trial was conducted with 84 infertile patients who had had at least two unsuccessful attempts of IVF. The patients were randomised in three groups: control (n=28), sham (n=28) and acupuncture (n=28). The sample size was calculated by assuming a pregnancy rate of 10% when embryo implantation had failed. The pregnancy rates of the current IVF cycle were evaluated by measurement of blood β human chorionic gonadotrophin (β hCG) and subsequent transvaginal ultrasound. Acupuncture was performed on the first and seventh day of ovulation induction, on the day before ovarian puncture and on the day after embryo transfer. In the acupuncture group, patients were treated with moxibustion at nine acupuncture points (BL18, BL22, BL23, BL52, CV3, CV4, CV5, CV7, GV4) and needling at 12 points. In the sham group needles were inserted in eight areas that did not correspond to known acupuncture points.

Results: The clinical pregnancy rate in the acupuncture group was significantly higher than that in the control and sham groups (35.7% vs 7.1% vs 10.7%; $p=0.0169$).

Conclusion: In this study, acupuncture and moxibustion increased pregnancy rates when used as an adjuvant treatment in women undergoing IVF, when embryo implantation had failed.

Effects of Chinese Medicines for Tonifying the Kidney on DNMT1 Protein Expression in Endometrium of Infertile Women During Implantation Period

Lian Fang et al *Jnl Alt Compl Med*, 2013, Vol 19, 4, 353–359
The Journal of Alternative and Complementary Medicine

In this country (Australia) it is preferred by IVF clinics that their patients do not take Chinese herbs. However in China it is more accepted and herbs are used during IVF cycles in some clinics. A recent study showed that taking herbs for three months prior to and during the IVF cycle improved egg quality and pregnancy rate with lower doses of FSH.

Abstract

Objectives: The purpose of this study was to explore the effects of Erzhi Tiangui Granule (ETG) on DNA methyltransferases (DNMT) 1 protein expression in endometrium of infertile women with Kidney-yin Deficiency syndrome.

Methods: A randomized, double-blinded, placebo-controlled clinical trial was conducted. Sixty-six (66) infertile patients who had Kidney-yin Deficiency syndrome and who were to undergo in vitro fertilization–embryo transfer (IVF-ET) were randomly assigned to either a treatment group or a control group according to a random table. Besides gonadotropin (Gn) therapy in both groups, the treatment group received ETG for 3 menstrual cycles before IVF, and the control group received placebo granules. The ETG and the placebo granules were made with similar color and shape, as well as in the same packaging. The scores of the Kidney-yin Deficiency syndrome were assessed. Other outcome measures included the dosage and duration of Gn, the number of retrieved oocytes, the rate of high-quality oocytes, the rate of high-quality embryos, the fertilization rate, and the clinical pregnancy rate. DNMT1 protein expression in the endometrium was measured in the midluteal phase.

Results: The difference in the syndrome score change before and after treatment between the two groups was statistically significant ($p < 0.05$). The dosage and duration of Gn were significantly lower in the treatment group than those in the control group ($p < 0.05$). The high-quality oocyte and embryo rates, and clinical pregnancy rate were all higher in the treatment group than those in the control group ($p < 0.05$). The fertilization rate was not significant when compared to the placebo group. No difference was found in the number of retrieved oocytes between the two groups. The DNMT1 protein expression in the endometrium was much more abundant in the treatment group than that in the control group ($p < 0.05$).

Conclusions: For the infertile patients undergoing IVF, the Chinese recipe for tonifying the Kidney as an adjunct treatment could reduce Gn dosage and treatment duration, alleviate clinical symptoms, and improve the clinical pregnancy rate. The increased level of DNMT1 protein expression after treatment may lead to enhanced endometrial receptivity. This finding may explain the improvement in clinical pregnancy rate.



Clinical Efficacy of Macrophage-activating Chinese Mixed Herbs (MACH) in Improvement of Embryo Qualities in Women with Long-term Infertility of Unknown Etiology

Ushiroyama T et al, Am J Chin Med. 2012;40(1):1-10.
American Journal of Chinese Medicine.

A pilot study in Japan, gave IVF patients with a history of cycle failure a Chinese herb formula designed to regulate the immune system. They found that use of the herbs was associated with significant improvement in the quality of the blastocysts.

Abstract

Despite the recent technological advances in in vitro fertilization and embryo transfer (IVF-ET), a significant proportion of women still do not become pregnant after long-term infertility, whether it is originally due to older age or other undetermined factors.

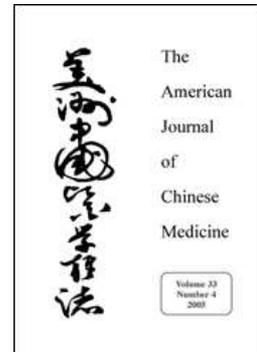
In the present study, macrophage activating Chinese herbs (MACH) were evaluated for their effects on embryo qualities in women who were undergoing repeated IVF-ET because of long-term infertility.

Method: Thirty women, who had significantly low rates of developing good quality cleaved embryos and did not become pregnant after three or more cycles of Assisted Reproductive Technology (ART) procedure, were included in the study. Oral administration of MACH significantly increased the percentage of good quality early stage blastocysts (the number of grade 1 or grade 2 cleaved embryos/the number of retrieved oocytes) from $18.7 \pm 16.2\%$ to $36.1 \pm 27.1\%$ (1.9-fold increase, $p < 0.01$). The rate of good quality early stage blastocysts increased in all patients. In 19 patients who desired embryo transfer using late stage blastocysts, MACH significantly increased the percentage of late stage blastocysts from the initial value of $14.8 \pm 11.2\%$ to $21.1 \pm 23.1\%$ (1.4-fold increase, $p < 0.05$). The rate of embryonic progress into late stage blastocyst increased in 52.6% (10/19) of the patients.

Furthermore, treatment with MACH significantly decreased the plasma follicle stimulating hormone (FSH) concentration on the day of oocyte retrieval from 14.4 ± 3.2 to 10.5 ± 2.4 mIU/ml ($p < 0.05$).

No adverse events were observed with MACH supplementation, and there was no patient dropout. Administration of MACH resulted in improved embryo quality in the difficult cases.

Conclusion: The present study demonstrates a new benefit of this herbal blend in women with refractory infertility of unknown etiology.



Acupuncture Treatment For Infertile Women Undergoing Intracytoplasmic Sperm Injection

Emmons S and Patton P, Medical Acupuncture 2000, 12 (2) 18 - 20

Medical Acupuncture

This pilot study is included here because it is the first of many studies which followed in subsequent years examining the effects of acupuncture on IVF patients. In this case several women were referred for acupuncture as a last resort after very poor response to high doses of FSH. More eggs were collected and more pregnancies were recorded in the acupuncture cycles compared to the non acupuncture cycles, possibly due to increased blood supply to the ovaries.



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.

A Randomized Double Blind Comparison of Real and Placebo Acupuncture in IVF Treatment

So et al, Hum Reprod. 2009 Feb;24(2):341-8.

Human Reproduction

While certain electroacupuncture protocols appear to increase blood flow to the uterus, the points (and no electroacupuncture) used at the time of embryo transfer have a different effect. This study showed that when these points were needled (either penetrating or pricking the acupuncture points) the vascularity of the lining of the uterus was reduced. The authors point out that a slightly hypoxic uterine environment may be beneficial for the embryo and its implantation.



Abstract

Background: Acupuncture has been used during IVF treatment as it may improve outcome, however, there are concerns about the true efficacy of this approach. This randomized double blind study aimed to compare real acupuncture with placebo acupuncture in patients undergoing IVF treatment.

Methods: On the day of embryo transfer (ET), 370 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received 25 min of real or placebo acupuncture before and after ET. The endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were evaluated before and after real and placebo acupuncture.

Results: The overall pregnancy rate was significantly higher in the placebo acupuncture group than that in the real acupuncture group (55.1 versus 43.8%, respectively, $P = 0.038$; Common odds ratio 1.578 95% confidence interval 1.047–2.378). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were observed following both real and placebo acupuncture, although there were no significant differences in the changes in all these indices between the two groups.

Conclusion: Placebo acupuncture was associated with a significantly higher overall pregnancy rate when compared with real acupuncture. Placebo acupuncture may not be inert.

Immunological Changes and Stress are Associated With Different Implantation Rates in Patients Undergoing In-vitro Fertilization–Embryo Transfer

*Gallinelli A et al, 2001 Fertil Steril 76, 1, 85
Fertility and Sterility*

This study examines the effect of stress on embryo transfer and explores its impact via the immune system. The researchers conclude that stress is associated with high amounts of activated T cells in the peripheral blood which is in turn associated with a reduced implantation rate in women undergoing IVF-ET. The subject of regulation of T cells by acupuncture is something we are examining currently and is one of the hypothesized mechanisms by which acupuncture may increase implantation in some women.



Abstract

Objective: To evaluate the possible correlation between immunological changes and implantation rates in patients who undergo in vitro fertilization–embryo transfer (IVF-ET).

Design: Controlled clinical study.

Setting: University hospital.

Patient(s): Forty infertile women undergoing IVF-ET.

Intervention(s): Stroop Color Word (CW) test, State-Trait Anxiety Inventory (STAI) test, blood sampling.

Main Outcome Measure(s): Heart rate and systolic and diastolic blood pressure responses to Stroop CW; circulating T, B, T-helper (CD4), and T-suppressor (CD8) lymphocytes.

Result(s): The total number of T lymphocytes increased significantly during superovulation, resulting in significantly higher levels in subjects achieving embryo implantation than in those showing a failure of implantation. An opposite trend was observed for the activated T cells. The number of T-helper lymphocytes and the T-helper/T-suppressor ratio showed a significant increase from baseline to the time of pick-up only in patients with implantation.

Conclusion(s): A prolonged condition of stress, which causes a decreased ability to adapt and a transitory anxious state, is associated with high amounts of activated T cells in the peripheral blood. Such a condition, in turn, is associated with a reduced implantation rate in women undergoing IVF-ET.

The Relationship Between Mental Work and Threatened Abortion

Huang Zhi Ying, 2002 Jnl Huaihai Medicine, Issue 1

Journal of Huaihai Medicine

Although some fine detail may have been lost in translation, this trial indicates that stress (mental work) increases the risk of miscarriage.

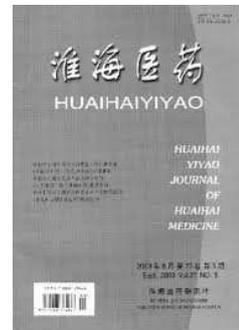
Abstract

Objective: To investigate the relationship between mental work and threatened abortion.

Methods: Pregnant women(620 cases, 1982~1999) were divided into mental worker and non mental worker groups. The incidence of threatened abortion was compared in the two groups.

Results: The incidence of threatened abortion was found to be significantly higher in the mental worker group(135 cases, 38%) than that in the non mental worker group(40 cases, 15%, $P < 0.01$). The higher incidence of threatened abortion was found in the older mental worker group($P < 0.05$).

Conclusion: The nervous mental work is significantly associated with threatened abortion.

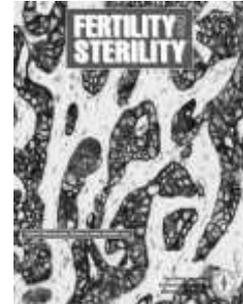


The Effect of Medical Clowning on Pregnancy Rates after In-vitro Fertilization and Embryo Transfer

Friedler S et al, Fertility and Sterility 2011, Vol 95, Issue 6 , Pg 2127

Fertility and Sterility

Dr. Friedler and colleagues tracked 219 women undergoing IVF treatment and, over a period of a year, treated half of them to a medical clown's 15-minute routine of jokes, magic tricks and other clowning immediately after their embryos were implanted. Those women who's stress was relieved with a good laugh after their transfer fell pregnant more often than did the control group.



Abstract

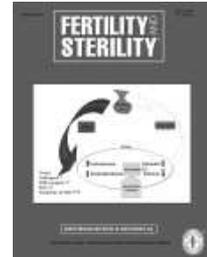
This experimental prospective quasi-randomized study examining the impact of a medical clowning encounter after embryo transfer (ET) after in vitro fertilization (IVF) found that the pregnancy rate in the intervention group was 36.4%, compared with 20.2% in the control group (adjusted odds ratio, 2.67; 95% confidence interval, 1.36–5.24). Medical clowning as an adjunct to IVF-ET may have a beneficial effect on pregnancy rates and deserves further investigation.

Effectiveness of Psychosocial Group Intervention for Reducing Anxiety in Women Undergoing In-vitro Fertilization: A Randomized Controlled Study

Chan CH et al, Fertil Steril. 2006 Feb;85(2):339-46.

Fertility and Sterility

A group of researchers from Hong Kong hypothesized that women who received certain interventions would experience a lower level of anxiety during the IVF treatment and therefore have better mental adjustment and psychosocial functioning during IVF. This programme includes instruction on principles of Chinese medicine emphasizing body-mind harmony and stress reduction techniques including Tai qi and meditation. However it did not include acupuncture. They found that anxiety was significantly reduced in the women who followed the programme.



Abstract

Objective: To evaluate the effect of the Eastern Body-Mind-Spirit (EBMS) group intervention on anxiety-reduction of Chinese women undergoing IVF.

Design: Randomized controlled study.

Setting: Tertiary assisted reproduction unit.

Participant(s): Two hundred twenty-seven women undergoing their first cycle of IVF treatment.

Intervention(s): The intervention group (n = 69) received four sessions of EBMS group counseling, while the control group (n = 115) did not receive any intervention.

Main Outcome Measure(s): State-Trait Anxiety Inventory.

Result(s): Compared with the control group, the intervention group had a significant drop in State Anxiety mean score following intervention. A comparable number of embryos were transferred for each group, but there was a nonsignificant trend of a higher pregnancy rate in the intervention group.

Conclusion(s): The Eastern Body-Mind-Spirit group intervention approach effectively reduces the anxiety level of women undergoing IVF treatment.

Stressful Life Events are Associated with a Poor In-vitro Fertilization (IVF) Outcome: A Prospective Study
Ebbesen S.M.S. Hum Reprod 2009;24(9):2173-2182.
Human Reproduction

This study examined the outcomes of IVF cycles for 800 women and found that the chance of success was related to chronic stress levels. They surmised that chronic stress levels may have a negative effect on follicle development in an IVF cycle. Since acupuncture has been shown to reduce stress hormones this may be the mechanism behind its benefit for IVF patients.

Abstract

Background: There is preliminary evidence to suggest an impact of stress on chances of achieving a pregnancy with in-vitro fertilization (IVF). The majority of the available research has focused on stress related to infertility and going through IVF-treatment, and it is still unclear whether non-fertility-related, naturally occurring stressors may influence IVF pregnancy chances. Our aim was to explore the association between IVF-outcome and negative, i.e. stressful, life-events during the previous 12 months.

Methods: Prior to IVF, 809 women (mean age: 31.2 years) completed the List of Recent Events (LRE) and questionnaires measuring perceived stress and depressive symptoms. Results: Women who became pregnant reported fewer non-fertility-related negative life-events prior to IVF (Mean: 2.5; SD: 2.5) than women who did not obtain a pregnancy (Mean: 3.0; SD: 3.0) ($t(465.28) = 2.390, P = 0.017$). Logistic regression analyses revealed that the number of negative life-events remained a significant predictor of pregnancy (OR: 0.889; $P = 0.02$), when controlling for age, total number of life-events, perceived stress within the previous month, depressive symptoms, and relevant medical factors related to the patient or treatment procedure, including duration of infertility, number of oocytes retrieved and infertility etiology. Mediation analyses indicated that the association between negative life events and IVF pregnancy was partly mediated by the number of oocytes harvested during oocyte retrieval.

Conclusion: A large number of life-events perceived as having a negative impact on quality of life may indicate chronic stress, and the results of our study indicate that stress may reduce the chances of a successful outcome following IVF, possibly through psychobiological mechanisms affecting medical end-points such as oocyte retrieval outcome.



Stress Reduces Conception Probabilities Across the Fertile Window: Evidence in Support of Relaxation

Buck Louis GM et al, Fertil Steril. 2011, 95, 7, pg 2184 - 2189

Fertility and Sterility

While this study did not involve IVF patients its conclusions nevertheless have relevance to women trying to fall pregnant with IVF. The study showed a clear relationship with higher stress levels and reduced conception rates. This may be one of the ways that acupuncture, which reduces stress hormones, can improve fertility.

Abstract

Objective To assess salivary stress biomarkers (cortisol and alpha-amylase) and female fecundity.

Design: Prospective cohort design.

Setting: United Kingdom.

Patient(s): 274 women aged 18 to 40 years who were attempting pregnancy.

Intervention(s): Observation for six cycles or until pregnancy; women collected basal saliva samples on day 6 of each cycle, and used fertility monitors to identify ovulation and pregnancy test kits for pregnancy detection.

Main Outcome Measure(s): Salivary cortisol (µg/dL) and alpha-amylase (U/mL) concentration measurements; fecundity measured by time-to-pregnancy and the probability of pregnancy during the fertile window as estimated from discrete-time survival and Bayesian modeling techniques, respectively.

Result(s): Alpha-amylase but not cortisol concentrations were negatively associated with fecundity in the first cycle (fecundity odds ratio = 0.85; 95% confidence interval 0.67, 1.09) after adjusting for the couples' ages, intercourse frequency, and alcohol consumption. Statistically significant reductions in the probability of conception across the fertile window during the first cycle attempting pregnancy were observed for women whose salivary concentrations of alpha-amylase were in the upper quartiles in comparison with women in the lower quartiles (highest posterior density: -0.284; 95% interval -0.540, -0.029).

Conclusion(s): Stress significantly reduced the probability of conception each day during the fertile window, possibly exerting its effect through the sympathetic medullar pathway.



The Relationship Between Perceived Stress, Acupuncture, and Pregnancy Rates Among IVF Patients: A Pilot Study

Balk J et al, Complement Ther Clin Pract. 2010 Aug;16(3):154-7).
Complementary Therapies in Clinical Practice

These investigators aimed to determine if acupuncture affects the levels of perceived stress at the time of embryo transfer, and whether either acupuncture or changes in stress levels play a role in the success rate in IVF. The patients who received acupuncture in this study had both higher rates of pregnancy, and lower levels of stress both before and after embryo transfer. They postulated that reducing stress at the time of embryo transfer could result in less vasoconstriction and improved uterine receptivity.



Abstract

The aim of this paper was to determine the effect of acupuncture on perceived stress levels in women on the day of embryo transfer (ET), and to determine if perceived stress levels at embryo transfer correlated with pregnancy rates. The study was an observational, prospective, cohort study based at the University IVF center.

Patient(s): 57 infertile patients undergoing IVF or IVF/ICSI.

Interventions(s): Patients were undergoing Embryo Transfer with or without acupuncture as part of their standard clinical care.

Main outcome measure(s): Perceive Stress Scale scores, pregnancy rates.

Result(s): women who received this acupuncture regimen achieved pregnancy 64.7%, whereas those without acupuncture achieved pregnancy 42.5%. When stratified by donor recipient status, only non-donor recipients potentially had an improvement with acupuncture (35.5% without acupuncture vs. 55.6% with acupuncture). Those who received this acupuncture regimen had lower stress scores both pre-ET and post-ET compared to those who did not. Those with decreased their perceived stress scores compared to baseline had higher pregnancy rates than those who did not demonstrate this decrease, regardless of acupuncture status.

Conclusions(s): The acupuncture regimen was associated with less stress both before and after embryo transfer, and it possibly improved pregnancy rates. Lower perceived stress at the time of embryo transfer may play a role in an improved pregnancy rate.

A Randomized Double Blind Comparison of Real and Placebo Acupuncture in IVF Treatment

So et al, Hum Reprod. 2009 Feb;24(2):341-8.

Human Reproduction

This paper which was included above amongst those describing the Embryo transfer trials, also investigated cortisol and anxiety levels before and after acupuncture was administered at precise points with either needles which penetrate the skin or "placebo" needles which prick the points but do not penetrate. No matter how the acupuncture was administered cortisol and perceived anxiety were significantly reduced after the treatment.



Abstract

Background: Acupuncture has been used during IVF treatment as it may improve outcome, however, there are concerns about the true efficacy of this approach. This randomized double blind study aimed to compare real acupuncture with placebo acupuncture in patients undergoing IVF treatment.

Methods: On the day of embryo transfer (ET), 370 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received 25 min of real or placebo acupuncture before and after ET. The endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were evaluated before and after real and placebo acupuncture.

Results: The overall pregnancy rate was significantly higher in the placebo acupuncture group than that in the real acupuncture group (55.1 versus 43.8%, respectively, $P = 0.038$; Common odds ratio 1.578 95% confidence interval 1.047–2.378). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were observed following both real and placebo acupuncture, although there were no significant differences in the changes in all these indices between the two groups.

Conclusions: Placebo acupuncture was associated with a significantly higher overall pregnancy rate when compared with real acupuncture. Placebo acupuncture may not be inert.

An Assessment of the Demand and Importance of Acupuncture to Patients of a Fertility Clinic During Investigations and Treatment

Hinks J and Coulson C, Hum Fert 2010 Vol 13, S1 Pg 3-21
Human Fertility

These authors working in a fertility clinic in the UK surveyed 200 patients who attended the clinic in August 2009. They discovered that there was a clear demand for acupuncture and that acupuncture may be valuable to improve the general wellbeing of women during infertility investigations and treatments. They also felt that patient resilience may be increased by the use of acupuncture alongside their IVF treatment such that patients would persevere with increased numbers of ART(Assisted Reproductive Technologies) cycles, thereby increasing their ultimate chance of a successful pregnancy.



Abstract

An assessment of the demand and importance of acupuncture to patients of a fertility clinic during investigations and treatment

Julie Hinks & Catherine Coulson

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Introduction: Despite a lack of studies clearly demonstrating clinical efficacy complementary medicine is frequently used by couples undergoing infertility treatment (Coulson 2005). In Bristol, acupuncture has become very popular among patients undergoing infertility treatment, thus this study sought to quantify this and examine the reasons why patients choose acupuncture.

Methods: Two hundred questionnaires were given to patients who attended the Bristol Centre for Reproductive Medicine (BCRM) for investigation or treatment of infertility in August 2009. Patients were asked to complete the questionnaire while waiting to see their doctor or nurse and 194 responses were returned. The questionnaires asked if patients had or wished to have acupuncture or other complementary medicine, and to indicate on a scale of one to ten (10 being the best) the relative importance of acupuncture in comparison to values such as pregnancy rates and continuity of care.

Results: Out of 58 respondents who use complementary medicine, 43 used acupuncture. 40 respondents use acupuncture regularly and 17 of those lived outside of Bristol. A further 52 respondents had considered using acupuncture. In terms of very high importance (score of 10) 135 respondents felt pregnancy rates scored 10, 84 felt having the same doctor scored 10, 71 scored 10 for having the same nurse, 31 felt in house acupuncture scored 10 and 21 scored 10 for other complementary medicine. Overall, 43 respondents felt acupuncture should be available at Bristol Centre for Reproductive Medicine. Thirty four respondents gave more importance to acupuncture than seeing the same doctor or nurse, and 32 deemed it equally important. In addition, 29 patients scored acupuncture as equally important to pregnancy rates and 5 scored acupuncture higher than pregnancy rates.

Discussion: Previous unpublished work at BCRM showed that 85% of the patients found the named nurse system important as a coping mechanism to support them by providing continuity of care through stressful treatment. The responses to the questionnaires indicate a clear demand for acupuncture and suggest that acupuncture may be valuable to improve the general wellbeing of women during infertility investigations and treatments. If acupuncture provides an effective coping mechanism, this could support patients to persevere with increased numbers of ART(Assisted Reproductive Technologies) cycles, thereby increasing their ultimate chance of a successful pregnancy.

Building Resilience: An Exploration of Women's Perceptions of the Use of Acupuncture as an Adjunct to IVF

De Lacey S, Smith C and Paterson C, BMC Complementary and Alternative Medicine 2009, 9:50
BioMed Central

Resilience is an interesting and important concept when applied to couples doing IVF.

Studies of acupuncture involving women dealing with chronic health issues have shown that women experienced relief of presenting symptoms but also increases in energy, increase in relaxation and calmness, reduction in the reliance of prescription drugs (such as analgesics), quicker healing from surgery and increased self awareness and well being. Such effects indicate a reduction of stress that in turn may diminish the number of treatment cycles needed for pregnancy to occur. But further, reducing the number of cycles a woman must undertake to reach her goal of motherhood reduces the overall cost of IVF.

Abstract

Background: In Vitro Fertilisation (IVF) is now an accepted and effective treatment for infertility, however IVF is acknowledged as contributing to, rather than lessening, the overall psychosocial effects of infertility. Psychological and counselling interventions have previously been widely recommended in parallel with infertility treatments but whilst in many jurisdictions counselling is recommended or mandatory, it may not be widely used. Acupuncture is increasingly used as an adjunct to IVF, in this preliminary study we sought to investigate the experience of infertile women who had used acupuncture to improve their fertility.

Methods: A sample of 20 women was drawn from a cohort of women who had attended for a minimum of four acupuncture sessions in the practices of two acupuncturists in South Australia. Eight women were interviewed using a semi-structured questionnaire. Six had sought acupuncture during IVF treatment and two had begun acupuncture to enhance their fertility and had later progressed to IVF. Descriptive content analysis was employed to analyse the data.

Results: Four major categories of perceptions about acupuncture in relation to reproductive health were identified: (a) Awareness of, and perceived benefits of acupuncture; (b) perceptions of the body and the impact of acupuncture upon it; (c) perceptions of stress and the impact of acupuncture on resilience; and (d) perceptions of the intersection of medical treatment and acupuncture.

Conclusion: This preliminary exploration, whilst confined to a small sample of women, confirms that acupuncture is indeed perceived by infertile women to have an impact to their health. All findings outlined here are reported cautiously because they are limited by the size of the sample. They suggest that further studies of acupuncture as an adjunct to IVF should systematically explore the issues of wellbeing, anxiety, personal and social resilience and women's identity in relation to sexuality and reproduction.

Understanding Women's Views Towards the use of Acupuncture While Undergoing IVF Treatment
Smith C and De Lacey S, 2008 In press
FSA conference 2008

This qualitative study found that most women who had acupuncture as an adjunct to IVF treatment reported increased well being, reduced anxiety and an increase in capacity to cope with the stresses of IVF and infertility treatments.

Abstract

Aim: There is interest in the use of acupuncture as an adjunct to fertility treatment. this study aimed to examine women's attitudes and beliefs in relation to the use of acupuncture for enhancing fertility or as an adjunct to ART.

Results: Participants all expressed confidence in the ability of acupuncture to contribute to their reproductive decision in a positive way. They described acupuncture as an adjunct to pregnancy attempts that was positive since it gave them a sense of control and a strategy for improving their chances. Women were unable to locate acupuncture as a causative factor in a resulting pregnancy however all women described acupuncture as instrumental in an increased sense of well being, self confidence, emotional balance and reduced anxiety. All experienced increased resilience.

Conclusion; Acupuncture is an effective and low intensity procedure for increasing women's resilience in the repetitive and stress inducing time of pregnancy attempts, with or without medical treatment. The instrumental role of the acupuncture therapist in increasing resilience is a finding that has not emerged in previous studies and has implications for patient management.



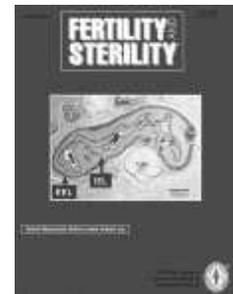
The Impact of Acupuncture on in Vitro Fertilization Outcome.

Domar A et al Fertil Steril 2009 Vol 91 Issue 3 pg 723 - 6

Fertility and Sterility

One of the trials that investigated the effect of acupuncture on IVF pregnancy rates also collected data on the subjective experience of these women. The authors write “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”.

Nobody knows how exactly acupuncture might boost IVF success, Domar said, although she suggests that it has something to do with a woman's mental state at the time of embryo transfer.



Abstract

Objective: To replicate previous research on the efficacy of acupuncture in increasing pregnancy rates (PR) in patients undergoing IVF and to determine whether such an increase was due to a placebo effect. Design: Prospective, randomized, controlled, single blind trial.

Setting: Private, academically affiliated, infertility clinic.

Patient(s): One hundred fifty patients scheduled to undergo embryo transfer.

Intervention(s): Subjects were randomized to either the acupuncture or control group. Acupuncture patients received the protocol, as first described by Paulus and his colleagues, for 25 minutes before and after embryo transfer. Control subjects laid quietly. All subjects then completed questionnaires on anxiety and optimism. The IVF staff remained blind to subject assignment.

Main Outcome Measure(s): Clinical PRs, anxiety, optimism.

Result(s): Before randomization both groups had similar demographic characteristics including age and psychological variables. There were no significant differences in PRs between the two groups. 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.

Conclusion(s): The use of acupuncture in patients undergoing IVF was not associated with an increase in PRs but they were more relaxed and more optimistic.

Acupuncture & IVF Poor Responders: A Cure?

Magarelli P, Cridennda D, Fertil Steril, 2004; 81 Suppl 3 S20 Fertility and Sterility

Conclusions: Significant increases in pregnancy outcomes were confirmed by this study and the data uniquely supported the advantage of acupuncture in patients with normal Pulsatility index. We also demonstrated that both acupuncture treatment protocols could be used together with a synergistic effect. Finally, this study is the first to demonstrate that the use of acupuncture in patients with poor prognoses (elevated Peak FSH, longer history of infertility, poor sperm morphology) can achieve similar pregnancy rates to normal prognosis patients.



Objective: The purpose of the study was to determine the influence of two acupuncture protocols on IVF outcomes and secondly to identify the appropriate patient groups that would most benefit from this adjunctive therapy.

Materials and Methods: In this retrospective study, data was extracted from medical records of patients RE&I clinic & acupuncture clinics between January 2001 and November 2003. All patients completing an IVF cycle with transfer were included. One RE&I provided the IVF care and a consortium of acupuncturists overseen by the author provided the strict acupuncture protocols. PR per transfer were the endpoints measured. Data was analyzed by student's t test and Multiregression with Wilcox ranking (MRW).

Results: 147 patients were included in the study and of those 53 had Acupuncture (Ac) and 94 did not (Non-Ac group). Demographic data between these Ac and Non-Ac groups respectively indicated remarkable equity (Table 1). Fertility Factors also demonstrated equity and there were no differences in Diagnoses, IVF Protocols and type of Gonadotrophin protocols used.

Factors that demonstrated significance were: Length of time infertile, Peak FSH, PI for total group without MRW; PI for MRW groups reversed this (Table 2) and finally average: Sperm Morphology, Peak E2, Peak P4 prior to HcG; and endometrial thickness. PR before Wilcox ranking were the same: 40% v 38%. MRW analysis revealed FSH, Length of time trying to get pregnant, Sperm Morphology and E2 levels as significant: 6.5, 4.1, 4.0 and 1.6 respectively. When the Ac group was modified (15 Ac patient dropped), PI was elevated from 1.76 to 1.94 resulting in a significant elevation compared to the Non-Ac group, p 0.01. Also PR changed from 40% before to 53% after and this value was significantly greater than the Non-Ac group (38%), p 0.01.

Efficacy of Traditional Chinese Herbal Medicine in the Management of Female Infertility: A Systematic Review

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Abstract

Objectives: To assess the effect of Traditional Chinese Herbal Medicine (CHM) in the management of female infertility and on pregnancy rates compared with Western Medical (WM) treatment.

Methods: We searched the Medline and Cochrane databases and Google Scholar until February 2010 for abstracts in English of studies investigating infertility, menstrual health and Traditional Chinese Medicine (TCM). We undertook meta-analyses of (non-)randomised controlled trials (RCTs) or cohort studies, and compared clinical pregnancy rates achieved with CHM versus WM drug treatment or in vitro fertilisation (IVF). In addition, we collated common TCM pattern diagnosis in infertility in relation to the quality of the menstrual cycle and associated symptoms.

Results: Eight RCTs, 13 cohort studies, 3 case series and 6 case studies involving 1851 women with infertility were included in the systematic review. Meta-analysis of RCTs suggested a 3.5 greater likelihood of achieving a pregnancy with CHM therapy over a 4-month period compared with WM drug therapy alone (odds ratio=3.5, 95% CI: 2.3, 5.2, $p<0.0001$, $n=1005$). Mean (SD) pregnancy rates were $60\pm 12.5\%$ for CHM compared with $32\pm 10\%$ using WM drug therapy. Meta-analysis of selected cohort studies ($n=616$ women) suggested a mean clinical pregnancy rate of 50% using CHM compared with IVF (30%) ($p<0.0001$).

Conclusions: Our review suggests that management of female infertility with Chinese Herbal Medicine can improve pregnancy rates 2-fold within a 4 month period compared with Western Medical fertility drug therapy or IVF. Assessment of the quality of the menstrual cycle, integral to TCM diagnosis, appears to be fundamental to successful treatment of female infertility.

Changes in Serum Cortisol and Prolactin Associated with Acupuncture During IVF

Magarelli, PC, D Cridennda, M Cohen. Fertil Steril 2009 in press Fertility and Sterility

Conclusion: The researchers found that the women who had acupuncture showed beneficial changes in serum levels of stress hormones compared to the control group of women who did not have acupuncture. This may have implications for both egg quality and implantation. In addition, the pregnancy and live birth rate was significantly higher in the acupuncture group.



A number of women going through IVF were given acupuncture to increase blood flow through the uterine arteries in the immediate weeks before egg collection. The researchers found that the women who had acupuncture showed beneficial changes in serum levels of stress hormones compared to the control group of women who did not have acupuncture. The acupuncture treatments appear to normalize levels of cortisol and prolactin which have been artificially depressed by the IVF drugs. This may have implications for both egg quality and implantation. In addition, the pregnancy and live birth rate was significantly higher in the acupuncture group.

Abstract

Objective: To determine whether changes in serum cortisol (CORT) and PRL are affected by acupuncture (Ac) in Ac-treated IVF patients.

Design: Prospective cohort clinical study.

Setting: Private practice reproductive endocrinology and infertility clinic and private practice acupuncture consortium.

Patient(s): Sixty-seven reproductive-age infertile women undergoing IVF.

Intervention(s): Blood samples were obtained from all consenting new infertility patients and serum CORT and serum PRL were obtained prospectively. Patients were grouped as controls (IVF with no Ac) and treated (IVF with Ac) according to acupuncture protocols derived from randomized controlled trials.

Main Outcome Measure(s): Serum levels of CORT and PRL were measured and synchronized with medication stimulation days of the IVF cycle (e.g., day 2 of stimulation, day 3, etc.). Reproductive outcomes were collected according to Society for Assisted Reproductive Technology protocols, and results were compared between controls and those patients treated with Ac.

Result(s): CORT levels in Ac group were significantly higher on IVF medication days 7, 8, 9, 11, 12, and 13 compared with controls. PRL levels in the Ac group were significantly higher on IVF medication days 5, 6, 7, and 8 compared with controls.

Conclusion(s): In this study, there appears to be a beneficial regulation of CORT and PRL in the Ac group during the medication phase of the IVF treatment with a trend toward more normal fertile cycle dynamics. (Fertil Steril 2008;88:1000-1005. 2008 by American Society for Reproductive Medicine.)

Increase of Success Rate for Women Undergoing Embryo Transfer by Transcutaneous Electrical Acupoint Stimulation - A Prospective Randomized Placebo-Controlled Study

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Transcutaneous electrical acupoint stimulation, especially double TEAS, significantly improved the clinical outcome of ET.

*Neuroscience Research Institute and Department of Neurobiology, Peking University Health Science Center, Key Laboratory of Neuroscience, The Ministry of Education and the Ministry of Public Health, Beijing, People's Republic of China



Objective: To evaluate the effect of transcutaneous electrical acupoint stimulation (TEAS) on pregnancy rates (PR) in women undergoing ET.

Design: Prospective, randomized, single-blinded placebo-controlled clinical trial.

Setting: Research and laboratory facilities.

Patient(s): A total of 309 patients, less than 45 years old, undergoing cryopreservation embryos transplant or fresh cycle IVF with or without intracytoplasmic sperm injection (ICSI).

Intervention(s): The subjects were randomly allocated to three groups: mock TEAS treatment: 30 minutes after ET (group I, n = 99); single TEAS treatment: 30 minutes after ET (group II, n = 110); and double TEAS treatments: 24 hours before ET and 30 minutes after ET (group III, n = 100).

Main Outcome Measure(s): Clinical PR, embryos implantation rate, live birth rate.

Result(s): The clinical PR, embryos implantation rate, and live birth rate of group I (29.3%, 15.0%, and 21.2%, respectively) were significantly lower than those in group II (42.7%, 25.7%, and 37.3%, respectively) and group III (50.0%, 25.9%, and 42.0%, respectively).

Conclusion(s): Transcutaneous electrical acupoint stimulation, especially double TEAS, significantly improved the clinical outcome of ET.

Effects of Acupuncture on LIF and IL-12 in Rats of Implantation Failure

Gui, Juan; Xiong, Fan; Li, Jing; Huang, Guangying 2012 American Journal of Reproductive Immunology. Am J Reprod Immunol. 1600-0897. 2012

According to the study, Acupuncture could improve the poor receptive state of endometrium by promoting LIF and IL-12 secretion to improve blastocyst implantation.

Abstract

Problem: Acupuncture has a positive effect on implantation obstacle but the mechanism is still not clear, so the aim of the experiment is to explore the possible role that acupuncture plays in implantation.

Method of study: Early pregnant rats were randomized into normal group (N), group treated with mifepristone (M), acupuncture treatment group (A), and progestin treatment group (P). The model of blastocyst implantation obstacle in groups M, A, and P was established with mifepristone. Bilateral "Housanli" and "Sanyinjiao" were needled in group A. The expression of interleukin (IL)-12, leukemia inhibitory factor (LIF), LIFR protein, and mRNA in endometrium were detected.

Results: Positivity of the protein expression of IL-12, LIF, and LIFR in the endometrium was significantly higher in groups N, A, and P; positivity of the mRNA of IL-12 and LIF in the endometrium was significantly higher in groups N, A, and P.

Conclusion: Acupuncture could improve the poor receptive state of endometrium by promoting LIF and IL-12 secretion to improve blastocyst implantation.



Effects of Acupuncture on Pregnancy Rates in Women Undergoing In-vitro Fertilization: A Systematic Review and Meta-analysis

Cui Hong Zheng, M.D.; Ph.D.^a, Guang Ying Huang, M.D., Ph.D.^a; Ming Min Zhang, M.D., Ph.D.^b; Wei Wang, M.D., Ph.D.^c. *Fertility and Sterility*. 1-11-2012.

Abstract

Acupuncture improves Clinical Pregnancy Rates (CPR) and Live Birth Rates (LBR) among women undergoing IVF

Objective: To evaluate the effect of acupuncture on in vitro fertilization (IVF) outcomes.

Design: Systematic review and meta-analysis.

Patient(s): Women undergoing IVF in randomized controlled trials (RCTs) who were evaluated for the effects of acupuncture on IVF outcomes.

Intervention(s): The intervention groups used manual, electrical, and laser acupuncture techniques. The control groups consisted of no, sham, and placebo acupuncture.

Main Outcome Measure(s): The major outcomes were clinical pregnancy rate (CPR) and live birth rate (LBR). Heterogeneity of the therapeutic effect was evaluated with a forest plot analysis. Publication bias was assessed by a funnel plot analysis.

Result(s): Twenty-four trials (a total of 5,807 participants) were included in this review. There were no significant publication biases for most of the comparisons among these studies. The pooled CPR (23 studies) from all of the acupuncture groups was significantly greater than that from all of the control groups, whereas the LBR (6 studies) was not significantly different between the two groups. The results were different when the type of control was examined in a sensitivity analysis. The CPR and LBR differences between the acupuncture and control groups were more obvious when the studies using the Streitberger control were ignored. Similarly, if the underlying effects of the Streitberger control were excluded, the LBR results tended to be significant when the acupuncture was performed around the time of oocyte aspiration or controlled ovarian hyperstimulation.

Conclusion(s): Acupuncture improves CPR and LBR among women undergoing IVF based on the results of studies that do not include the Streitberger control. The Streitberger control may not be an inactive control. More positive effects from using acupuncture in IVF can be expected if an appropriate control and more reasonable acupuncture programs are used.



Influence of Acupuncture on the Pregnancy Rate in Patients Who Undergo Assisted Reproduction Therapy
Paulus W et al, Fertil Steril 2002 Vol 77, pg 721-724
Fertility and Sterility

Abstract

Objective: To evaluate the effect of acupuncture on the pregnancy rate in assisted reproduction therapy (ART) by comparing a group of patients receiving acupuncture treatment shortly before and after embryo transfer with a control group receiving no acupuncture.

Design: Prospective randomized study.

Setting: Fertility center.

Patient(s): After giving informed consent, 160 patients who were undergoing ART and who had good quality embryos were divided into the following two groups through random selection: embryo transfer with acupuncture (n = 80) and embryo transfer without acupuncture (n = 80).

Intervention(s): Acupuncture was performed in 80 patients 25 minutes before and after embryo transfer. In the control group, embryos were transferred without any supportive therapy.

Main Outcome Measure(s): Clinical pregnancy was defined as the presence of a fetal sac during an ultrasound examination 6 weeks after embryo transfer.

Result(s): Clinical pregnancies were documented in 34 of 80 patients (42.5%) in the acupuncture group, whereas pregnancy rate was only 26.3% (21 out of 80 patients) in the control group.

Conclusion(s): Acupuncture seems to be a useful tool for improving pregnancy rate after ART.



A Randomized Double Blind Comparison of Real and Placebo Acupuncture in IVF Treatment

So et al, Hum Reprod. 2009 Feb;24(2):341-8.

Human Reproduction

Researchers in Hong Kong found no significant difference between the effects of placebo and regular acupuncture in clinical or ongoing pregnancy rates however on initial hCG testing the placebo group had more positive tests.

Both placebo and regular acupuncture significantly reduced vascularity of the uterus, reduced stress hormones and anxiety levels. These findings lead the researchers to suggest that placebo acupuncture is in fact not inert. Placebo acupuncture needles prick the skin at the acupuncture point but do not penetrate the skin. Many Japanese acupuncturists (who routinely use minimal stimulation of acupuncture points) would argue strongly that this is not an inert placebo procedure but a therapeutic one.

Unfortunately there was no control group in this trial which received no acupuncture.

Abstract

Background: Acupuncture has been used during IVF treatment as it may improve outcome, however, there are concerns about the true efficacy of this approach. This randomized double blind study aimed to compare real acupuncture with placebo acupuncture in patients undergoing IVF treatment.

Method: On the day of embryo transfer (ET), 370 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received 25 min of real or placebo acupuncture before and after ET. The endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were evaluated before and after real and placebo acupuncture.

Results: The overall pregnancy rate was significantly higher in the placebo acupuncture group than that in the real acupuncture group (55.1 versus 43.8%, respectively, $P = 0.038$; Common odds ratio 1.578 95% confidence interval 1.047–2.378). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were observed following both real and placebo acupuncture, although there were no significant differences in the changes in all these indices between the two groups.

Conclusions: Placebo acupuncture was associated with a significantly higher overall pregnancy rate when compared with real acupuncture. Placebo acupuncture may not be inert.



Effect of Acupuncture on the Pregnancy Rate in Embryo Transfer and Mechanisms: A Randomized and Controlled Study

Zhang M et al, *Chin Acup and Moxabustion* 2003, Jan 23 (1): 3 - 5
Chinese Acupuncture and Moxabustion

210 IVF patients were randomly placed in groups that received real acupuncture or placebo or no treatment on the day of embryo transfer. The pregnancy rate was significantly higher in the group who received real acupuncture. Additionally this trial showed that the women who received real acupuncture had fewer uterine contractions after the transfer.

Abstract

Objective: To observe the effect of acupuncture on the pregnancy rate in assisted reproduction therapy such as in-vitro-fertilisation (IVF) and intracytoplasmic spermatozoen injection (ICSI), and mechanisms.

Methods: 210 cases undergoing IVF or ICSI were divided randomly into three groups: acupuncture treatment group, placebo group and control group. The acupuncture treatment group and the placebo group were treated respectively with body acupuncture and placebo acupuncture before and after embryo transfer, and in the control group embryos were transferred without any supportive therapy. Contraction frequency of the uterine junctional zone and the pregnancy rate were observed.

Results: The contraction frequency before embryo transfer was not significantly different among the three groups, but after embryo transfer in the acupuncture treatment group was lower than that in the placebo group and the control group, respectively. The pregnancy rate was 44.3% (31/70) in the acupuncture treatment group, and 27.1% (19/70) in the placebo group and 24.3% (17/70) in the control group. The pregnancy rate in the acupuncture treatment group was significantly higher than that in the placebo acupuncture group and the control group (P0.05).

Conclusion: Acupuncture is a powerful tool for improving pregnancy rate after assisted reproduction therapy.



Use of Acupuncture Before and After Embryo Transfer

Dalton-Brewer N et al, Hum Fert 2010 Vol 12 No 4 212 - 255

Human Fertility (abstracts from UK Fertility Societies Conference 2009)

This report describes outcomes for all patients who attended The London Bridge Fertility, Gynaecology and Genetics Centre in London over a 2 year period and who had acupuncture. In the acupuncture group positive pregnancy rates/ET were 44.6% comparing favourably with the non-acupuncture historic control group. When they analysed outcomes in different age groups they discovered that acupuncture intervention was particularly effective in woman in the 35 - 39 and the over 40 group.



Abstract

Use of Acupuncture before and after embryo transfer

Nick Dalton-Brewer, David Gillott, Nataly Atalla, Mohamed Menabawey, Pauline Wright, & Alan Thornhill
The London Bridge Fertility, Gynaecology and Genetics Centre, London, UK

All IVF cases in which acupuncture was administered before and after embryo transfer at a large private infertility centre were reviewed for a 2 year period. All patients were treated by the same practitioner (NDB) using Traditional Chinese Acupuncture (TCA). Patients received acupuncture to the protocol developed by Paulus, W.E., Zhang, M., Strehler, E., El-Danasouri, I., & Sterzik, K. (2002). Influence of acupuncture on the pregnancy rate in patients who undergo assisted reproduction therapy. *Fertility & Sterility*, 77, 721–724: Liver 3, Spleen 8, Stomach 29, Pericardium 6, GV 20 were manually stimulated five times over a 40-min period, at Bridge, approximately 10–20 minutes prior to embryo transfer. Embryo transfer was carried out under ultrasound guidance as per routine at Bridge. Ten minutes following embryo transfer acupoints Spleen 6, Stomach 36, Spleen 10, Large Intestine 4 were manually stimulated five times over a 40-min period before discharging the patient. Ear points 34, 55 and 58 were used in both treatments and not stimulated.

A total of 71 patients underwent 74 cycles involving acupuncture before and after embryo transfer.

Overall, positive pregnancy rates/ET were 44.6% comparing favourably with the non-acupuncture historic control group.

When analysed by maternal age at time of treatment, biochemical pregnancy results for acupuncture treated women were as follows: <35 years–52%; 35–39 years – 45%; 40–45 years – 35%.

Results for women aged 35–39 years and those over 40 years were markedly better than controls suggesting that acupuncture intervention of this type may be more effective in older women. No side effects or complications were experienced by women receiving acupuncture. Acupuncture is a safe, adjunct therapy in IVF and in other randomised clinical trials has been shown to significantly improve outcomes when used at the IVF centre before and after embryo transfer. Our preliminary data are encouraging and suggest that a trial involving older women may be effective.

Point- and Frequency-specific Response of the Testicular Artery to Abdominal Electroacupuncture in Humans

*Cakmak Y et al, Fertil Steril 2008;90:1732–8
Fertility and Sterility*



Just as electroacupuncture can increase blood flow to the ovaries and uterus (see reports above) so it can to the testicles. These authors demonstrate that particular frequencies applied for just 5 minutes are effective in increasing blood flow in the testes, and suggest that such a stimulus may address the damaged microcirculation associated with varicoceles, and with aging. They note that decreased testicular arterial blood flow may result in impaired spermatogenesis from defective metabolism in the microcirculatory bed and suggest that further research is needed to discover if electroacupuncture can improve sperm manufacture in this instance.

Abstract

Objective: To clarify the role of the abdominal acupuncture points and the frequency of short-term electroacupuncture (EA) stimulation on testicular blood flow (TBF) in humans.

Design: A prospective, randomized study.

Setting: University hospital, Department of Radiology, ultrasound unit.

Patient(s): Eighty healthy male volunteers were randomly allocated to three groups in stage one and to a single group in stage two. In the first stage of the study, the abdominal acupuncture points ST-29 (guilai) were stimulated using simple needle insertion, 2 Hz burst EA or 10 Hz EA, in three different groups. In the second stage of the study, abdominal acupuncture points ST-25 (tianshu) were stimulated with the frequency found to be more effective in stage one. Stimulation was for 5 minutes in each group.

Intervention(s): Electroacupuncture and Doppler flowmeter.

Main Outcome Measure(s): Four groups were compared for volume flow and other related parameters of TBF.

Result(s): The 10-Hz EA stimulation of ST-29 (guilai) increased TBF, but simple needle insertion and 2-Hz burst stimulation did not. The 10-Hz EA stimulation of ST-25 (tianshu) did not result in significant changes in TBF.

Conclusion(s): For the first time point- and frequency-specific effects of abdominal EA on TBF are shown in humans.

Further investigation is required to ascertain whether these findings may be helpful in the clinical treatment of infertile men.

A Prospective Randomized Placebo-Controlled Study of the Effect of Acupuncture in Infertile Patients with Severe Oligoasthenozoospermia

Dieterle et al Fertil Steril 2009 Oct; 92 (4): 1340-3

Fertility and Sterility

This recent small clinical trial randomised 57 patients who had extremely low sperm counts, to acupuncture and placebo acupuncture groups. After receiving acupuncture twice weekly for 6 weeks motility of sperm (but not overall count) was found to increase significantly. The authors conclude that the results of the present study support the significance of acupuncture in male patients with severe oligoasthenozoospermia. More evidence with larger trials needs to be accumulated before the efficacy and effectiveness of acupuncture in male infertility can be evaluated.



Abstract

In this first prospective, randomized, single-blind, placebo-controlled study, 28 infertile patients with severe oligoasthenozoospermia received acupuncture according to the principles of traditional Chinese medicine (TCM) and 29 infertile patients received placebo acupuncture. A significantly higher percentage of motile sperm (World Health Organization categories A–C), but no effect on sperm concentration, was found after acupuncture compared with placebo acupuncture.

Effects of Acupuncture and Moxa Treatment in Patients with Semen Abnormalities

Gurfinkel E et al *Asian J Androl.* 2003 Dec; 5(4): 345-8.

Asian Journal of Andrology

In a prospective, controlled and blind study, a group of infertile men (married for 3 - 11 years without children) were randomized into two groups, the treatment group receiving 10 acupuncture treatments and the control group receiving sham acupuncture treatments. The patients in the acupuncture group demonstrated a significant increase in the percentage of normal forms compared to the control group.

Abstract

Aim: To evaluate the effect of Chinese Traditional Medicine, acupuncture and moxa treatment, on the semen quality in patients with semen abnormalities.

Methods: In a prospective, controlled and blind study, nineteen patients, aged 24 years ~ 42 years and married for 3 years ~ 11 years without children with semen abnormalities in concentration, morphology and/or progressive motility without apparent cause, were randomized into two groups and submitted to acupuncture and moxa treatment at the therapeutic (Study Group) and the indifferent points (Control Group), respectively, for 10 weeks. Semen analyses were performed before and after the treatment course.

Results: The patients of the Study Group presented a significant increase in the percentage of normal-form sperm compared to the Control Group (calculated $U=16.0$, critical $U=17.0$).

Conclusion: The Chinese Traditional Medicine acupuncture and moxa techniques significantly increase the percentage of normal-form sperm in infertile patients with oligoasthenoteratozoospermia without apparent cause.



Does Acupuncture Treatment Affect Sperm Density in Males with Very Low Sperm Count? A Pilot Study
Siterman S et al Andrologia. 2000 Jan;32(1):31-9.
Andrologia

This pilot study once again showed a positive effect of acupuncture on sperm count - but this time on men with such low sperm counts (or no sperm) that they would usually require a testicular biopsy to extract sperm for use in an IVF cycle. Seven of the 15 men with no sperm at all produced sperm detectable by the light microscope after a course of 10 acupuncture treatments ($p < 0.01$) ie enough sperm could be produced for ICSI to be performed without recourse to testicular biopsy. The control group with similar semen analysis had no treatment and showed no change after 3 months.



Abstract

Classic therapies are usually ineffective in the treatment of patients with very poor sperm density. The aim of this study was to determine the effect of acupuncture on these males. Semen samples of 20 patients with a history of azoospermia were examined by light microscope (LM) and scanning electron microscope (SEM), with which a microsearch for spermatozoa was carried out.

These examinations were performed before and 1 month after acupuncture treatment and revealed that the study group originally contained three severely oligoteratoasthenozoospermic (OTA), two pseudoazoospermic and 15 azoospermic patients.

The control group was comprised of 20 untreated males who underwent two semen examinations within a period of 2–4 months and had initial andrological profiles similar to those of the experimental group.

No changes in any of the parameters examined were observed in the control group. There was a marked but not significant improvement in the sperm counts of severely OTA males following acupuncture treatment (average = $0.7 \pm 1.1 \times 10^6$ spermatozoa per ejaculate before treatment vs. $4.3 \pm 3.2 \times 10^6$ spermatozoa per ejaculate after treatment). A definite increase in sperm count was detected in the ejaculates of 10 (67%) of the 15 azoospermic patients. Seven of these males exhibited post-treatment spermatozoa that were detected even by LM. The sperm production of these seven males increased significantly, from 0 to an average of $1.5 \pm 2.4 \times 10^6$ spermatozoa per ejaculate ($Z = -2.8$, $P \leq 0.01$). Males with genital tract inflammation exhibited the most remarkable improvement in sperm density (on average from $0.3 \pm 0.6 \times 10^6$ spermatozoa per ejaculate to $3.3 \pm 3.2 \times 10^6$ spermatozoa per ejaculate; $Z = -2.4$, $P \leq 0.02$).

Two pregnancies were achieved by the IVF-ICSI procedure. It is concluded that acupuncture may be a useful, nontraumatic treatment for males with very poor sperm density, especially those with a history of genital tract inflammation.

See also a report of acupuncture helping an azoospermic patient to produce sperm. Bidoué F et al, Effect of acupuncture on azoospermic male. Saudi J Kidney Dis Transp, 2011;22;1039

Effect of Acupuncture on Sperm Parameters of Males Suffering From Subfertility Related to Low Sperm Quality

Siterman S et al Arch Androl. 1997 Sep-Oct;39(2):155-61

Archives of Andrology



A group of infertile men with abnormal semen analysis were randomly divided into 2 groups; one group was given 10 acupuncture treatments over 5 weeks, and the other group, no treatment. Significant improvements ($p < 0.05$) were demonstrated in the acupuncture group compared to the control group, in particular improved motility and morphology

Abstract

The aim of this prospective controlled study was to assess the effect of acupuncture on the sperm quality of males suffering from subfertility related to sperm impairment.

Semen samples of 16 acupuncture-treated subfertile patients were analyzed before and 1 month after treatment (twice a week for 5 weeks). In parallel, semen samples of 16 control untreated subfertile males were examined. Two specimens were taken from the control group at an interval of 2-8 months. The expanded semen analysis included routine and ultramorphological observations.

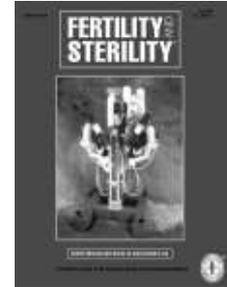
The fertility index increased significantly ($p < \text{or} = .05$) following improvement in total functional sperm fraction, percentage of viability, total motile spermatozoa per ejaculate, and integrity of the axonema ($p < \text{or} = .05$), which occurred upon treatment. The intactness of axonema and sperm motility were highly correlated ($\text{corr.} = .50$, $p < \text{or} = .05$).

Thus, patients exhibiting a low fertility potential due to reduced sperm activity may benefit from acupuncture treatment.

Quantitative Evaluation of Spermatozoa Ultrastructure After Acupuncture Treatment for Idiopathic Male Infertility

Pei J et al Fertil Steril. 2005 Jul;84(1):141-7

Fertility and Sterility



A group of infertile men who had pathological semen analyses according to WHO criteria, were treated with acupuncture twice a week for 5 weeks. A statistically significant increase after acupuncture in the percentage and number of sperm with no structural defects was demonstrated compared to the control group of patients who received no treatment. They concluded that male infertility patients could benefit from having acupuncture. A general improvement of sperm quality, specifically in the ultrastructural integrity of spermatozoa, was seen after acupuncture

Abstract

Objective: To evaluate the ultramorphologic sperm features of idiopathic infertile men after acupuncture therapy.

Design: Prospective controlled study.

Setting: Christian-Lauritzen-Institut, Ulm, IVF center Munich, Germany, and Department of General Biology, University of Siena, Siena, Italy.

Patient(s): Forty men with idiopathic oligospermia, asthenospermia, or teratozoospermia. I

Interventions(s): Twenty eight of the patients received acupuncture twice a week over a period of 5 weeks. The samples from the treatment group were randomized with semen samples from the 12 men in the untreated control group.

Main Outcome Measure(s): Quantitative analysis by transmission electron microscopy (TEM) was used to evaluate the samples, using the mathematical formula based on submicroscopic characteristics.

Result(s): Statistical evaluation of the TEM data showed a statistically significant increase after acupuncture in the percentage and number of sperm without ultrastructural defects in the total ejaculates. A statistically significant improvement was detected in acrosome position and shape, nuclear shape, axonemal pattern and shape, and accessory fibers of sperm organelles. However, specific sperm pathologies in the form of apoptosis, immaturity, and necrosis showed no statistically significant changes between the control and treatment groups before and after treatment.

Conclusion(s): The treatment of idiopathic male infertility could benefit from employing acupuncture. A general improvement of sperm quality, specifically in the ultrastructural integrity of spermatozoa, was seen after acupuncture, although we did not identify specific sperm pathologies that could be particularly sensitive to this therapy.

A Pilot Study Evaluating the Combination of Acupuncture with Sildenafil on Endometrial Thickness

Yu W et.al. Presented at the Pacific Coast Reproductive Society Annual Conference 2007

This small pilot study examined the effect of Viagra and acupuncture on the uterine linings of women who had a history of thin linings (<8mm) in previous IVF cycles (including patients who had previously used Viagra alone). They used the above mentioned protocols which improve blood flow to the ovaries and uterus. The researchers found that after acupuncture treatment the thickness of the lining improved to 10 mm or more in all participating patients



Abstract

Endometrial thickness has been shown to be an important prognostic factor of successful embryo implantation. If the endometrial thickness is less than 9 mm there is a significant reduction in live birth rates. Though there is conflicting data, preliminary evidence suggests that the administration of vaginal Sildenafil can markedly improve endometrial thickness and result in increased live IVF births.

Our clinical observations are consistent with this. However, other clinics report inconsistent results. Therefore, we hypothesized that the difference in response between clinics may involve other factors. When we looked into this, we found that many of our patients were simultaneously receiving acupuncture treatments.

Studies on acupuncture have demonstrated positive effects on implantation rates, ongoing pregnancy rates and the number of live births. Acupuncture has also been shown, via measurements of pulsatility index, to significantly increase blood flow to the uterus. Decreases in pulsatility index have been shown to significantly improve pregnancy rates.

Researchers have also found that acupuncture has direct effects on the endometrium. Some of these include increases in progesterone receptor concentration, a reduction in COX-2, and an increase in the activity of nitric oxide synthase.

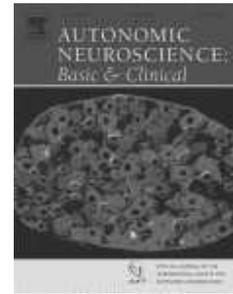
Therefore, the purpose of our investigation was to evaluate the effects of combining acupuncture and Sildenafil suppositories on endometrial lining.

Results: All four subjects achieved endometrial lining thickness of greater than or equal to 10 mm following the administration of the combination of acupuncture and Sildenafil: including one patient whose lining did not exceed 5 mm in a previous cycle. Another patient, who had not responded to Sildenafil alone in a prior IVF cycle, responded to the combination of Sildenafil and acupuncture. We also noted that endometrial thickness in most patients continued to increase post-hCG administration.

Conclusions: This pilot study is consistent with previous reports that acupuncture improves uterine lining measurements over previous cycles. This preliminary data supports the potential for a synergistic action between acupuncture and Sildenafil. We hypothesize these effects may be due to acupuncture's ability to upregulate nitric oxide synthase. However, we cannot rule out other mechanisms of action since acupuncture has also been shown to affect many other parameters. The results of this preliminary data may also suggest a role for a similar combination in treating erectile dysfunction. Further testing and data is necessary to verify these results.

Ovarian Blood Flow Responses to Electro-Acupuncture Stimulation at Different Frequencies and Intensities in Anaesthetized Rats

*Stener-Victorin E et al Autonomic Neuroscience 2003, Vol 108, Issues 1-2, Pg 50-55
Autonomic Neuroscience*



The blood flow to the ovaries has also been shown to be enhanced by acupuncture by the same researchers. This study was done on anaesthetized rats, however we can assume a similar mechanism will operate in women.

Abstract

The purpose of the present study was to investigate changes in ovarian blood flow (OBF) in response to electro-acupuncture (EA) stimulation at different frequencies and intensities in anaesthetized rats. Whether the ovarian sympathetic nerves were involved in OBF responses was elucidated by severance of the ovarian sympathetic nerves. In addition, how changes in the systemic circulation affected OBF was evaluated by continuously recording blood pressure. OBF was measured on the surface of the left ovary using laser Doppler flowmeter. Acupuncture needles with a diameter of 0.3 mm were inserted bilaterally into the abdominal and the hindlimb muscles and connected to an electrical stimulator.

Two frequencies—2 Hz (low) and 80 Hz (high)—with three different intensities—1.5, 3, and 6 mA—were applied for 35 s. Both low- and high-frequency EA at 1.5 mA and high-frequency EA at 3 mA had no effect on OBF or mean arterial blood pressure (MAP). Low-frequency EA at 3 and 6 mA elicited significant increases in OBF. In contrast, high-frequency EA with an intensity of 6 mA evoked significant decreases in OBF, followed by decreases in MAP. After severance of the ovarian sympathetic nerves, the increases in the OBF responses to low-frequency EA at 3 and 6 mA were totally abolished, and the responses at 6 mA showed a tendency to decrease, probably because of concomitant decreases in MAP.

The decreased OBF and MAP responses to high-frequency EA at 6 mA remained after the ovarian sympathectomy, and the difference in the responses before and after ovarian sympathectomy was nonsignificant.

In conclusion, the present study showed that low-frequency EA stimulation increases OBF as a reflex response via the ovarian sympathetic nerves, whereas high-frequency EA stimulation decreases OBF as a passive response following systemic circulatory changes.

Reduction of Blood Flow Impedance in the Uterine Arteries of Infertile Women with Electro-Acupuncture

Stener-Victorin E, et al Hum Reprod 1996; 11: 1314-1317.

Human Reproduction

Previous studies have shown that reduced blood flow in the uterine arteries is associated with a decreased pregnancy rate following IVF-embryo transfer. This study reported in *Human Reproduction* (the official journal of the European Society of Human Reproduction and Embryology) shows that after 8 acupuncture treatments blood flow to the uterus was markedly increased. Research carried out by one group of IVF clinics in California has shown that using this protocol to increase blood flow to the uterus, combined with acupuncture on the day of transfer has resulted in a significant improvement in pregnancy rates.

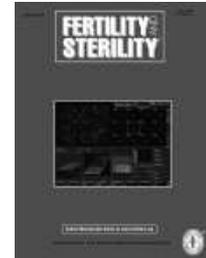


Abstract

In order to assess whether electro-acupuncture (EA) can reduce a high uterine artery blood flow impedance, 10 infertile but otherwise healthy women with a pulsatility index (PI) ≥ 3.0 in the uterine arteries were treated with EA in a prospective, non-randomized study. Before inclusion in the study and throughout the entire study period, the women were down-regulated with a gonadotrophin-releasing hormone analogue (GnRHa) in order to exclude any fluctuating endogenous hormone effects on the PI. The baseline PI was measured when the serum oestradiol was ≤ 0.1 nmol/l, and thereafter the women were given EA eight times, twice a week for 4 weeks. The PI was measured again closely after the eighth EA treatment, and once more 10–14 days after the EA period. Skin temperature on the forehead (STFH) and in the lumbosacral area (STLS) was measured during the first, fifth and eighth EA treatments. Compared to the mean baseline PI, the mean PI was significantly reduced both shortly after the eighth EA treatment ($P < 0.0001$) and 10–14 days after the EA period ($P < 0.0001$). STFH increased significantly during the EA treatments. It is suggested that both of these effects are due to a central inhibition of the sympathetic activity.

Immunological Changes and Stress are Associated with Different Implantation Rates in Patients Undergoing In-vitro Fertilization–Embryo Transfer

*Gallinelli A et al, 2001 Fertil Steril 76, 1, 85
Fertility and Sterility*



This study examines the effect of stress on embryo transfer and explores its impact via the immune system. The researchers conclude that stress is associated with high amounts of activated T cells in the peripheral blood which is in turn associated with a reduced implantation rate in women undergoing IVF-ET. The subject of regulation of T cells by acupuncture is something we are examining currently and is one of the hypothesized mechanisms by which acupuncture may increase implantation in some women

Abstract

Objective: To evaluate the possible correlation between immunological changes and implantation rates in patients who undergo in vitro **fertilization–embryo** transfer (IVF-ET).

Design: Controlled clinical study.

Setting: University hospital.

Patient(s): Forty infertile women undergoing IVF-ET.

Intervention(s): Stroop Color Word (CW) test, State-Trait Anxiety Inventory (STAI) test, blood sampling.

Main Outcome Measure(s): Heart rate and systolic and diastolic blood pressure responses to Stroop CW; circulating T, B, T-helper (CD4), and T-suppressor (CD8) lymphocytes.

Result(s): The total number of T lymphocytes increased significantly during superovulation, resulting in significantly higher levels in subjects achieving embryo implantation than in those showing a failure of implantation. An opposite trend was observed for the activated T cells. The number of T-helper lymphocytes and the T-helper/T-suppressor ratio showed a significant increase from baseline to the time of pick-up only in patients with implantation.

Conclusion(s): A prolonged condition of stress, which causes a decreased ability to adapt and a transitory anxious state, is associated with high amounts of activated T cells in the peripheral blood. Such a condition, in turn, is associated with a reduced implantation rate in women undergoing IVF-ET.

The Relationship Between Mental Work and Threatened Abortion

Huang Zhi Ying, 2002 Jnl Huaihai Medicine, Issue 1

Journal of Huaihai Medicine

Although some fine detail may have been lost in translation, this trial indicates that stress (mental work) increases the risk of miscarriage

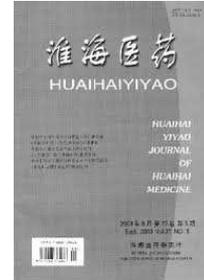
Abstract

Objective: To investigate the relationship between mental work and threatened abortion.

Methods: Pregnant women(620 cases, 1982~1999) were divided into mental worker and non mental worker groups. The incidence of threatened abortion was compared in the two groups.

Results: The incidence of threatened abortion was found to be significantly higher in the mental worker group(135 cases,38%)than that in the non mental worker group(40 cases,15%, P 0.01). The higher incidence of threatened abortion was found in the older mental worker group(P 0.05).

Conclusion: The nervous mental work is significant associated with threatened abortion.

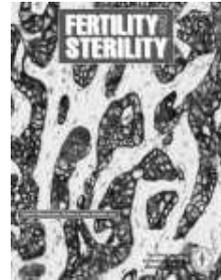


The Effect of Medical Clowning on Pregnancy Rates After In-vitro Fertilization and Embryo Transfer

Friedler S et al, Fertility and Sterility 2011, Vol 95, Issue 6 , Pg 2127

Fertility and Sterility

Dr. Friedler and colleagues tracked 219 women undergoing IVF treatment and, over a period of a year, treated half of them to a medical clown's 15-minute routine of jokes, magic tricks and other clowning immediately after their embryos were implanted. Those women who's stress was relieved with a good laugh after their transfer fell pregnant more often than did the control group.



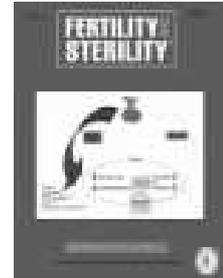
Abstract

This experimental prospective quasi-randomized study examining the impact of a medical clowning encounter after embryo transfer (ET) after in vitro fertilization (IVF) found that the pregnancy rate in the intervention group was 36.4%, compared with 20.2% in the control group (adjusted odds ratio, 2.67; 95% confidence interval, 1.36–5.24). Medical clowning as an adjunct to IVF-ET may have a beneficial effect on pregnancy rates and deserves further investigation.

Effectiveness of Psychosocial Group Intervention for Reducing Anxiety in Women Undergoing In-vitro Fertilization: A Randomized Controlled Study

*Chan CH et al, Fertil Steril. 2006 Feb;85(2):339-46.
Fertility and Sterility*

A group of researchers from Hong Kong hypothesized that women who received certain interventions would experience a lower level of anxiety during the IVF treatment and therefore have better mental adjustment and psychosocial functioning during IVF. This programme includes instruction on principles of Chinese medicine emphasizing body-mind harmony and stress reduction techniques including Tai qi and meditation. However it did not include acupuncture. They found that anxiety was significantly reduced in the women who followed the programme.



Abstract

Objective: To evaluate the effect of the Eastern Body-Mind-Spirit (EBMS) group intervention on anxiety-reduction of Chinese women undergoing IVF.

Design: Randomized controlled study.

Setting: Tertiary assisted reproduction unit.

Participant(s): Two hundred twenty-seven women undergoing their first cycle of IVF treatment.

Intervention(s): The intervention group (n = 69) received four sessions of EBMS group counseling, while the control group (n = 115) did not receive any intervention.

Main Outcome Measure(s): State-Trait Anxiety Inventory.

Result(s): Compared with the control group, the intervention group had a significant drop in State Anxiety mean score following intervention. A comparable number of embryos were transferred for each group, but there was a nonsignificant trend of a higher pregnancy rate in the intervention group.

Conclusion(s): The Eastern Body-Mind-Spirit group intervention approach effectively reduces the anxiety level of women undergoing IVF treatment.

Stressful Life Events are Associated with a Poor In-vitro Fertilization (IVF) Outcome: A Prospective Study
Ebbesen S.M.S. Hum Reprod 2009;24(9):2173-2182.
Human Reproduction

This study examined the outcomes of IVF cycles for 800 women and found that the chance of success was related to chronic stress levels. They surmised that chronic stress levels may have a negative effect on follicle development in an IVF cycle. Since acupuncture has been shown to reduce stress hormones this may be the mechanism behind its benefit for IVF patients.



Abstract

Background: There is preliminary evidence to suggest an impact of stress on chances of achieving a pregnancy with in-vitro fertilization (IVF). The majority of the available research has focused on stress related to infertility and going through IVF-treatment, and it is still unclear whether non-fertility-related, naturally occurring stressors may influence IVF pregnancy chances. Our aim was to explore the association between IVF-outcome and negative, i.e. stressful, life-events during the previous 12 months.

Methods: Prior to IVF, 809 women (mean age: 31.2 years) completed the List of Recent Events (LRE) and questionnaires measuring perceived stress and depressive symptoms.

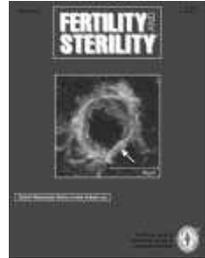
Results: Women who became pregnant reported fewer non-fertility-related negative life-events prior to IVF (Mean: 2.5; SD: 2.5) than women who did not obtain a pregnancy (Mean: 3.0; SD: 3.0) ($t(465.28) = 2.390, P = 0.017$). Logistic regression analyses revealed that the number of negative life-events remained a significant predictor of pregnancy (OR: 0.889; $P = 0.02$), when controlling for age, total number of life-events, perceived stress within the previous month, depressive symptoms, and relevant medical factors related to the patient or treatment procedure, including duration of infertility, number of oocytes retrieved and infertility etiology. Mediation analyses indicated that the association between negative life events and IVF pregnancy was partly mediated by the number of oocytes harvested during oocyte retrieval.

Conclusion: A large number of life-events perceived as having a negative impact on quality of life may indicate chronic stress, and the results of our study indicate that stress may reduce the chances of a successful outcome following IVF, possibly through psychobiological mechanisms affecting medical end-points such as oocyte retrieval outcome.

Stress reduces Conception Probabilities Across the Fertile Window: Evidence in Support of Relaxation

Buck Louis GM et al, Fertil Steril. 2011, 95, 7, pg 2184 - 2189

Fertility and Sterility



While this study did not involve IVF patients its conclusions nevertheless have relevance to women trying to fall pregnant with IVF. The study showed a clear relationship with higher stress levels and reduced conception rates. This may be one of the ways that acupuncture, which reduces stress hormones, can improve fertility.

Abstract

Objective: To assess salivary stress biomarkers (cortisol and alpha-amylase) and female fecundity.

Design: Prospective cohort design.

Setting: United Kingdom.

Patient(s): 274 women aged 18 to 40 years who were attempting pregnancy.

Intervention(s): Observation for six cycles or until pregnancy: women collected basal saliva samples on day 6 of each cycle, and used fertility monitors to identify ovulation and pregnancy test kits for pregnancy detection.

Main Outcome Measure(s): Salivary cortisol (µg/dL) and alpha-amylase (U/mL) concentration measurements; fecundity measured by time-to-pregnancy and the probability of pregnancy during the fertile window as estimated from discrete-time survival and Bayesian modeling techniques, respectively.

Result(s): Alpha-amylase but not cortisol concentrations were negatively associated with fecundity in the first cycle (fecundity odds ratio = 0.85; 95% confidence interval 0.67, 1.09) after adjusting for the couples' ages, intercourse frequency, and alcohol consumption. Statistically significant reductions in the probability of conception across the fertile window during the first cycle attempting pregnancy were observed for women whose salivary concentrations of alpha-amylase were in the upper quartiles in comparison with women in the lower quartiles (highest posterior density: -0.284; 95% interval -0.540, -0.029).

Conclusion(s): Stress significantly reduced the probability of conception each day during the fertile window, possibly exerting its effect through the sympathetic medullar pathway.

The Relationship Between Perceived Stress, Acupuncture, and Pregnancy Rates Among IVF Patients: A Pilot Study

*Balk J et al, Complement Ther Clin Pract. 2010 Aug; 16(3):154-7.
Complementary Therapies in Clinical Practice*

These investigators aimed to determine if acupuncture affects the levels of perceived stress at the time of embryo transfer, and whether either acupuncture or changes in stress levels play a role in the success rate in IVF. The patients who received acupuncture in this study had both higher rates of pregnancy, and lower levels of stress both before and after embryo transfer. They postulated that reducing stress at the time of embryo transfer could result in less vasoconstriction and improved uterine receptivity



Abstract

The aim of this paper was to determine the effect of acupuncture on perceived stress levels in women on the day of embryo transfer (ET), and to determine if perceived stress levels at embryo transfer correlated with pregnancy rates. The study was an observational, prospective, cohort study based at the University IVF center.

Patient(s): 57 infertile patients undergoing IVF or IVF/ICSI.

Interventions(s): Patients were undergoing Embryo Transfer with or without acupuncture as part of their standard clinical care.

Main outcome measure(s): Perceive Stress Scale scores, pregnancy rates.

Result(s): women who received this acupuncture regimen achieved pregnancy 64.7%, whereas those without acupuncture achieved pregnancy 42.5%. When stratified by donor recipient status, only non-donor recipients potentially had an improvement with acupuncture (35.5% without acupuncture vs. 55.6% with acupuncture). Those who received this acupuncture regimen had lower stress scores both pre-ET and post-ET compared to those who did not. Those with decreased their perceived stress scores compared to baseline had higher pregnancy rates than those who did not demonstrate this decrease, regardless of acupuncture status.

Conclusions(s): The acupuncture regimen was associated with less stress both before and after embryo transfer, and it possibly improved pregnancy rates. Lower perceived stress at the time of embryo transfer may play a role in an improved pregnancy rate.

A Randomized Double Blind Comparison of Real and Placebo Acupuncture in IVF Treatment

So et al, Hum Reprod. 2009 Feb;24(2):341-8.

Human Reproduction

This paper which was included above amongst those describing the Embryo transfer trials, also investigated cortisol and anxiety levels before and after acupuncture was administered at precise points with either needles which penetrate the skin or "placebo" needles which prick the points but do not penetrate. No matter how the acupuncture was administered cortisol and perceived anxiety were significantly reduced after the treatment.



Abstract

Background: Acupuncture has been used during IVF treatment as it may improve outcome, however, there are concerns about the true efficacy of this approach. This randomized double blind study aimed to compare real acupuncture with placebo acupuncture in patients undergoing IVF treatment.

Method: On the day of embryo transfer (ET), 370 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received 25 min of real or placebo acupuncture before and after ET. The endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were evaluated before and after real and placebo acupuncture.

Results: The overall pregnancy rate was significantly higher in the placebo acupuncture group than that in the real acupuncture group (55.1 versus 43.8%, respectively, $P = 0.038$; Common odds ratio 1.578 95% confidence interval 1.047–2.378). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and subendometrial vascularity, serum cortisol concentration and the anxiety level were observed following both real and placebo acupuncture, although there were no significant differences in the changes in all these indices between the two groups.

Conclusion: Placebo acupuncture was associated with a significantly higher overall pregnancy rate when compared with real acupuncture. Placebo acupuncture may not be inert.

An Assessment of the Demand and Importance of Acupuncture to Patients of a Fertility Clinic During Investigations and Treatment

*Hinks J and Coulson C, Hum Fert 2010 Vol 13, S1 Pg 3-21
Human Fertility*



These authors working in a fertility clinic in the UK surveyed 200 patients who attended the clinic in August 2009. They discovered that there was a clear demand for acupuncture and that acupuncture may be valuable to improve the general wellbeing of women during infertility investigations and treatments. They also felt that patient resilience may be increased by the use of acupuncture alongside their IVF treatment such that patients would persevere with increased numbers of ART (Assisted Reproductive Technologies) cycles, thereby increasing their ultimate chance of a successful pregnancy.

Abstract

An assessment of the demand and importance of acupuncture to patients of a fertility clinic during investigations and treatment

Julie Hinks & Catherine Coulson

North Bristol NHS Trust, Bristol, United Kingdom

Introduction: Despite a lack of studies clearly demonstrating clinical efficacy complementary medicine is frequently used by couples undergoing infertility treatment (Coulson 2005). In Bristol, acupuncture has become very popular among patients undergoing infertility treatment, thus this study sought to quantify this and examine the reasons why patients choose acupuncture.

Methods: Two hundred questionnaires were given to patients who attended the Bristol Centre for Reproductive Medicine (BCRM) for investigation or treatment of infertility in August 2009. Patients were asked to complete the questionnaire while waiting to see their doctor or nurse and 194 responses were returned. The questionnaires asked if patients had or wished to have acupuncture or other complementary medicine, and to indicate on a scale of one to ten (10 being the best) the relative importance of acupuncture in comparison to values such as pregnancy rates and continuity of care.

Results: Out of 58 respondents who use complementary medicine, 43 used acupuncture. 40 respondents use acupuncture regularly and 17 of those lived outside of Bristol. A further 52 respondents had considered using acupuncture. In terms of very high importance (score of 10) 135 respondents felt pregnancy rates scored 10, 84 felt having the same doctor scored 10, 71 scored 10 for having the same nurse, 31 felt in house acupuncture scored 10 and 21 scored 10 for other complementary medicine. Overall, 43 respondents felt acupuncture should be available at Bristol Centre for Reproductive Medicine. Thirty four respondents gave more importance to acupuncture than seeing the same doctor or nurse, and 32 deemed it equally important. In addition, 29 patients scored acupuncture as equally important to pregnancy rates and 5 scored acupuncture higher than pregnancy rates.

Discussion: Previous unpublished work at BCRM showed that 85% of the patients found the named nurse system important as a coping mechanism to support them by providing continuity of care through stressful treatment. The responses to the questionnaires indicate a clear demand for acupuncture and suggest that acupuncture may be valuable to improve the general wellbeing of women during infertility investigations and treatments. If acupuncture provides an effective coping mechanism, this could support patients to persevere with increased numbers of ART (Assisted Reproductive Technologies) cycles, thereby increasing their ultimate chance of a successful pregnancy.

Building Resilience: An Exploration of Women's Perceptions of the Use of Acupuncture as an Adjunct to IVF
De Lacey S, Smith C and Paterson C, BMC Complementary and Alternative Medicine 2009, 9:50
BioMed Central

Resilience is an interesting and important concept when applied to couples doing IVF.



Studies of acupuncture involving women dealing with chronic health issues have shown that women experienced relief of presenting symptoms but also increases in energy, increase in relaxation and calmness, reduction in the reliance of prescription drugs (such as analgesics), quicker healing from surgery and increased self awareness and well being. Such effects indicate a reduction of stress that in turn may diminish the number of treatment cycles needed for pregnancy to occur. But further, reducing the number of cycles a woman must undertake to reach her goal of motherhood reduces the overall cost of IVF.

Abstract

Background: In Vitro Fertilisation (IVF) is now an accepted and effective treatment for infertility, however IVF is acknowledged as contributing to, rather than lessening, the overall psychosocial effects of infertility. Psychological and counselling interventions have previously been widely recommended in parallel with infertility treatments but whilst in many jurisdictions counselling is recommended or mandatory, it may not be widely used. Acupuncture is increasingly used as an adjunct to IVF, in this preliminary study we sought to investigate the experience of infertile women who had used acupuncture to improve their fertility.

Methods: A sample of 20 women was drawn from a cohort of women who had attended for a minimum of four acupuncture sessions in the practices of two acupuncturists in South Australia. Eight women were interviewed using a semi-structured questionnaire. Six had sought acupuncture during IVF treatment and two had begun acupuncture to enhance their fertility and had later progressed to IVF. Descriptive content analysis was employed to analyse the data.

Results: Four major categories of perceptions about acupuncture in relation to reproductive health were identified: (a) Awareness of, and perceived benefits of acupuncture; (b) perceptions of the body and the impact of acupuncture upon it; (c) perceptions of stress and the impact of acupuncture on resilience; and (d) perceptions of the intersection of medical treatment and acupuncture.

Conclusion: This preliminary exploration, whilst confined to a small sample of women, confirms that acupuncture is indeed perceived by infertile women to have an impact to their health. All findings outlined here are reported cautiously because they are limited by the size of the sample. They suggest that further studies of acupuncture as an adjunct to IVF should systematically explore the issues of wellbeing, anxiety, personal and social resilience and women's identity in relation to sexuality and reproduction.

Understanding Women's Views Towards the use of Acupuncture While Undergoing IVF Treatment

Smith C and De Lacey S, 2008 In press

FSA conference 2008

This qualitative study found that most women who had acupuncture as an adjunct to IVF treatment reported increased well being, reduced anxiety and an increase in capacity to cope with the stresses of IVF and infertility treatments



Abstract

Aim: There is interest in the use of acupuncture as an adjunct to fertility treatment. this study aimed to examine women's attitudes and beliefs in relation to the use of acupuncture for enhancing fertility or as an adjunct to ART.

Results: Participants all expressed confidence in the ability of acupuncture to contribute to their reproductive decision in a positive way. They described acupuncture as an adjunct to pregnancy attempts that was positive since it gave them a sense of control and a strategy for improving their chances. Women were unable to locate acupuncture as a causative factor in a resulting pregnancy however all women described acupuncture as instrumental in an increased sense of well being, self confidence, emotional balance and reduced anxiety. All experienced increased resilience.

Conclusion: Acupuncture is an effective and low intensity procedure for increasing women's resilience in the repetitive and stress inducing time of pregnancy attempts, with or without medical treatment. The instrumental role of the acupuncture therapist in increasing resilience is a finding that has not emerged in previous studies and has implications for patient management.

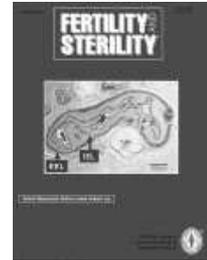
The Impact of Acupuncture on in Vitro Fertilization Outcome

Domar A et al Fertil Steril 2009 Vol 91 Issue 3 pg 723 - 6

Fertility and Sterility

One of the trials that investigated the effect of acupuncture on IVF pregnancy rates also collected data on the subjective experience of these women. The authors write “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”.

Nobody knows how exactly acupuncture might boost IVF success, Domar said, although she suggests that it has something to do with a woman's mental state at the time of embryo transfer.



Abstract

Objective: To replicate previous research on the efficacy of acupuncture in increasing pregnancy rates (PR) in patients undergoing IVF and to determine whether such an increase was due to a placebo effect. Design: Prospective, randomized, controlled, single blind trial.

Setting: Private, academically affiliated, infertility clinic.

Patient(s): One hundred fifty patients scheduled to undergo embryo transfer.

Intervention(s): Subjects were randomized to either the acupuncture or control group. Acupuncture patients received the protocol, as first described by Paulus and his colleagues, for 25 minutes before and after embryo transfer. Control subjects laid quietly. All subjects then completed questionnaires on anxiety and optimism. The IVF staff remained blind to subject assignment.

Main Outcome Measure(s): Clinical PRs, anxiety, optimism.

Result(s): Before randomization both groups had similar demographic characteristics including age and psychological variables. There were no significant differences in PRs between the two groups. 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.

Conclusion(s): The use of acupuncture in patients undergoing IVF was not associated with an increase in PRs but they were more relaxed and more optimistic.