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PUBLICATIONS

IVF

Complement Ther Med. 2011 Dec;19(6):319-31. doi: 10.1016/j.ctim. 2011.09.003. Epub 2011 Oct 5.

Efficacy of Traditional Chinese Herbal Medicine in the management of female infertility: a systematic review.

Ried K1, Stuart K.

Author information

1Discipline of General Practice, School of Population Health & Clinical Practice, The University of Adelaide, South Australia.

INCREASE OF SUCCESS RATE FOR WOMEN UNDERGOING EMBRYO TRANSFER BY TRANSCUTANEOUS ELECTRICAL ACUPOINT STIMULATION

(read more for below)

I. 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

October 2011

INCREASE OF SUCCESS RATE FOR WOMEN UNDERGOING EMBRYO TRANSFER BY TRANSCUTANEOUS ELECTRICAL ACUPOINT STIMULATION

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

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

**Correspondence: Ji-Sheng Han, M.D., Neuroscience Research Institute, Peking University, 38 Xueyuan Road, Beijing 100191, PR 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.

2>EFFICACY OF TRADITIONAL CHINESE HERBAL MEDICINE IN THE MANAGEMENT OF FEMALE INFERTILITY: A SYSTEMATIC REVIEW Efficacy of Traditional Chinese Herbal Medicine in the management of female infertility: A systematic review.

Ried K, Stuart K. October 05 2011

Source

Discipline of General Practice, School of Population Health & Clinical Practice, The University of Adelaide, South Australia 5005, Australia. 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. Metaanalysis 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 $60\pm12.5\%$ for CHM compared with $32\pm10\%$ 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.

Complement Ther Med. 2011 Dec;19(6):319-31. Epub 2011 Oct 5. Author:

Ried K, Stuart K. Publication Date: October 05 2011

Publisher:

Discipline of General Practice, School of Population Health & Clinical Practice, The University of Adelaide, South Australia 5005, Australia

>EFFECTS OF ACUPUNCTURE ON PREGNANCY RATES IN WOMEN UNDERGOING IN VITRO FERTILIZATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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

"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. 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 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.

Author:

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. Publication Date: 1-11-2012 Publisher: Fertility and Sterility

>COMMENTARY ON THE COCHRANE REVIEW OF ACUPUNCTURE AND ASSISTED CONCEPTION

Elisabet Stener-Victorin, RPT, PhD1,2,* and Eric Manheimer, MS3,* (2013). Manheimer, Eric, Daniëlle van der Windt, Ke Cheng, Kristen Stafford, Jianping Liu, Jayne Tierney, Lixing Lao, Brian M. Berman, Patricia Langenberg, and Lex M. Bouter. "The effects of acupuncture on rates of clinical pregnancy among women undergoing in vitro fertilization: a systematic review and meta-analysis." Human reproduction update

<u>4> Chinese herbal medicine for infertility with anovulation:</u> <u>a systematic review.ui Hong Zheng, M.D.; Ph.D.a, Guang</u> <u>Ying Huang, M.D., Ph.D.a; Ming Min Zhang, M.D., Ph.D.b;</u> <u>Wei Wang, M.D., Ph.D.c.</u>

<u>1-11-2012</u>

J Altern Complement Med. 2012 Dec;18(12):1087-100. doi: 10.1089/acm. 2011.0371.

Chinese herbal medicine for infertility with anovulation: a systematic review.

Tan L, Tong Y, Sze SC, Xu M, Shi Y, Song XY, Zhang TT. Source

YueYang Hospital of Integrative Chinese & Western Medicine Affiliated with Shanghai University of Traditional Chinese Medicine, Shang Hai, China.

Abstract

The aim of this systematic review is to assess the effectiveness and safety of Chinese herbal medicine (CHM) in treatment of anovulation and infertility in women. Eight (8) databases were extensively retrieved. The Chinese electronic databases included VIP Information, CMCC, and CNKI. The English electronic databases included AMED, CINAHL, Cochrane Library, Embase, and MEDLINE(®). Randomized controlled

trials using CHM as intervention were included in the study selection. The quality of studies was assessed by the Jadad scale and the criteria referred to Cochrane reviewers' handbook. The efficacy of CHM treatment for infertility with anovulation was evaluated by meta-analysis. There were 692 articles retrieved according to the search strategy, and 1659 participants were involved in the 15 studies that satisfied the selection criteria. All the included trials were done in China. Meta-analysis indicated that CHM significantly increased the pregnancy rate (odds ratio [OR] 3.12, 95% confidence interval [CI] 2.50-3.88)

and reduced the miscarriage rate (OR 0.2, 95% CI 0.10-0.41) compared to clomiphene.

In addition, CHM also increased the ovulation rate (OR 1.55, 95% CI 1.06-2.25) and improved the cervical mucus score (OR 3.82, 95% CI 1.78-8.21) compared to clomiphene, while there were no significant difference between CHM and clomiphene combined with other medicine. CHM is effective in treating infertility with anovulation. Also, no significant adverse effects were identified for the use of CHM from the studies included in this review. However, owing to the low quality of the studies investigated, more randomized controlled trials are needed before evidence-based recommendation regarding the effectiveness and safety of CHM in the management of infertility with anovulation can be provided. PMID: 23198826 [PubMed - indexed for MEDLINE]

5>EFFECT OF ACUPUNCTURE ON THE PREGNANCY RATE IN EMBRYO TRANSFER AND MECHANISMS: A RANDOMIZED AND CONTROLLED STUDY

10 IVF patients were randomly placed in groups that received real acupuncture or a 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), intracytoplasmatic 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.

Author: Zhang M et al Publication Date: 2003, Jan 23 (1): 3 - 5 Publisher: Chinese Acupuncture and Moxabustion

6> CHANGES IN SERUM CORTISOL AND PROLACTIN ASSOCIATED WITH ACUPUNCTURE DURING IVF

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.

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

Listen to a wonderful podcast about his research and how it can help you have a baby

Click this link: <u>http://www.creatingafamily.org/radioshow.html</u>. There's a little box in the center of the page that says "blogtalkradio" and the show title, "Acupuncture, Traditional Chinese Medicine."

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 Sterile 2008;-:---. 2008 by American Society for Reproductive Medicine.)

Magarelli, PC, D Cridennda, M Cohen 2009

<u>7 >ACUPUNCTURE & IVF POOR RESPONDERS: A CURE?</u>

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

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 Gonadatrophin 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.

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.

Author: Magarelli P, Cridennda D Publication Date: 2004 Publisher: 81 Suppl 3 S20 Fertility and Sterility

<u>ACUPUNCTURE AND BLOOD FLOW</u> <u>Stener-Victorin E, et al</u> <u>1996</u>

REDUCTION OF BLOOD FLOW IMPEDANCE IN THE UTERINE ARTERIES OF INFERTILE WOMEN WITH ELECTRO-ACUPUNCTURE

Previous studies have shown that reduced blood flow in the uterine arteries is associated with a decreased pregnancy rate following IVFembryo transfer. This study reported in Human Reproduction (the official journal of the European Society of Human Reproduction and Embryology) shows that after eight 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. **See also:**

Acupuncture & IVF Poor Responders: A Cure?

Acupuncture and IVF: State of the ART of Integrative Research 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) \geq 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 \leq 0.1 nmol/1, 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

<u>treatment, and once more 10–14 days after the EA period. Skin</u> <u>temperature on the forehead (STFH) and in the lumbosacral area</u> (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.

ELECTROACUPUNCTURE REDUCES UTERINE ARTERY BLOOD FLOW IMPEDANCE IN INFERTILE WOMEN

<u>Ming H et al</u> 2009 Vol 48, Issue 2, Pages 148-151 <u>Read more</u>

<u>A PILOT STUDY EVALUATING THE COMBINATION OF</u> <u>ACUPUNCTURE WITH SILDENAFIL ON ENDOMETRIAL THICKNESS</u> <u>Yu W et.al</u> 20

ACUPUNCTURE AND STRESS AND FERTILITY

1>BUILDING RESILIENCE: AN EXPLORATION OF WOMEN'S PERCEPTIONS OF THE USE OF ACUPUNCTURE AS AN ADJUNCT TO IVF

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 well-being, anxiety, personal and social resilience, and women's identity in relation to sexuality and reproduction.

http://www.biomedcentral.com/1472-6882/9/50

2>THE IMPACT OF ACUPUNCTURE ON IN VITRO FERTILIZATION OUTCOMES Domar A et al 2009

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." Domar said nobody knows how exactly acupuncture might boost IVF success, 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): 150 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.

<u>3>UNDERSTANDING WOMEN'S VIEWS TOWARDS THE USE OF</u> <u>ACUPUNCTURE WHILE UNDERGOING IVF TREATMENT</u>

Smith C and De Lacey S 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 contibute 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 though all women described acupuncture as instrumental in an increased sense of well-being, selfconfidence, 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 RELATIONSHIP BETWEEN MENTAL WORK AND THREATENED ABORTION Huang Zhi Ying

Huang Zhi Ying 2002 Read more

STRESSFUL LIFE EVENTS ARE ASSOCIATED WITH A POOR IN VITRO FERTILIZATION (IVF) OUTCOME: A PROSPECTIVE STUDY Ebbesen S.M.S. 2009 Read more

STRESS REDUCES CONCEPTION PROBABILITIES ACROSS THE FERTILE WINDOW: EVIDENCE IN SUPPORT OF RELAXATION Buck Louis GM et al 2011 Read more

IMMUNOLOGICAL CHANGES AND STRESS ARE ASSOCIATED WITH DIFFERENT IMPLANTATION RATES IN PATIENTS UNDERGOING IN VITRO FERTILIZATION–EMBRYO TRANSFER

Gallinelli A et al 2001 <u>Read more</u>

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 2009

BUILDING RESILIENCE: AN EXPLORATION OF WOMEN'S PERCEPTIONS OF THE USE OF ACUPUNCTURE AS AN ADJUNCT TO IVF

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.

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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.

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http://www.biomedcentral.com/1472-6882/9/50

Author:

De Lacey S, Smith C and Paterson C **Publication Date:** 2009 **Publisher:** BMC Complementary and Alternative Medicine **Condition Term:** IVF/IUI Services Stress Section:

Stress and Fertility

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.

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 well-being 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 treatments (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 1-10 (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 of these 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 felt having the same nurse scored 10, 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, 34 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.

Balk J et al 2010 Aug;16(3):154-7)

STRESS AND FERTILITY

Section: Complement Ther Clin Pract. Author manuscript; available in PMC Aug 1, 2011.

Published in final edited form as: Complement Ther Clin Pract. Aug 2010; 16(3): 154-157. Published online Dec 24, 2009. doi: 10.1016/j.ctcp.2009.11.004

PMCID: PMC2904299 NIHMSID: NIHMS164753

The relationship between perceived stress, acupuncture, and pregnancy rates among IVF patients: a pilot study

Judith Balk, MD MPH, Janet Catov, PhD, Brandon Horn, LAc, JD, PhD, Kimberly Gecsi, MD, and Anthony Wakim, MD Author information
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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.

Keywords: Acupuncture, infertility, perceived stress

Introduction

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Acupuncture is a therapy of inserting, manipulating and retaining very fine needles in specific "acupoints". It appears to be helpful in improving the success rate of assisted reproductive techniques, although not all studies are positive 1-5. A recent systematic review and meta-analysis concluded that preliminary evidence suggests a role for acupuncture in infertility<u>6</u>. The mechanisms by which acupuncture affects pregnancy rates are not known.

Currently at our institution (Magee-Womens Hospital), women are given the option to undergo acupuncture at the time of embryo transfer and/or earlier during the IVF cycle, and patients either self-select acupuncture or they self-select to not have acupuncture. In this pilot study, we compare subjects undergoing embryo transfer without acupuncture to those who have embryo transfer in conjunction with acupuncture to evaluate whether acupuncture improves stress levels, and whether either acupuncture or stress levels are associated with improved pregnancy rates.

The Perceived Stress Scale, which is a 10-item questionnaire is a valid and reliable tool that measures the degree to which situations in one's life are appraised as stressful7. The PSS is sensitive to both stress from expectations concerning future events and to chronic stress deriving from ongoing life circumstances, both of which are potentially relevant for the IVF population. We hypothesized that an increased perception of stress at the time of embryo transfer could lead to lower IVF success rates, potentially through a sympathetic activation pathway, although the mechanism was not specifically studied in this pilot study.

Stress and anxiety are very common in infertility patients, especially those undergoing IVF8. Anxiety and depression are considered causes of early drop-out after the first IVF cycle and are related to lower pregnancy rates 9–11. Acute and chronic stress in patients undergoing assisted reproduction affects biologic end points (i.e. number of oocytes retrieved and fertilized), as well as pregnancy, live birth delivery, birth weight and multiple gestations12, 13. Thus, reducing stress and anxiety can be helpful in IVF patients. True acupuncture decreases anxiety levels when compared to sham acupuncture14, {Kober, 2003 #38}.

We 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. We chose to measure stress levels at the time of embryo transfer for several reasons. We postulated that reducing stress at the time of embryo transfer could

result in less vasoconstriction and improved uterine receptivity. Embryo transfer data collection was logistically feasible; in addition, because all participants were receiving the same embryo transfer procedure, the study groups were fairly homogenous, with one key difference between groups being whether or not acupuncture was performed. To keep the group receiving acupuncture homogenous, the protocol used for all acupuncture patients was the same, that described by Paulus, which involves acupuncture before and after embryo transfer, on the day of embryo transfer1. This same protocol was found to improve pregnancy rates in a later study by a different investigator15. We chose this protocol because we have found, both within the University of Pittsburgh, and in the community, this is the common acupuncture approach used in conjunction with embryo transfer. Paulus notes that he chose the points based on "acupuncture points that relax the uterus according to the principles of TCM."

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Materials and methods

This study was an observational prospective cohort study comparing stress levels of In Vitro Fertilization (IVF) patients either receiving acupuncture or not receiving acupuncture on the day of their embryo transfer. The inclusion criteria were that the subjects were receiving an embryo transfer in the Reproductive Endocrinology and Infertility (REI) office at Magee-Womens Hospital of the University of Pittsburgh Medical Center. The only exclusion criterion was that gestational carriers, ie surrogates, were not enrolled. All acupuncture was conducted by a physician acupuncturist and licensed in the state of Pennsylvania. The study was approved by the University of Pittsburgh Institutional Review Board prior to initiating the study. Study procedures conform to the Declaration of Helsinki for Medical Research involving Human Subjects.

A total of 57 subjects were recruited for this study. The REI nurses and physicians approached patients regarding the study upon arrival to the office on the day of the ET. When patients agreed to participate, they signed an informed consent form prior to initiation of any study procedures. The nurses and physicians explained that the study involved completing a 10-item questionnaire twice, once before ET and once after ET. All patients undergoing ET were eligible with the exception of gestational carriers. As part of each patient's IVF protocol, patients selfselected into the acupuncture group or to the non-acupuncture group prior to the day of ET. There were no attempts to manipulate either the

self-selection of acupuncture or the IVF protocols as part of this research study.

After informed consent was signed, the patient was given the Perceived Stress Scale7 to fill out. Those patients in the acupuncture group completed the Perceived Stress Scale (PSS), and then had acupuncture for 25 minutes before undergoing embryo transfer. The acupuncture regimen used in this study is described in Paulus et al, 20021. Those patients in the non-acupuncture group completed the Perceived Stress Scale and then rested for 25 minutes prior to embryo transfer. All patients underwent embryo transfer using their physician's standard procedure.

Once embryo transfers were completed, patients returned to the recovery room. After emptying their bladders, they either received 25 more minutes of acupuncture according to the Paulus protocol<u>1</u> followed by completion of the PSS, or they were given the PSS to complete if they were not receiving acupuncture. All patients were at bedrest for 30 minutes after ET. Once the questionnaire was completed it was returned to the nurse and placed in an envelope marked with the patient's study number and placed with her previously completed stress scale and informed consent. These were kept in a locked file cabinet.

Statistical analysis

The primary outcome variable is the change in stress level before and after embryo transfer, as measured by the perceived stress scale (PSS), described in Cohen et al, 19837. A change of 7.5 on the PSS is considered to be clinically significant. Our sample size analysis determined that with an alpha of 0.05 and a beta of .2 (80% power), we needed twenty subjects in each group to detect this level of change. In order to recruit both acupuncture and non-acupuncture patients during the same time period, without specifically selecting for the acupuncture group, we enrolled subjects until we had 20 subjects in the acupuncture group. To enroll 20 acupuncture subjects, we projected that roughly 35 non-acupuncture subjects would need to be enrolled, for a total enrollment of approximately 55. We stopped enrollment when 20 acupuncture subjects were enrolled, regardless of the number of control subjects.

We defined good quality embryos as those that were 6cell, grade A, and better, as determined by the embryologists' standard clinical practice. Poor prognosis embryos were those that were 6B or worse. Endometrial

lining thickness was the last ultrasound measurement prior to embryo transfer. All transfers were on day 3.

Differences in the mean score for the Perceived Stress Scale in each group (acupuncture and non-acupuncture) before and after embryo transfer were evaluated using paired t-tests. The chi-squared test was used to evaluate the pregnancy rates between the two groups. Pearson correlation coefficients were used to compare continuous variables, such as the relationship between age and stress scores. We used a t-test to compare stress levels between those who achieved pregnancy and those who did not, and multivariate logistic regression was used to evaluate the relation between acupuncture and stress to pregnancy rates independent of relevant covariates.

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Results

A total of 57 women were included in the study. Two women had more than one embryo transfer; we included only the cycle with acupuncture or the last cycle if all were conducted with acupuncture. The characteristics of the subject population are displayed in <u>Table I</u>.

Table 1			
Characteristics of women w	with and without acupuncts	ine, mean (SD) or n ((percent)
	No acupuncture (n=40)	Acupuncture (n=17)	p- value*
Age (years)	35.8 (4.4)	37.5 (5.4)	0.21
Failed cycles (no.)	1.6 (1.7)	1.8 (1.2)	0.70
Uterine lining	11.0 (3.1)	9.9 (2.8)	0.20
Nulliparous	27 (67.5)	9 (52.9)	0.29
Good embryo quality	19 (47.5)	12 (75.0)	0.06
Donor egg	9 (22.5)	0 (47.1)	0.06
Number of embryos transferred	2.6 (0.7)	2.4 (0.9)	0.43
Same	17 (42.5)	11 (64.7)	0.13
S and	17.3 (6.5)	132136	

Table 1

Characteristics of women with and without acupuncture, mean (SD) or n (percent)

Women with acupuncture tended to be older compared to women with no acupuncture. They were more likely to have had donor eggs transferred which, as expected, tended to be of better quality. Women with acupuncture at the time of embryo transfer had lower levels of perceived stress before and after acupuncture compared to women with no acupuncture. Both groups had less perceived stress after embryo transfer, but there was no difference in the mean change in scores

between the two groups (p=0.66) nor in the likelihood of having a reduction in stress >= 2 points (p=0.76). Age was the only factor that was significantly correlated with the mean change in perceived stress scores (r=-0.28, p=0.04), as shown in Figure I. In these data, stress levels decreased as maternal age increased. Differences in stress according to acupuncture group, however, were unchanged when adjusted for maternal age.

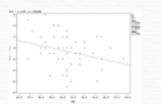


Figure I Relations hip between change in stress score and age (r=-0.28, p=0.04)

Overall, 28 women (49.1%) achieved pregnancy following embryo transfer. Women with acupuncture tended to achieve pregnancy more often compared to women without acupuncture (64.7% vs. 42.5%, p=0.13). There was no difference, however, in the change in perceived stress among women who did and did not achieve pregnancy (-0.93 vs. -0.45, p=0.52). However, women with perceived stress scores that were reduced by 2 or more points compared to baseline (21% of the study group) had higher pregnancy rates than those with more modest reductions or increases in perceived stress (75.0% vs. 42.2%, p=0.04). Although precision was compromised when results were stratified by

donor egg status, the effect of acupuncture on pregnancy rates appeared to be limited to those without donor eggs (35.5% without acupuncture vs. 55.6% with acupuncture, p=0.28; <u>Table 2</u>). In addition, stress reduction in women with or without acupuncture was not different according to donor egg status.

regnancy rates and stress reduction among women with and without as institled by donor egg status				
	No acupuncture	Acupuncture	p-value [*]	
No donor egg (n=+0)				
Achieved pregnancy	11/01 (35.5)	5/9 (55.6)	0.28	
Stress reduction >==2	5/31 (16.1)	2/9 (22.2)	0.67	
Donor egg (n=17)				
Achieved pregnancy	6/9 (95.7)	6/8 (75.0)	0.71	
Stress reduction >=-2	3/9 (33.3)	2/8 (25.0)	0.71	

Table 2

Pregnancy rates and stress reduction among women with and without acupuncture, stratified by donor egg statusAcupuncture was associated with a 3.0 fold increased rate of pregnancy (95% CI 0.8, 8.0). Although estimates were quite imprecise due to limited sample size, this relation appeared to be independent of embryo quality, uterine lining thickness, maternal age and changes in perceived stress measured before and after embryo transfer (OR 3.4, 95% CI 0.6, 18.6).

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Discussion

Overall, our study confirms that the chosen acupuncture regimen appears to increase pregnancy rates in IVF patients. When we model the relationship of this acupuncture regimen to pregnancy success, women with acupuncture were 3.0-times more likely to become pregnant. However, the confidence interval is extremely large and overlaps 1 Cl (0.5–17.9). One commonly reported action of acupuncture is stress reduction. Given that a stress response causes vasoconstriction<u>16</u>, which could acutely decrease uterine perfusion, it seems plausible that excessive stress on the day of embryo transfer could lower pregnancy rates. It also seems that techniques that elicit the relaxation response, leading to vasodilation, at the time of ET could improve pregnancy rates. Future studies could evaluate other relaxation techniques at the time of embryo transfer.

Those who received this protocol of acupuncture had both higher rates of pregnancy, and lower levels of stress both before and after embryo transfer. The vast majority of acupuncture patients had been receiving acupuncture prior to the day of ET, which could explain why the pre-ET stress scores were lower. However, the particular acupuncture protocol we used in this study did not seem to lower stress scores significantly from before embryo transfer to after embryo transfer. Therefore, the mechanism by which pregnancies were increased with this protocol remains unknown. Because this is not an attention-controlled study, it is possible that merely having the attention from acupuncture, rather than the actual acupuncture, resulted in lower stress scores. Based on the results of this study, it would be interesting to try new acupuncture protocols targeted at reducing stress levels at the time of ET.

When subjects in either group had a significant reduction in stress from before the embryo transfer to after it, pregnancy rates increased. It is possible that those who had a reduction in perceived stress scores had that reduction because they had excellent quality embryos, whereas those who had increased stress did so because they were less optimistic about their outcome. Thus, the decrease in stress could have occurred because the chances of pregnancy were higher, not that the decrease in stress resulted in higher pregnancy rates. However, when we examined this, embryo quality was not related to the change in stress scores (p=0.78), the pretest scores (p=0.97), or the post-test scores (p=0.91).

One limitation to this study is that it is small, with only 57 subjects. Previous studies have indicated that acupuncture improves pregnancy rates; however, the selection bias for acupuncture is unknown. If poor prognosis patients tend to choose acupuncture, then an improvement in pregnancy rates is very important. If good prognosis patients choose acupuncture, then a high pregnancy rate is less impressive. We found that donor oocyte recipients were more likely to choose acupuncture when compared with non-donor oocyte patients. We believe this is due to our clinical donor program, where the patients have a one-on-one relationship with the donor coordinator, and are more likely to hear all the options available to them.

Another major limitation is that this study is not-randomized, blinded, or placebo-controlled. Given the large financial and emotional investment in IVF, it is difficult to recruit for a randomized, placebo-controlled trial. Lack of a placebo arm means that this study is testing the whole acupuncture regimen, not just needling of the specific points. Also, while the

measurement of the stress scores was prospective, the chart review for the variables was retrospective. Thus, some variables, such as the use of ICSI, was not collected prospectively and was difficult to obtain reliably from a clinical chart review. Another weakness of the study is that we did not control for the amount of acupuncture that the subjects received prior to the day of ET. Some received it only on the day of ET, whereas others had multiple sessions of acupuncture. This study is too small to determine a dose-response relationship, but future studies should explore this possibility. Lastly, the acupuncture protocol used was the Paulus protocol, and it was the same used for all subjects. It is possible that individualizing acupuncture, rather than using a formulaic approach. would lead to different results. We chose this protocol because it is commonly used on the day of ET, and when modifications are made to this protocol with respect to point selection or timing of acupuncture, or the protocol is individualized based on TCM diagnosis, the results appear to be less positive than using the Paulus protocol5, 15, 17. Our results only refer to the acupuncture regimen chosen; other acupuncture regimens might have different results.

Although more involved questionnaires might be useful to provide additional information, we chose a short, validated questionnaire to have minimal burden on the subject and the healthcare team. This study did not have a funded research recruiter, so we needed to be able to enroll subjects with minimal disruption to clinical care. Future studies could investigate serial cortisol concentrations, anxiety measurements, and measurements of autonomic function, such as heart rate variability.

One of the strengths of this study is that it is innovative. It is the first study to investigate the effects of acupuncture on perceived stress at time of ET, and we believe it is the first study to investigate the effects of perceived stress at the time of ET on pregnancy rates. In addition, our study assessed subjects based on what is done in clinical care, where some patients choose acupuncture and others do not, although the acupuncture regimen in clinical care is not uniform for all subjects, as it was in this study.

Finally, even with our small sample size, we were able to demonstrate that acupuncture was associated with less stress both before and after embryo transfer, and that acupuncture may improve pregnancy rates. It is possible that lower perceived stress at the time of embryo transfer may plan a role in an improved pregnancy rate. Future studies should investigate a dose-response relationship, mechanisms of action, and the

types of biases and directions of the biases that may confound the relationship between acupuncture and pregnancy success.

Acknowledgments

This publication was supported by funds received from the NIH/NCRR GCRC Grant MO1-RR000056 and the CTSA Grant 1 UL1 RR024153–01

Financial support: Institutional support from Magee-Womens Hospital Department of Obstetrics and Gynecology and support from NIH/NCRR GCRC Grant MO1-RR000056 and the CTSA Grant 1 UL1 RR024153-0

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