



Summary of Acupuncture Studies related to Reproductive Medicine

Compiled from Journals, Internet, and Website resources as a tool to aid ABORM members understand the depth and breadth of Western Style research related to our fields.

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Meta-Analysis

Acupuncture and herbal medicine in in vitro fertilization: a review of the evidence for clinical practice

Cheong Y et al, Hum Fert 2010, Vol. 13, No. 1, Pg 3-12.

Human Fertility

A further analysis by the authors of the previously published Cochrane databases included more trials in their analysis of the benefit of acupuncture at embryo transfer. They included a trial which had previously been excluded due to the fact that its methodology introduced too much heterogeneity - this plus the inclusion of another trial which controversially used placebo acupuncture reduced the measurable benefits of acupuncture to IVF patients in this analysis.

Abstract

The objectives of this systematic review were to determine the effectiveness of (a) acupuncture and (b) Chinese herbal medicine on the treatment of male and female subfertility by assisted reproductive technologies (ART). All reports from RCTs of acupuncture and/or Chinese herbal medicine in ART were obtained via searches through The Cochrane Menstrual Disorders and Sub-fertility Group's Specialized Register of controlled trials, and other major databases. The outcome measures were determined prior to starting the search, and comprised: live birth rate, ongoing pregnancy rate, clinical pregnancy rate, the incidence of ovarian hyperstimulation syndrome and multiple pregnancy, miscarriage rate and adverse effects arising from treatment. Overall, 14 trials (a total of 2670 subjects) were included in the meta-analysis. The results provided no evidence of benefit in the use of acupuncture during assisted conception. Further studies should attempt to explore the potential placebo, as well as treatment, effects of this complimentary therapy. Essential elements for a quality RCT will be the size of the trial, the use of a standardized acupuncture method and of placebo needles.

Acupuncture and assisted conception

Cheong Y et al, Cochrane Database of Systematic Reviews 2009 Issue 1

Cochrane Database

A newer version of this data base by the same authors as the one listed above concluded that there is an increase in live birth rate when acupuncture is performed on day of embryo transfer.

Abstract

Background

Acupuncture has recently been studied in assisted reproductive treatment (ART) although its role in reproductive medicine is still debated.

Objectives

To determine the effectiveness of acupuncture in the outcomes of ART.

Search strategy

All reports which describe randomized controlled trials of acupuncture in assisted conception were obtained through searches of the Menstrual Disorders and Subfertility Group Specialized Register, CENTRAL, Ovid MEDLINE (1996 to August 2007), EMBASE (1980 to August 2007), CINAHL (Cumulative Index to Nursing & Allied Health Literature) (1982 to August 2007), AMED, National Research Register, Clinical Trials register (www.clinicaltrials.gov), and the Chinese database of clinical trials.

Selection criteria

Randomized controlled trials of acupuncture for couples who were undergoing ART comparing acupuncture treatment alone or acupuncture with concurrent ART versus no treatment, placebo or sham acupuncture plus ART for the treatment of primary and secondary infertility. Women with medical illness deemed contraindications for ART or acupuncture were excluded.

Data collection and analysis

Sixteen randomized controlled trials were identified that involved acupuncture and assisted conception. Thirteen trials were included in the review and three were excluded. Quality assessment and data extraction were performed independently by two review authors. Meta-analysis was performed using odds ratio (OR) for dichotomous outcomes. The outcome measures were live birth rate, clinical ongoing pregnancy rate, miscarriage rate, and any reported side effects of treatment.

Main results

There is evidence of benefit when acupuncture is performed on the day of embryo transfer (ET) on the live birth rate (OR 1.86, 95% CI 1.29 to 2.77) but not when it is performed two to three days after ET (OR 1.79, 95% CI 0.93 to 3.44). There is no evidence of benefit on pregnancy outcomes when acupuncture is performed around the time of oocyte retrieval.

Authors' conclusions

Acupuncture performed on the day of ET shows a beneficial effect on the live birth rate; however, with the present evidence this could be attributed to placebo effect and the small number of women included in the trials. Acupuncture should not be offered during the luteal phase in routine clinical practice until further evidence is available from sufficiently powered RCTs.

The data from this meta-analysis suggests that acupuncture does increase the live birth rate with in vitro fertilization (IVF) treatment when performed around the time of embryo transfer. However, this could be attributed to placebo effect and the small number of trials included in the review. Larger studies are necessary to confirm the results. Acupuncture may have potential

harmful effects in early pregnancy and hence clinicians should be cautious when giving advice regarding the use of acupuncture in early pregnancy.

Effects of acupuncture on rates of pregnancy and live birth among women undergoing in vitro fertilization: systematic review and meta-analysis.

Manheimer E et al. BMJ 2008;336 pg 545-549

British Medical Journal

Early in 2008, the prestigious British Medical journal published its own analysis of the acupuncture in a meta-analysis of 7 of these trials; i.e. they chose only those which met strict research criteria.

The authors concluded,

“The odds ratio of 1.65 suggests that acupuncture increased the odds of clinical pregnancy by 65% compared with the control groups... In absolute terms 10 patients would need to be treated with acupuncture to bring about one additional clinical pregnancy. These are clinically relevant benefits.”

And when they analyzed the 4 trials that measured live births in addition to pregnancy rates, they found that acupuncture increased the odds by 91% and that the number of patients who would need to be treated to bring about an additional pregnancy dropped to 9.

Impressive as these results are they may still be an underestimate, since the authors included women whose IVF cycles were cancelled before transfer.

The accompanying editorial in the BMJ makes the comment that adding acupuncture to IVF improved pregnancy rates more than any other recent improvement or advance in IVF technology.

Abstract

Objective - To evaluate whether acupuncture improves rates of pregnancy and live birth when used as an adjuvant treatment to embryo transfer in women undergoing in vitro fertilization.
Design - Systematic review and meta-analysis.

Data sources - Medline, Cochrane Central, Embase, Chinese Biomedical Database, hand searched abstracts, and reference lists.

Review methods - Eligible studies were randomized controlled trials that compared needle acupuncture administered within one day of embryo transfer with sham acupuncture or no adjuvant treatment, with reported outcomes of at least one of clinical pregnancy, ongoing pregnancy, or live birth. Two reviewers independently agreed on eligibility; assessed methodological quality; and extracted outcome data. For all trials, investigators contributed

additional data not included in the original publication (such as live births). Meta-analyses included all randomized patients.

Data synthesis - Seven trials with 1366 women undergoing in vitro fertilization were included in the meta-analyses. There was little clinical heterogeneity. Trials with sham acupuncture and no adjuvant treatment as controls were pooled for the primary analysis. Complementing the embryo transfer process with acupuncture was associated with significant and clinically relevant improvements in clinical pregnancy (odds ratio 1.65, 95% confidence interval 1.27 to 2.14; number needed to treat (NNT) 10 (7 to 17); seven trials), ongoing pregnancy (1.87, 1.40 to 2.49; NNT 9 (6 to 15); five trials), and live birth (1.91, 1.39 to 2.64; NNT 9 (6 to 17); four trials). Because we were unable to obtain outcome data on live births for three of the included trials, the pooled odds ratio for clinical pregnancy more accurately represents the true combined effect from these trials rather than the odds ratio for live birth.

The results were robust to sensitivity analyses on study validity variables. A prespecified subgroup analysis restricted to the three trials with the higher rates of clinical pregnancy in the control group, however, suggested a smaller non-significant benefit of acupuncture (odds ratio 1.24, 0.86 to 1.77).

Conclusions - Current preliminary evidence suggests that acupuncture given with embryo transfer improves rates of pregnancy and live birth among women undergoing in vitro fertilization.

A Systematic Review and Meta -analysis of the effect of Acupuncture on Outcome of in Vitro Fertilization Treatment

El-Toukhy T et al BJOG 2008 115 (10); 1203 -13

British Journal of Obstetrics and Gynecology

Another meta-analysis also reported at an annual fertility conference indicated that in the trials they chose to include they found no effect of acupuncture on IVF treatment. This meta-analysis included a trial which had been excluded from the previous analysis because it employed different methodology and therefore introduced a degree of heterogeneity which reduces the validity of this meta-analysis.

Abstract

BACKGROUND: Numerous randomized studies have reported pregnancy outcome in women who received acupuncture during their in vitro fertilization (IVF) treatment cycle. **OBJECTIVE:** The objective of this study was to conduct a systematic review with meta-analysis of the trials of acupuncture during IVF treatment on the outcomes of clinical pregnancy and live birth rates. **SEARCH STRATEGY:** Searches were conducted in MEDLINE, EMBASE, Cochrane Library, ISI Proceedings and SCISEARCH. **SELECTION CRITERIA:** All randomized controlled trials that evaluated the effects of acupuncture compared with no treatment or sham acupuncture in women undergoing IVF-intracytoplasmic sperm injection treatment were included. **DATA**

COLLECTION AND ANALYSIS: Study selection, quality appraisal and data extraction were performed independently and in duplicate. A sensitivity analysis was conducted where the meta-analysis was restricted to trials in which sham acupuncture was used in the control group. Meta-regression analysis was used to explore the association between study characteristics and pregnancy rates. **MAIN RESULTS:** Thirteen relevant trials, including a total of 2500 women randomized to either acupuncture or control group, were identified. No evidence of publication bias was found (Begg's test, $P = 0.50$). Five trials ($n = 877$) evaluated IVF outcome when acupuncture was performed around the time of transvaginal oocyte retrieval, while eight trials ($n = 1623$) reported IVF outcome when acupuncture was performed around the time of embryo transfer (ET). Meta-analysis of the five studies of acupuncture around the time of egg collection did not show a significant difference in clinical pregnancy (relative risks [RR] = 1.06, 95% CI 0.82-1.37, $P = 0.65$). Meta-analysis of the eight studies of acupuncture around the time of ET showed no difference in the clinical pregnancy rate (RR = 1.23, 95% CI 0.96-1.58, $P = 0.1$). Live birth data were available from five of the eight studies of acupuncture around the time of ET. Meta-analysis of these studies did not show a significant increase in live birth rate with acupuncture (RR = 1.34, 95% CI 0.85-2.11). Using meta-regression, no significant association between any of the studied covariates and clinical pregnancy rate was found ($P > 0.05$ for all covariates). **CONCLUSION:** Currently available literature does not provide sufficient evidence that adjuvant acupuncture improves IVF clinical pregnancy rate.

Traditional Chinese medicine and infertility.

Huang, S T and Chen, A P C, Current Opinion in Obstetrics & Gynecology. 2008, 2(3):211-215.

Current Opinion in Obstetrics & Gynecology

A recent review of current medical literature carried out by researchers in Taiwan noted that "traditional Chinese medicine could regulate the gonadotropin-releasing hormone to induce ovulation and improve the uterus blood flow and menstrual changes of endometrium. In addition, it also has impacts on patients with infertility resulting from polycystic ovarian syndrome, anxiety, stress and immunological disorders." Their review concludes "Integrating the principles and knowledge from well characterized approaches and quality control of both traditional Chinese medicine and Western medical approaches should become a trend in existing clinical practice and serve as a better methodology for treating infertility."

Abstract

Purpose of review: The present review gives an overview of the potential use of traditional Chinese medicine in the treatment of infertility, including an evidence-based evaluation of its efficacy and tolerance.

Recent findings: Recent studies demonstrated that traditional Chinese medicine could regulate the gonadotropin-releasing hormone to induce ovulation and improve the uterus blood flow and menstrual changes of endometrium.

In addition, it also has impacts on patients with infertility resulting from polycystic ovarian syndrome, anxiety, stress and immunological disorders.

Although study design with adequate sample size and appropriate control for the use of traditional Chinese medicine is not sufficient, the effective studies have already indicated the necessity to explore the possible mechanisms, that is, effective dose, side effect and toxicity of traditional Chinese medicine, in the treatment of infertility by means of prospective randomized control trial.

Summary: The growing popularity of traditional Chinese medicine used alone or in combination with Western medicine highlights the need to examine the pros and cons of both Western and traditional Chinese medicine approaches. Integrating the principle and knowledge from well characterized approaches and quality control of both traditional Chinese medicine and Western medical approaches should become a trend in existing clinical practice and serve as a better methodology for treating infertility.

The Role of Acupuncture in the Management of Subfertility

Ng E H et al Fertil Steril. 2008 Jul;90(1):1-13.

Fertility and Sterility

Another review of the literature from a group in Hong Kong concludes that the positive effect of acupuncture in the treatment of subfertility may be related to the central sympathetic inhibition by the endorphin system, the change in uterine blood flow and motility, and stress reduction.

Abstract

OBJECTIVE: To review systematically the use of acupuncture in the management of subfertility.

DESIGN: A computer search was performed via several English and Chinese databases to identify journals relevant to the subject.

RESULT(S): The positive effect of acupuncture in the treatment of subfertility may be related to the central sympathetic inhibition by the endorphin system, the change in uterine blood flow and motility, and stress reduction. Acupuncture may help restore ovulation in patients with polycystic ovary syndrome, although there are not enough randomized studies to validate this.

There is also no sufficient evidence supporting the role of acupuncture in male subfertility, as most of the studies are uncontrolled case reports or case series in which the sample sizes were small. Despite these deficiencies, acupuncture can be considered as an effective alternative for pain relief during oocyte retrieval in patients who cannot tolerate side effects of conscious sedation.

The pregnancy rate of IVF treatment is significantly increased, especially when acupuncture is administered on the day of embryo transfer.

CONCLUSION(S): Although acupuncture has gained increasing popularity in the management of subfertility, its effectiveness has remained controversial.

Miscellaneous

Effect of acupuncture on the outcome of in vitro fertilization and intracytoplasmic sperm injection: a randomized, prospective, controlled clinical study

Dieterle S et al, Fertil Steril 2006 Vol 85, pg 1347-1351

Fertility and Sterility

Abstract

OBJECTIVE: To determine the effect of luteal-phase acupuncture on the outcome of IVF / intracytoplasmic sperm injection (ICSI).

DESIGN: Randomized, prospective, controlled clinical study.

SETTING: University IVF center.

PATIENT(S): Two hundred twenty-five infertile patients undergoing IVF/ICSI.

INTERVENTION(S): In group I, 116 patients received luteal-phase acupuncture according to the principles of traditional Chinese medicine. In group II, 109 patients received placebo acupuncture.

MAIN OUTCOME MEASURE(S): Clinical and ongoing pregnancy rates.

RESULT(S): In group I, the clinical pregnancy rate and ongoing pregnancy rate (33.6% and 28.4%, respectively) were significantly higher than in group II (15.6% and 13.8%).

CONCLUSION(S): Luteal-phase acupuncture has a positive effect on the outcome of IVF/ICSI.

Acupuncture: Impact on Pregnancy Outcomes in IVF Patients

12th World Congress on Human Reproduction, Venice Italy March 2005

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Abstract

Take Home babies' rates (THB) have been the sine quo non of IVF outcomes. Pregnancy rates (PR) can overestimate the expected success of a high-technology treatment for patients and many clinics use PR as means of marketing their practices. This has caused disillusionment in patients and government regulation (especially in the U.S.). Each IVF program strives to improve reproductive outcomes (low ectopic rates, low miscarriage rates and improved take

home baby rates - live births). Usually the approach to these improvements are changes in IVF protocols, media adjustments in the IVF lab, patient selection, and subtle nudges towards egg donors for poor responders. Another approach has been the inclusion of alternative medical modalities: acupuncture, massage therapy, stress reduction techniques, herbal medicine. We, and others, have chosen to incorporate Acupuncture into our IVF treatment protocols. Recently we presented two studies that demonstrated improvements in pregnancy rates in Good and Poor IVF Responders with the inclusion of two specific Acupuncture Protocols (Steiner-Victorin and Paulus et. Al). In the poor responders group we demonstrated a positive adjustment to Poor Responders pregnancy rates (PR) with improvements in PR in the Poor Responders group equivalent to good responders. In the Good Responders study we demonstrated a trend towards improved PR (5% above controls, not significant at $p < 0.05$). With these observations noted we have continued our investigation and are reporting on reproductive outcomes in all IVF patients treated with Acupuncture compared to those untreated.

Materials and Methods: In this study 130 IVF cycles were reviewed in a retrospective fashion. Patients demographics, years infertile, age of male partners, sperm parameters, Day 3 FSH, Pulsatility Indices, Weight, BMI, infertility diagnoses, IVF treatment protocols were statistically similar for both the Controls (C) and Acupuncture (Ac) treatment groups. All patients that completed an IVF cycle (retrieval, transfer) were included. There were 82 in the C group (non acupuncture) and 48 in the Ac group. For the C vs. Ac groups a summary of their statistics are as follows: Mean Age was 32.6 vs. 32.7, Day 3 FSH was 5.5 vs. 6.4, Pulsatility Indices for right and left uterine arteries were 1.5 and 1.2 vs. 1.4 and 1.0; Sperm counts were 69 vs. 67 million/ml; Sperm motility (%) were 48 vs. 53%, and Sperm morphologies were 6 % normal vs. 7%.

Results: Pregnancy rates for the Ac group were statistically similar, although numerically higher, versus C (50% v 45% at $P < 0.05$). Ac miscarriage rates (SAB) were statistically lower than the C (8 % vs. 11% at $p < 0.01$). There were no ectopic pregnancies in the Ac group ($P < 0.01$). Live Births were significantly better in the Ac v C groups (42% v 38%). A surprising observation was that multiples pregnancies were significantly lower in the Ac vs. C groups (17 % vs. 22%). Average eggs retrieved were statistically similar 15 vs. 15 for Ac and C respectively.

Conclusions: IVF programs can significantly improve their IVF outcomes (PR, THB, SAB and Ectopic) by adding acupuncture protocols, specifically Steiner Victorin and Paulus. Further studies of Traditional Chine Medicine modalities of treatment are underway. We are organizing a multi-center prospective study to confirm our observations.

Acupuncture & IVF poor responders: a cure?

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

Abstract

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 Gonadotropin 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 PI (prior studies were done on patient with PI). 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.

Acupuncture and Good Prognosis IVF Patients: Synergy

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FERTILITY AND STERILITY®, Proceedings from the 2004 ASRM meeting in Philadelphia

OBJECTIVE: To determine the role of electro stimulation acupuncture and traditional combined with auricular acupuncture on IVF outcomes in good prognosis patients.

DESIGN: Retrospective case controlled clinical study. Acupuncture Consortium for treatment standardization. Reproductive Endocrinology & Infertility IVF Private Practice and Traditional Chinese Medicine Acupuncture Clinics.

MATERIALS AND METHODS: One hundred fourteen infertile patients undergoing controlled ovarian hyperstimulation with gonadotropins and GnRH agonist and antagonist for IVF-ET (2001 to 2003) in private practice IVF clinic. Only IVF patients with normal Day 3 FSH, normal

uterine artery Pulsatility indices, sperm morphologies over 7% normal by Kruger Strict Criteria and good response to ovarian hyperstimulation protocols (i.e., E2 over 2000 pg/ml) were analyzed. Intervention (s): Electrostimulation acupuncture - reduction of Pulsatility Index (PI) of the uterine artery and Traditional combined with Auricular acupuncture - Pre/Post embryo transfer protocols were used alone or in combination and resultant pregnancy outcomes were measured after IVF treatments. Main Outcome Measure(s): Cycles were grouped according to those that received No Acupuncture (Non-Ac) and those that received either one or both acupuncture treatments (Ac). Comparisons were made between Acupuncture treated IVF patients and Non-Acupuncture treated IVF patients in clinical pregnancies, ongoing pregnancies and birth outcomes. The statistics used for this analysis included; Tests for normal distribution: chi-square test, Kolmogorov-Smirnov Test Unpaired T-tests Stepwise Multiple regression Variance ratio test (F-Test) One-Way analysis of variance (ANOVA) with Student-Newman-Keuls (SNK) test for pair wise comparison of subgroups.

RESULTS: Total IVF cases 114, 53 with Acupuncture (Ac) and 61 without Acupuncture (Non-Ac). Demographics, Infertility Diagnoses, and Treatment Protocols were statistically the same between both groups and by design, the following parameters were similar: Sperm Morphology; Peak Day 3 FSH; Average Pulsatility Index; Peak E2 at hCG; and Post hCG P4. These parameters earned the designation of Good Prognosis group. Pregnancy rates (PR) and Miscarriage rates (SAB) were statistically improved at the $p < 0.05$ levels in those patients that received Acupuncture (51% v 36% PR and 8% v 20% SAB in the AC v Non-Ac groups). There were no ectopic pregnancies in the Ac group and 9% in the Non-Ac group, $p < 0.008$. Finally, Birth rates (BR) per cycle start and per pregnancy were significantly higher in the Ac group, with 23% more births/pregnancy significant at the $p < 0.05$ level.

CONCLUSION: The use of adjunctive therapies in IVF protocols is gaining popularity. In previously published data, Acupuncture was reserved for Poorer Prognosis patients and enhanced outcomes were observed. In this study, we demonstrated that Good Prognosis patients would also benefit from inclusion of published Acupuncture protocols. This is also the first publication of Birth outcome data in Acupuncture treated IVF patients. Acupuncture significantly increased birth outcomes; it significantly decreased ectopic pregnancies and miscarriage rates. These data uniquely support a definitive role of both Electrostimulation and Traditional combined with Auricular Acupuncture in IVF in Good Prognosis IVF patients. Supported by: None.

Quintero R et al, Fertil Steril 2004 Vol 81 Suppl 3, pg S11-12

Fertility and Sterility

Abstract

Objective: The purpose of this study was to determine if there are benefits of standard acupuncture compared to sham acupuncture as an adjunct to IVF.

Materials and Methods: A randomized, controlled, double-blind, cross over pilot trial was performed using a needle-like device (sham acupuncture) as a control. Approval from GAMC's

Investigational Review Board was acquired. Inclusion criteria were women aged 18 to 42 years with a history of failed IVF cycle(s); the presence of both ovaries; and a normal uterine cavity. Exclusion criteria was Kruger morphology <4%.

Results: Seventeen subjects were enrolled and seven subjects completed both arms of the study. The mean age was 36.2 years (range 28-41 years). The mean Day 3 FSH=3 D6.8 IU (range 3-13 IU). There were four ongoing pregnancies after the first cycle, equally distributed. Seven subjects were crossed over after the first cycle. Of these, four from the standard acupuncture group and one from the sham acupuncture group attained pregnancy. Two subjects of the standard acupuncture group were on-going pregnancies and one from the sham group. Only the sham group had two IVF cancellations. An unpaired Mann-Whitney Test using a two-sided p value was performed.

Conclusions: Our study shows a significantly lower amount of gonadotropins used when IVF is combined with standard acupuncture. A 70% pregnancy rate was also achieved with standard acupuncture and IVF, compared to 25%. Larger prospective trials are necessary.

Reduction of blood flow impedance in the uterine arteries of infertile women with electro-acupuncture.

Hum Reprod. 1996 Jun;11(6):1314-7.

Stener-Victorin E, Waldenström U, Andersson SA, Wikland M.

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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.

In anovulatory infertility cases the hyperactive sympathetic system can be depressed by electro acupuncture and the function of the hypothalamus-pituitary-ovarian axis can be regulated by electro acupuncture via central sympathetic system

Relationship between Blood Radioimmunoreactive Beta-Endorphin and Hand Skin Temperature During The Electro-Acupuncture Induction of Ovulation

By Chen Bo Ying M.D. Lecturer of Neurobiology Institute of Acupuncture Research, and Yu Jin, MD., Prof of Gynecology Obstetrics and Gynecology Hospital Shanghai Medical University Shanghai, People's Republic of China

Abstract:

Thirteen cycles of anovulation menstruation in 11 cases were treated with Electro-Acupuncture (EA) ovulation induction. In 6 of these cycles which showed ovulation, the hand skin temperature (HST) of these patients was increased after EA treatment. In the other 7 cycles ovulation was not induced. There were no regular changes in HST of 5 normal subjects. The level of radioimmunoreactive beta-endorphin ($r\beta$ -E) fluctuated, and returned to the preacupunctural level in 30 min. after withdrawal of needles in normal subjects. After EA, the level of blood $r\beta$ -E in cycles with ovulation declined or maintained the range of normal subjects. But the level of blood $r\beta$ -E and increase of HST after EA ($r=-0.677$, $P < 0.01$). EA is able to regulate the function of the hypothalamic pituitary-ovarian axis. Since a good response is usually accompanied with the increase of HST, monitoring HST may provide a rough but simple method for predicating the curative effect of EA. The role of $r\beta$ -E in the mechanism of EA ovulation induction was discussed.

KEYWORDS: Electro-Acupuncture (EA), Hand Skin Temperature (HST), radioimmunoreactive beta-endorphin ($r\beta$ -E), ovulation, radioimmunoassay

How acupuncture stimulates ovulation (the mechanism)

Clinical studies on the mechanism for acupuncture stimulation of ovulation

Mo X; Li D; Pu Y; Xi G; Le X; Fu Z Zhejiang College of Traditional Chinese Medicine, Hangzhou.

Ovulatory dysfunction is commonly seen in gynecology clinic. It may cause infertility, anemia, functional uterine bleeding and a variety of complications. This research according to TCM theory records treating with acupuncture 34 patients suffering from ovulatory dysfunction. Changes in clinical symptoms and some relative targets are reported, plus findings in animal experiments. The theory concerning the generative and physiologic axis of women, this research involved the following points; Ganshu (UB 18), Shenshu (UB 23), Guanyuan (Ren 4), Zhongji (Ren 3), and Sanyinjiao (Sp 6). The reinforcement and reduction of acupuncture enables it to strengthen liver and kidney. Through the Chong and Ren channels it nourishes

uterus to adjust the patient's axis function and recover ovulation. Treated on an average of 30 times, the patients' symptoms improved to varying degrees. The marked effective rate was 35.29%, the total effective rate being 82.35%. BBT, VS, CMS, and B ultrasonic picture all improved to some degree. The results also showed that acupuncture may adjust FSH, LH, and E2 in two directions and raise the progesterone level, bringing them to normal. The animal experiments confirmed this result. Results showed that acupuncture may adjust endocrine function of the generative and physiologic axis of women, thus stimulating ovulation. The results of this research will provide some scientific basis for treating and further studying this disorder.

Acupuncture and embryo transfer, other publication

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 favorably with the non-acupuncture historic control group. When they analyzed 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 favorably with the non-acupuncture historic control group.

When analyzed 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 randomized 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.

The relationship between perceived stress, acupuncture, and pregnancy rates among IVF patients: A 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.

A Randomized double blind comparison of real and placebo acupuncture in IVF treatment.

So EWS et al. Human Reproduction 2009; 24: 341-8.

A randomized controlled trial that compared real acupuncture with sham acupuncture before and after embryo transfer in 370 patients undergoing IVF treatment. The sham treatment used pressure at the same locations as used for real acupuncture, in effect a comparison of acupuncture and acupressure, not a placebo. The clinical pregnancy rate was significantly higher in the sham acupuncture group than the real acupuncture group (55.1 versus 43.8%, respectively, $p=0.038$). No significant differences were found in rates of ongoing pregnancy and live birth between the two groups. Reduction of endometrial and sub-endometrial vascularity, serum cortisol concentrations and anxiety levels were observed in both groups. The researchers concluded that placebo acupuncture was associated with a significantly higher overall pregnancy rate than real acupuncture, but that placebo acupuncture may not be inert.

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 increased blood flow to 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 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

Abstract

This study showed no acupuncture effect and the researchers felt this was due to the fact that they included many women who didn't have good quality embryos available for transfer. While acupuncture may help a woman become pregnant after the transfer of a healthy embryo, the researcher noted in an interview, it can't repair an embryo with chromosomal defects or other abnormalities. She added, "Despite the results of my own study, I still recommend acupuncture to women going through IVF"

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 lay 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 performed before and after embryo transfer improves pregnancy rates.

Youran D et al Fertil Steril 2008 Vol. 90, Suppl 1, pg S240

Fertility and Sterility

Abstract

OBJECTIVE: Conflicting evidence exists on whether acupuncture is beneficial for patients undergoing In Vitro Fertilization (IVF) cycles. Therefore, this study was undertaken to determine whether on-site acupuncture, performed both before and after embryo transfer, affects clinical outcomes.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: The Acupuncture Group consisted of 49 patients who received acupuncture on-site before and after embryo transfer in 2007. The treatment did not follow the Paulus protocol. The Control Group were 212 patients with no acupuncture undergoing IVF cycles in the same time period. The data was subdivided by SART age classifications to determine if acupuncture differentially benefitted certain age groups. Clinical Pregnancy Rate (CPR) was defined as the presence of fetal cardiac activity. Loss Rate was the percentage of pregnancies that did not proceed from a positive hCG to a clinical pregnancy. Data were analyzed using the unpaired t-test and Fisher's exact test, with significance defined as $P < 0.05$.

RESULTS: Patients with a positive hCG were significantly higher in the Acupuncture Group for women less than 35 years old (63.3% vs. 43.2%, $p = 0.048$). The Acupuncture Group also had a higher CPR in the under 35 category (60.0% vs. 34.6%, $p = 0.01$). There were no differences in the other age groups. Combining all the age groups, the cycle parameters between the two Groups were equivalent, while the CPR was higher and the Loss Rate lower for the Acupuncture group (Table 1).

TABLE 1. Cycle Data for All Age Groups

	Acupuncture	No Acupuncture	P Value
N	49	212	
Age	32.6 + 4.2	32.0 + 3.8	0.33
No. Oocytes	13.7 + 6.6	13.2 + 6.9	0.65

Cell Number	6.8 + 2.0	7.0 + 2.1	0.36
Fragmentation Score	2.5 + 0.6	2.5 + 0.6	1.00
No. Embryos Frozen	2.5 + 3.2	2.7 + 3.5	0.85
No. Embryos Transferred	2.3 + 0.6	2.2 + 0.6	0.29
Positive hCG (%)	57.1 (28/49)	45.8 (97/212)	0.16
Clinical Pregnancy (%)	55.1 (27/49)	34.4 (75/212)	0.01
Loss Rate (%)	3.6 (1/28)	22.7 (22/97)	0.02

CONCLUSIONS: Although other studies regarding acupuncture have been inconclusive, perhaps these positive results are related to two important factors. The treatments were performed on-site, eliminating the stress of traveling to another site before and after the embryo transfer. Also, the acupuncture treatment protocol did not follow the traditional Paulus protocol, thereby suggesting there is still more research to be done on how best to treat infertility issues with acupuncture

Laser acupuncture before and after embryo transfer improves ART delivery rates.

Fratterelli JL et al Fertil Steril 2008 Vol 90, Suppl 1,pg S105

Fertility and Sterility

Abstract

This study reports an increase in implantation rates with the use of laser acupuncture however the overall pregnancy rates for laser or needle acupuncture were not significantly different to control groups. The control groups in this trial had a high clinical pregnancy rate i.e. over 50%.

DESIGN: Prospect randomized double blind and placebo controlled.

MATERIALS AND METHODS: On the day of transfer, participants were randomly assigned to a study group; needle acupuncture (AC), laser acupuncture (LZ AC), sham laser acupuncture (LZ sham), relaxation (RX), or no treatment (NT). The AC and LZ AC puncture groups were considered treatment groups, the RX controls for the additional rest before and after transfer, and NT is the non-intervention group. Most significantly, the LZ Sham group provided an important control group. The laser acupuncture device was randomly preprogrammed per case to either fire (and provide LZ AC) or to not fire and thus provide a true double blind control group (LZ sham). It was not possible for the patient or acupuncturist to know if the laser fired. No contact occurs with the patient in laser acupuncture so there is no acupressure effect or contact with the wrong meridians. All treatments were administered for 25 minutes before and after embryo transfer. Outcomes were compared by Chi-square and multiple logistic regression

analysis to control for the potential confounders including female age, embryo quality, and day of transfer (Table 1).

RESULTS: All treatments were well tolerated. No differences in terms of patient demographics, cycle type, stimulation outcomes, embryo number and quality, day of embryo transfer, transferring physician, or acupuncturist were found between the 5 study groups. Implantation rates were significantly improved with laser acupuncture. Traditional needle acupuncture had outcomes equivalent to the 3 control groups. Sub analyses of patient age and embryo transfer day produced similar findings with laser acupuncture enhancing outcome rates.

CONCLUSIONS: This large prospective randomized and well controlled study consistently demonstrated benefit to LZ AC. Treatment was well tolerated and significantly improved implantation rates.

Table 1.

Clinical Outcomes (%) Rates

	AC	LZ AC	LZ Sham	RX	NT	P Values
Impl	28.9	33.7	26.8	24.9	30.2	< 0.05
Chem Preg	61.5	60.9	53.0	53.7	60.4	0.22
Clin Preg	51.5	54.5	43.9	45.3	50.3	0.19
Cont Preg	39.0	42.1	35.4	37.4	39.6	0.71

The effect of acupuncture on outcomes in in-vitro fertilization (IVF)

Udoff L. C. et al, Fertil Steril 2007 Vol 86, Issue 3, pg S145

Fertility and Sterility

Abstract

OBJECTIVE: To develop a protocol that could be used in future studies to evaluate whether acupuncture improves pregnancy and delivery rates in patients undergoing IVF. **DESIGN:** Randomized, sham treatment controlled pilot study.

MATERIALS AND METHODS: Patients planning to undergo IVF who meet inclusion/exclusion criteria (age 40 years old at start of stimulation, highest basal FSH 10mIU/mL, 3 prior failed IVF attempts, acupuncture naive) were randomly assigned to an acupuncture treatment group or a sham treatment group.

Treatment sessions occurred before the start of gonadotropin stimulation, the day before the oocyte retrieval, the day before the embryo transfer and the day after the embryo transfer.

Acupuncture was performed using manual manipulation at 6 to 10 points depending on the timing of the acupuncture treatment. Sham treated patients had needles placed in non-meridian points at a shallow depth. Patients were also given a questionnaire regarding their impressions of acupuncture treatment and were asked to guess their group assignment.

Data was analyzed using chi-squared for dichotomous outcome variables (e.g. clinical pregnancy rate, number of take home babies) and t-tests for continuous outcomes (e.g. age).

RESULTS: Twenty-two IVF cycles (19 patients) were randomized with thirteen patients completing the study (14 cycles). Five cycles were not completed due to poor response to ovarian stimulation (4 in the sham group, one in the real group). Other reasons for incomplete cycles (all in the sham group) included a persistent ovarian cyst, no viable embryos for transfer and personal reasons. The overall cycle cancellation rate was 32% compared to a 22% cycle cancellation rate for non-study patients of a similar age treated at this center during a similar time period (p.05).

In the 13 patients analyzed, the mean age was 35 years old (SD4.03). There was no statistical difference between true and sham acupuncture groups with respect to age (Sham: Mean35, SD4.6, Real: Mean34, SD4.6). Additionally, there was no significant difference between groups in highest basal FSH, number of oocytes retrieved, or number of embryos transferred. There was a significantly higher chemical pregnancy rate (80% versus 11.0%) in patients receiving true acupuncture compared to sham acupuncture (p.05). The clinical pregnancy rates and the take home baby rates showed a strong trend towards a higher rate with acupuncture treatment though the difference was not statistically significant (60% real treatment vs. 11% sham treatment, p.05.).

Regarding the questionnaire, only one patient correctly guessed their group assignment (real acupuncture). All patients rated their experience as very positive or positive.

CONCLUSION: It is feasible to conduct a randomized, blinded, sham control trial to study the impact of acupuncture on IVF success rates. Such a protocol is well accepted by patients. Preliminary data shows a statistically significant improvement in the biochemical pregnancy rate with acupuncture treatment. Additionally, acupuncture was associated with a strong trend towards higher clinical pregnancy rates and take home baby rates, though more patients will need to be studied to reach any final conclusions.

The effect of acupuncture in assisted reproduction techniques

Teshima D. R. K et al, Fertil Steril 2007 Vol 88, Suppl 1, pg S330

Fertility and Sterility

Abstract

OBJECTIVE: The aim of this study was to evaluate the effects of acupuncture on embryo transfer by comparing the rates of clinical pregnancy.

DESIGN: Retrospective, interventional and longitudinal study.

MATERIALS AND METHODS: Study with a total of 111 cycles of patients who underwent assisted reproduction techniques: in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) from June/2005 to January/ 2007: 52 cycles with acupuncture and 59 cycles without acupuncture. Acupuncture was performed, in specific points of the body including the ear, immediately before and after the embryo transfer procedure and the needles were retained for 30 minutes per session. The embryo transfer was carried out under ultrasound guidance and luteal phase support was given by trans-vaginal progesterone administration (Utrogestan) and intramuscular progesterone. Outcome measure was clinical pregnancy rate.

RESULTS: The clinical pregnancy rate per cycle was observed in 27 of 52 (51.9%) patients in the acupuncture group and 21 of 59 (35.6%) patients in the control group (P 140,083). The mean age was 36.1 6.1 years in the control group and 36.4 years in the acupuncture group (P140.785). The mean number of embryo transferred was 3.3 in the control group and 3.6 in the acupuncture group (P140.462). The technique of embryo transfer was 5 cycles of IVF and 54 cycles of ICSI in the control group and 5 cycles IVF and 47 cycles of ICSI in the acupuncture group (P 141.000). Both groups did not show statistics difference in the mean age, number of embryo transferred and the technique procedure.

CONCLUSIONS: Although there was a higher pregnancy rate in the acupuncture group, this difference was not statistically significant, probably because of the small number of patients in both group. Acupuncture seems to be an important coadjutant in the treatment of infertility with IVF or ICSI, and further research is needed to demonstrate its precisely effect.

Acupuncture in IVF Linked to Lower Miscarriage and Ectopic Rates

Cridennda Diane K, Magarelli Paul, Cohen Mel

Research Presented at ASRM 2007

PHILADELPHIA - Women who receive acupuncture during the stimulation phase of an in vitro fertilization cycle and again immediately after embryo transfer have a higher live-birth rate than do controls, according to the first acupuncture study with this end point.

"Other studies have looked at pregnancy rates, but what is really important is whether or not there is a baby," said Paul C. Magarelli, M.D., who reported his findings at the annual meeting of the American Society for Reproductive Medicine.

The retrospective study included 131 women who were undergoing standard in vitro fertilization (IVF) or Intracytoplasmic sperm injection (ICSI). All of these women were considered good prognosis candidates for IVF/ICSI and were given the choice of having acupuncture. A total of 83 women declined (controls) and 48 accepted. There were no significant differences between the two groups in terms of infertility diagnoses, demographics, and treatment protocols, except that sperm morphology was slightly better in the partners of women receiving acupuncture (7.3% vs. 5.9 % normal forms with strict criteria evaluation), and the average uterine artery Pulsatility index was lower in the acupuncture group (1.57 vs. 1.72), said Dr. Magarelli of the

department of ob.gyn. at the University of New Mexico, Albuquerque. The study found that pregnancy rates per embryo transfer were not significantly different between the two groups (50% in the acupuncture group and 45% in controls). The miscarriage rate was almost halved in the acupuncture group (8% vs. 14%). In addition, the rate of ectopic pregnancies was significantly lower in the acupuncture group-0 of 24 pregnancies (0%) vs. 2 of 37 pregnancies (9%), said Dr. Magarelli, who is also in private practice in Colorado Springs and Albuquerque. Thus, the live-birth rate per IVF/ICSI cycle was significantly higher in the acupuncture group than in controls (21% vs. 16%).

"The live-birth rate per pregnancy is an even more telling number, since some cycles get cancelled. There was a 42% live-birth rate per pregnancy in the acupuncture group, compared to a 35% rate in the non-acupuncture group," Dr. Magarelli said in an interview with this newspaper. "We believe that what we are doing is improving the uterine environment such that implantation is improved," he added. The study used two acupuncture protocols. The Stener-Victorin electro stimulation protocol-which has been shown to reduce high uterine artery blood flow impedance, or Pulsatility index (Hum. Reprod. 1996;11:1314-7)-was used for nine treatments during ovarian stimulation. The second acupuncture technique-the Paulus protocol, which has been associated with improved pregnancy rates (Fertil. Steril. 2002;77:721-4)-was used within 24 hours before the embryo transfer and 1 hour after.

"This protocol has demonstrated reductions in uterine contractility, so by relaxing the uterus before the embryo transfer and immediately after, we felt we were setting up a better environment for implantation," Dr. Magarelli said.

RESULTS: The proportion of patients with a positive pregnancy test was higher in the control group (36/46) than the acupuncture group (25/48) (78.3% vs. 52.1%, respectively; $P=0.01$). More importantly, the clinical pregnancy rate was higher in the control group than in the acupuncture group (69.6% vs. 43.8%, respectively; $P=0.03$). The groups were statistically similar with respect to age, peak estradiol, number of oocytes retrieved, fertilization method, fertilization rate, number of embryos transferred, and the proportion with blastocyst transfer.

CONCLUSIONS: In contrast to previous reports, acupuncture before and after embryo transfer was associated with lower biochemical and clinical pregnancy rates when compared to the control group. The value of acupuncture in patients undergoing IVF needs to be further examined before recommending it to patients.

Acupuncture lowers pregnancy rates when performed before and after embryo transfer

Craig L. B et al, Fertil Steril 2007 Vol 88, Suppl 1, pg S40

Fertility and Sterility

Abstract (not published)

OBJECTIVE: Acupuncture performed onsite before and after embryo transfer has been reported to improve in vitro fertilization (IVF) outcome in patients with good quality embryos. The purpose of this investigation was to evaluate whether acupuncture before and after embryo transfer would alter pregnancy rates in patients undergoing IVF regardless of embryo quality if the treatment was performed offsite.

DESIGN: Multi-center, prospective, randomized study.

MATERIALS AND METHODS: 107 patients undergoing IVF were randomized to acupuncture vs. control group. The treatment group received acupuncture by one of two licensed acupuncturists at an offsite location for 25 minutes before and after embryo transfer using a modified Paulus protocol (protocol described by Paulus et. al. 2002 with the addition of Cv6 before and K3 after transfer). The control group underwent embryo transfer without any other intervention. The IVF protocol was determined by the treating physician who was blinded to assigned group. The main outcome measures were a positive quantitative hCG, clinical pregnancy as manifested by fetal cardiac activity, and live birth (data pending). Chi-squared analysis and Student's t-test were used for statistical analyses. Of the 107 patients randomized, 94 completed the study (10 IVF cycles canceled, 3 patients withdrew).

Acupuncture and IVF embryo transfer, ART and PCOS

Acupuncture Med. 2006 Dec;24(4):157-63.

Use of acupuncture in female infertility and a summary of recent acupuncture studies related to embryo transfer.

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During the last five years the use of acupuncture in female infertility as an adjuvant to conventional treatment in assisted reproductive technology (ART) has increased in popularity. The present paper briefly discusses clinical and experimental data on the effect of acupuncture on uterine and ovarian blood flow, as an analgesic method during ART, and on endocrine and metabolic disturbances such as polycystic ovary syndrome (PCOS). Further it gives a summary of recent studies evaluating the effect of acupuncture before and after embryo transfer on pregnancy outcome. Of the four published RCTs, three reveal significantly higher pregnancy rates in the acupuncture groups compared with the control groups. But the use of different study protocols makes it difficult to draw definitive conclusions. It seems, however, that acupuncture has a positive effect and no adverse effects on pregnancy outcome.

Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer

Smith C et al, Fertil Steril 2006 Vol 85, pg 1352-1358

Fertility and Sterility

Abstract

OBJECTIVE: To evaluate the effects of acupuncture on clinical pregnancy rates for women undergoing ET.

DESIGN: Single-blind, randomized controlled trial using a noninvasive sham acupuncture control.

SETTING: Repromed, The Reproductive Medicine Unit of The University of Adelaide.

PATIENT(S): Women undergoing IVF.

INTERVENTION(S): Women were randomly allocated to acupuncture or noninvasive sham acupuncture with the placebo needle. All women received three sessions, the first undertaken on day 9 of stimulating injections, the second before ET, and the third immediately after ET.

MAIN OUTCOME MEASURE(S): The primary outcome was pregnancy. Secondary outcomes were implantation, ongoing pregnancy rate at 18 weeks, adverse events, and health status.

RESULT(S): Two hundred twenty-eight subjects were randomized. The pregnancy rate was 31% in the acupuncture group and 23% in the control group. For those subjects receiving acupuncture, the odds of achieving a pregnancy were 1.5 higher than for the control group, but the difference did not reach statistical significance. The ongoing pregnancy rate at 18 weeks was higher in the treatment group (28% vs. 18%), but the difference was not statistically significant.

CONCLUSION(S): There was no significant difference in the pregnancy rate between groups; however, a smaller treatment effect cannot be excluded. Our results suggest that acupuncture was safe for women undergoing ET.

Acupuncture on the day of embryo transfer significantly improves the reproductive outcome in infertile women: a prospective, randomized trial

Westergaard L et al, Fertil Steril 2006 Vol 85, pg 1341-1346

Fertility and Sterility

Abstract

OBJECTIVE: To evaluate the effect of acupuncture on reproductive outcome in patients treated with IVF/intracytoplasmic sperm injection (ICSI). One group of patients received acupuncture on the day of ET, another group on ET day and again 2 days later (i.e., closer to implantation day), and both groups were compared with a control group that did not receive acupuncture.

DESIGN: Prospective, randomized trial.

SETTING: Private fertility center.

PATIENT(S): During the study period all patients receiving IVF or ICSI treatment were offered participation in the study. On the day of oocyte retrieval, patients were randomly allocated (with sealed envelopes) to receive acupuncture on the day of ET (ACU 1 group, n = 95), on that day and again 2 days later (ACU 2 group, n = 91), or no acupuncture (control group, n = 87).

INTERVENTION(S): Acupuncture was performed immediately before and after ET (ACU 1 and 2 groups), with each session lasting 25 minutes; and one 25-minute session was performed 2 days later in the ACU 2 group.

MAIN OUTCOME MEASURE(S): Clinical pregnancy and ongoing pregnancy rates in the three groups.

RESULT(S): Clinical and ongoing pregnancy rates were significantly higher in the ACU 1 group as compared with controls (37 of 95 [39%] vs. 21 of 87 [26%] and 34 of 95 [36%] vs. 19 of 87 [22%]). The clinical and ongoing pregnancy rates in the ACU 2 group (36% and 26%) were higher than in controls, but the difference did not reach statistical difference.

CONCLUSION(S): Acupuncture on the day of ET significantly improves the reproductive outcome of IVF/ICSI, compared with no acupuncture. Repeating acupuncture on ET day +2 provided no additional beneficial effect.

Impact of acupuncture before and after embryo transfer on the outcome of in vitro fertilization cycles: A prospective single blind randomized study

Benson M. R. et al, Fertil Steril 2006 Vol 86, Issue 3, pg S135

Fertility and Sterility

Abstract

OBJECTIVE: The study was conducted to examine several adjunct treatment regimens administered before and after embryo transfer and determine if one treatment was more efficacious than any of the alternative regimens on in vitro fertilization (IVF) outcome. We compared two different acupuncture stimulation modes, needle and laser acupuncture, with sham laser acupuncture, relaxation, or no intervention treatment on implantation and pregnancy rates in women undergoing IVF.

DESIGN: Prospective single blind randomized trial. **MATERIALS AND METHODS:** Patients (n258) who had been scheduled for embryo transfer (ET), signed informed consent and were randomly assigned to one of 5 study treatment regimens; needle acupuncture (AC; 53), laser acupuncture (LZ AC; n53), sham laser acupuncture (placebo)(LZ sham; n52), relaxation (RX; n50), or no intervention treatment (NT; n50). All treatments were administered 25 minutes before ET and immediately after ET. The patient and acupuncturist were unaware of whether the laser system was active which allowed for a double-blind control group for the laser acupuncture treatment. Comparisons of various parameters between groups were conducted by 2 tests and one-way ANO- As.. Multinomial logistic regression analysis was used to control for the potentially confounding effects of day of embryo transfer (day 3 vs.5) and number of embryos transferred which are known to relate to IVF outcome, to further analyze the impact of adjunct treatment regimens on implantation and pregnancy rates. Probability of P 0.05 was considered to be statistically significant.

RESULTS: No differences in terms of cycle type, day of embryo transfer, or physician performing transfer were found between treatment groups. Neither day of transfer (p0.079) or egg number (P 0.082) were significant independent predictors of implantation or conception when interactions between parameters were considered in all 5 groups. All acupuncture treatments were well tolerated.

CONCLUSION: Conception and implantation rates were highest with traditional needle acupuncture. IVF treatment outcomes did not differ between patients treated with laser or sham laser acupuncture. This study did not have the statistical power to detect treatment differences in pregnancy rates between needle acupuncture and no treatment (i.e., at least 200 subjects are needed to detect differences in CP rates of 54.7 and 44% with 80% power) which may be due to sample size, transfer of embryos of varying quality and variations in stimulation protocols. However, while not statistically significant, needle acupuncture produced a clinically significant effect (greater than 10% increase in clinical pregnancy rate) compared with relaxation or no treatment which warrants further investigation.

The impact of acupuncture on IVF outcome

Domar A et al, Fertil Steril 2006 Vol 86 Suppl 2, pg S378-379

Fertility and Sterility

Abstract

OBJECTIVE: The purpose of this study was to replicate previous research on the efficacy of acupuncture in increasing pregnancy rates in IVF and determine if the increase in conceptions was due to a placebo effect.

DESIGN: This was a randomized, controlled, prospective, single blind design.

MATERIALS AND METHODS: 83 women scheduled to undergo embryo transfer from a fresh cycle using their own eggs were recruited to participate in the study. Subjects completed a battery of demographic and psychological questionnaires prior to randomization and were then

assigned to either the acupuncture or control condition. Acupuncture subjects received the protocol first described by Paulus et al, 2002, which included 22 needles, for 25 minutes prior to and again 25 minutes following embryo transfer. Control subjects lay quietly for the same amounts of time.

All subjects completed another battery of psychological questionnaires following their second acupuncture/control session which focused on their sense of optimism about the outcome of the cycle. All IVF staff remained blind to subject assignment.

RESULTS: The mean age of the acupuncture patients was 36.5 and for the control subjects was 35.3 ($p < 0.05$). The mean number of embryos transferred for the acupuncture patients was 2.58 and for the controls 2.56 ($p < 0.05$). The pregnancy rate (defined as a positive HCG level 11 days following ET) was 53.84% in the acupuncture group and 52.94% in the control group ($p < 0.05$). There were also no significant differences between the two groups in optimism level post-embryo transfer, although there was a trend for the acupuncture group to express more optimism.

CONCLUSION: The use of acupuncture with IVF patients was not associated with an increase in pregnancy rates or optimism. This study did not replicate previous research. Possible explanations include the fact that this study differed in three ways from the Paulus et al study:

all ET patients were eligible, not just patients with good embryo quality,

all staff were blind to subject assignment, not just the attending physician,

patients completed several psychological questionnaires which might have impacted them in some way.

Since there were no differences in pregnancy rates, it was not possible to determine if acupuncture is associated with a placebo effect.

Improvement of IVF Outcomes by Acupuncture: Are egg and embryo qualities involved?

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FERTILITY AND STERILITY®, May 2005, VOL 83, SUP 2, Proceeding from the 2005 Pacific Coast Reproductive Society annual meeting in Palm Springs

Objective: In this study, we examine the impact of Acupuncture on the embryology characteristics of IVF patients, i.e., are there changes in the numbers of eggs generated, embryos fertilized, embryos transferred or remaining embryos for freezing in those patients receiving acupuncture therapy.

Design: Retrospective clinical study

Setting: Private infertility practice and Traditional Chinese Medicine practice

Patients: Two hundred eight IVF cycles were reviewed, 95 received acupuncture (Ac) and 113 were controls (C).

Interventions: Patients randomly chose Ac to complement their IVF treatments. Two published Ac protocols were used. Standard IVF protocols were used and done in one clinic by one physician. The MD was not aware of who received Ac in addition to their IVF. After three years the data were collected and analyzed.

Main Outcome Measures: Number of eggs retrieved, number of eggs fertilized normally, number of embryos implanted, number of embryos frozen, number of embryos transferred, day of transfer, number of prior IVF cycles, Day 3 FSH, Pulsatility Indices, weight, infertility diagnoses, IVF treatment protocols, pregnancy rates, SAB rates, ectopic rates, and multiple pregnancy rates.

Results: Number of prior IVF cycles, Day 3 FSH, Pulsatility Indices, Weight, Infertility diagnoses, IVF treatment protocols were statistically similar. Pregnancy rates for the Ac group were statistically significantly higher than the C group ($P \leq 0.05$), SAB rates were lower and multiple pregnancy rates were lower ($P < 0.06$, not statistically significant). Ectopic pregnancy rates were statistically lower in the Ac group ($P \leq 0.05$). There were no statistically significant differences between the C and Ac treated groups for the following embryology parameters: number of eggs retrieved, number of eggs fertilized normally, number of embryos implanted, number of embryos frozen, number of embryos transferred, and day of transfer.

Conclusions: There were no discernable statistical differences between embryology characteristics in patients treated with or without Acupuncture. These data suggests that the mechanism of action of Acupuncture on IVF outcomes may be related to affects in the host (the egg provider and the embryo recipient) rather than in direct changes to the eggs retrieved and the embryos created.

Key Words: IVF, acupuncture, adjuvant therapies, electro stimulation acupuncture, embryology, eggs

Acupuncture and In Vitro Fertilization: Does the Number of Treatments Impact Reproductive Outcomes?

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Objective: The purpose of this study was to determine the optimal number of acupuncture treatments that provide the patient with the best IVF outcomes, i.e., pregnancy.

Materials and Methods: Retrospective clinical study in private practice Acupuncture and IVF center. Data were compiled in a group of infertile patients ($n = 216$) who received acupuncture during their IVF treatment cycle between 2001 and 2005. Data were analyzed to determine the

optimal number of Electrical Stimulation (e-Stim) acupuncture treatments (Stener-Victorin protocol) that would result in a clinical pregnancy. Two hundred sixteen patients over a 4 year period were included in this study. Based on our previous studies, we determined a significant improvement in IVF outcomes when patients were treated with Acupuncture (Ac). We utilized two protocols: Stener-Victorin et al 1996 (reported on uterine blood flow) and Paulus et al. 2002 protocol (reported on acupuncture given just before and just after embryo transfer). Patients received a combination of both protocols. This population was stratified into pregnant and non-pregnant groups and then evaluated by Student T-test and Chi-Square analysis for age, FSH levels, weight, BMI and E-2 levels. The pregnant and non-pregnant groups were further subdivided into those that received or did not receive acupuncture and were analyzed by Chi-square analysis. Since all patients received acupuncture consisting of e-Stim, their distribution was analyzed utilizing Kaplan- Meier survival analysis for pregnancy and no pregnancy to determine the number of e-stimulation that would provide the greatest chance for pregnancy.

Results: Patients age, day 3 FSH levels, weight, BMI (body mass index) and E2 (estrogen level at embryo transfer) were not statistically significantly different between the Non Acupuncture (No Ac) and the Acupuncture (Ac) groups. There was a statistically significant improvement ($p < 0.01$) in pregnancy rates in the group that received Ac (49 patients of 106 (37.4%) in the No Ac became pregnant vs. 77 patients of 111 (61.1%) of the Ac group became pregnant). This is over 23% increase in pregnancy rates in the Ac group. When the data were compared between e-Stim treatments in the Ac only group, an average of 6.5 treatments were found in the non-pregnant Ac group and 5.9 treatments in pregnant Ac group (not statistically significantly different). When the data were plotted comparing pregnant vs. non pregnant Ac patients, there was a trend towards numerically more e-Stim treatments in those who achieved a pregnancy. In order to confirm or refute differences in these two groups, Kaplan Meier's survival analyses were done. Based on these analyses, the average accumulated affect in the non-pregnant Ac group was 5.1 e-Stim treatments and 8.4 e-Stim treatments in the pregnant Ac group. This was statistically significantly different at the $p < 0.05$.

Conclusion: In traditional Chinese medicine the basic theory is that only when the body is balanced will it function at its optimal level. Acupuncture helps restore balance which results in a higher chance of achieving pregnancy. In our study, we found that patients who received more than 8 e-Stim treatments appeared to have the maximum benefit for IVF outcomes: pregnancy ($p < 0.05$). In our study, we also reviewed the independent effects of the Paulus protocol, however due to small numbers; we could not perform the analyses. In the IVF center included in this study, patients receive Valium (diazepam) to reduce smooth muscle contractility. This treatment may provide all that is needed to reduce uterine contractility and therefore the additional impact of Ac at the pre and post transfer (Paulus protocol) may well be masked by the medication. More study of these and other treatments must be done. We are currently investigating the role of Ac in stress hormone circulating levels.

Source : No outside source of funding.

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

A randomized, controlled, double-blind, cross-over study evaluating acupuncture as an adjunct to IVF

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-fertilization (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 ($P < 0.05$).

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

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.

Acupuncture and IVF Miscellaneous

Acupuncture on the day of embryo transfer: a randomized controlled trial of 635 patients.

Andersen D, Løssl K, Andersen AN, Fürbringer J, Bach H, Simonsen J, Larsen EC

The Fertility Clinics, Copenhagen University Hospital, Rigshospitalet, 2100 Copenhagen, Denmark. Reprod Biomed Online. 2010 Apr 7. [Epub ahead of print]

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

Acupuncture and herbal medicine in in vitro fertilization: a review of the evidence for clinical practice

Cheong Y et al. . Hum Fertil 2010 Jan 7. [Epub ahead of print]

A systematic review and meta-analysis that looked at the effectiveness of acupuncture and Chinese herbal medicine in the treatment of male and female subfertility by assisted reproductive technologies (ART). It included 14 randomized controlled trials involving a total of 2,670 participants of acupuncture and/or Chinese herbal medicine in ART. The outcome measures were: live birth rate, ongoing pregnancy rate, clinical pregnancy rate, the incidence of ovarian hyperstimulation syndrome and multiple pregnancy, miscarriage rate and adverse effects arising from treatment. Adjunctive acupuncture improved live birth and pregnancy rates but the superiority over control groups was not statistically significant. Hence the reviewers concluded that there was no evidence of benefit in the use of acupuncture during assisted conception.

Acupuncture for frozen-thawed embryo transfer cycles: a double-blind randomized controlled trial.

So EW, Ng EH, Wong YY, Yeung WS, Ho PC. Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Hong Kong Special Administrative Region, People's Republic of China.

Reprod Biomed Online. 2010 Jun;20(6):814-821. Epub 2010 Mar 4.

Abstract

The role of acupuncture on the pregnancy rate has not been evaluated in frozen-thawed embryo transfer (FET) cycles. This randomized double-blind study aimed to determine whether acupuncture performed on the day of FET improves clinical outcomes. On the day of FET, 226 patients were randomly allocated to either real or placebo acupuncture according to a computer-generated randomization list in sealed opaque envelopes. They received a session of real or placebo acupuncture for 25min on site immediately after FET. The anxiety level and serum cortisol concentration were evaluated before and after real and placebo acupuncture. There were no significant differences in rates of overall pregnancy, clinical pregnancy, ongoing pregnancy, live birth and implantation in the placebo acupuncture group, when compared with the real acupuncture group. The anxiety level and serum cortisol concentration were similar for both groups. Only the placebo acupuncture group had significantly higher ongoing pregnancy ($P=0.022$) and implantation rates ($P=0.038$) than those who declined to join the study and received no acupuncture. In conclusion, comparable pregnancy and live birth rates of FET treatment were found in patients who had one session of real or placebo acupuncture after FET

Randomized controlled trial: effects of acupuncture on pregnancy rates in women undergoing in vitro fertilization.

Moy I, Milad MP, Barnes R, Confino E, Kazer RR, Zhang X. Fertil Steril. 2010 Jun 19. [Epub ahead of print]

Abstract

OBJECTIVE: To evaluate the influence of "true" versus "sham" acupuncture on pregnancy rates (PRs) in women undergoing IVF.

DESIGN: Randomized controlled trial, double-blinded with independent observer.

SETTING: Academic infertility clinic.

PATIENT(S): One hundred sixty patients <38 years old undergoing IVF with or without intracytoplasmic sperm injection.

INTERVENTION(S): Subjects were randomly allocated to the true or sham group and underwent acupuncture 25 minutes before and after ET. Subjects completed a McGill Pain Questionnaire regarding their clinical symptoms during ET.

MAIN OUTCOME MEASURE(S): Clinical PR and clinical symptoms during ET.

RESULT(S): While the overall clinical PR was 51.25%, there was no significant difference between the arms of the study (true = 45.3% vs. sham = 52.7%); 33.1% of the patients had ultrasound-documented singleton pregnancy, and 15% of patients had twin gestations, while one patient in the true arm had a triplet gestation. There were significant differences in the subjective, affective, and total pain experience between both arms. The subjects in the true arm described their acupuncture session as being more "tiring" and "fearful" and experienced more "achiness" compared with their sham counterparts.

CONCLUSION(S): There was no statistically significant difference in the clinical or chemical PRs between both groups. Patients undergoing true acupuncture had differing sensory experiences compared with patients in the sham arm. There were no significant adverse effects observed during the study, suggesting that acupuncture is safe for women undergoing ET.

Background: In vitro fertilization (IVF) is a widely accepted method to treat infertility; however, the average success rate in the United States is only 40.2%. Acupuncture has been shown to increase blood flow to the uterus, so it is reasonable to project that it could aid the success rate of IVF. Objective: To compare 3 acupuncture methods to evaluate which method is most effective for IVF. Design, Setting, and Patients: A total of 52 IVF patients aged between 29 and 45 years (mean age, 38) were selected for this study. This study was conducted from 2004 to 2008 at Acupuncture and Chinese Medical Center, Ann Arbor, MI. Interventions: Patients were randomly assigned to receive traditional Chinese acupuncture (TCA) plus electro acupuncture (EA), TCA alone (control), or EA alone (second control). Main Outcome Measures: Comparisons of IVF effectiveness rates were made for each method. Results: All 3 acupuncture methods increased the success rate for IVF. There was a marked increase with the combination of TCA and EA (81.8% success-twice the US average for IVF alone) ($P < .01$). The success rates for the control groups TCA and EA were 64.3% and 62.5%, respectively ($P > .05$). Conclusions: Our study suggests that the combination of TCA and EA is a promising new technique for the treatment of infertility with a higher IVF success rate than that of TCA or EA alone.

Acupuncture as an adjunct to in vitro fertilization: A randomized trial.

Kong S. Hughes A Medical Acupuncture. 21(3)(pp 179-182), 2009.

Abstract

Background: In vitro fertilization (IVF) is a widely accepted method to treat infertility; however, the average success rate in the United States is only 40.2%. Acupuncture has been shown to increase blood flow to the uterus, so it is reasonable to project that it could aid the success rate of IVF. Objective: To compare 3 acupuncture methods to evaluate which method is most effective for IVF. Design, Setting, and Patients: A total of 52 IVF patients aged between 29 and 45 years (mean age, 38) were selected for this study. This study was conducted from 2004 to 2008 at Acupuncture and Chinese Medical Center, Ann Arbor, MI. Interventions: Patients were randomly assigned to receive traditional Chinese acupuncture (TCA) plus electro acupuncture (EA), TCA alone (control), or EA alone (second control). Main Outcome Measures: Comparisons of IVF effectiveness rates were made for each method. Results: All 3 acupuncture

methods increased the success rate for IVF. There was a marked increase with the combination of TCA and EA (81.8% success-twice the US average for IVF alone) ($P < .01$). The success rates for the control groups TCA and EA were 64.3% and 62.5%, respectively ($P > .05$). Conclusions: Our study suggests that the combination of TCA and EA is a promising new technique for the treatment of infertility with a higher IVF success rate than that of TCA or EA alone.

Acupuncture as an adjunct to in vitro fertilization: A randomized trial.

Kong S. Hughes A. Medical Acupuncture 2009;21:179-82.

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

Acupuncture intervention combined with assisted reproductive technology: Its different effects at different time points during the in vitro fertilization-embryo transfer course

Guo J. Li D. Zhang Q.-F.

Department of Traditional Chinese Medicine and Acupuncture, Peking University Third Hospital, Beijing 100191, China [in Chinese] Journal of Chinese Integrative Medicine. 6(12)(pp 1211-1216), 2008.

Recently the combination of acupuncture with assisted reproductive technology (ART) to increase the outcomes of ART is being widely studied. In this article, the literatures concerning random controlled clinical trials since 2002 are reviewed and the designs of the trials, especially the timing of acupuncture, are evaluated. Over the past 5 years, the related clinical trials have primarily showed that acupuncture done immediately before and after embryo transfer might increase the assisted reproduction rates, but still requiring further high quality trials with large samples; in addition, different stimulation modes could produce different result, and so far there has not been a consensus as to the optimal time-point for the acupuncture intervention during the in vitro fertilization-embryo transfer (IVF-ET) course. Since the effects of acupuncture change with women's endocrine cycles, it is important and possible to make a breakthrough in ART outcomes if acupuncture is performed at a suitable time point during the cycle of IVF/ET combined with ART.

A matched controlled study to evaluate the efficacy of acupuncture for improving pregnancy rates following in vitro fertilization-embryo transfer.

Wang W., Check J.H., Liss J.R., Choe J.K. Clinical and Experimental Obstetrics and Gynecology. 34(3)(pp 137-138), 2007

Clinical and Experimental Obstetrics and Gynecology. 34(3)(pp 137-138), 2007

Purpose: To determine if acupuncture performed during the follicular phase and luteal phase but not on the day of embryo transfer could improve the outcome following IVF-ET compared to controls. Methods: Acupuncture was started biweekly from day 5 of the follicular phase through the luteal phase but not on the day of the transfer. Controls were matched according to age, same number of previous failed IVF cycles and same type of embryo transfer (fresh or frozen). Results: The clinical and ongoing (delivered pregnancy rates per transfer) for 32 women undergoing IVF-ET and acupuncture was 40.6% and 37.5%, respectively vs. 53.1% and 43.7% for controls. The median number of previous failed IVF cycles was three. Conclusions: Acupuncture performed twice weekly during the follicular and luteal phase does not seem to improve pregnancy rates following IVF-ET

In vitro fertilization and acupuncture: clinical efficacy and mechanistic basis.

Anderson BJ, Haimovici F, Ginsburg ES, Schust DJ, Wayne PM. Pacific College of Oriental Medicine, New York, USA. Altern Ther Health Med. 2007 May-Jun;13(3):38-48.

OBJECTIVE: To provide an overview of the use of acupuncture as an adjunct therapy for in vitro fertilization (IVF), including an evidence-based evaluation of its efficacy and safety and an examination of possible mechanisms of action. DESIGN: Literature review using PubMed, the Science Citation Index, The Cochrane Library (Database of Systematic Reviews and Central Register of Controlled Trials), the New England School of Acupuncture library databases, and a cross-referencing of published data, personal libraries, and Chinese medicine textbooks. RESULTS: Limited but supportive evidence from clinical trials and case series suggests that acupuncture may improve the success rate of IVF and the quality of life of patients undergoing IVF and that it is a safe adjunct therapy. However, this conclusion should be interpreted with caution because most studies reviewed had design limitations, and the acupuncture interventions employed often were not consistent with traditional Chinese medical principles. The reviewed literature suggests 4 possible mechanisms by which acupuncture could improve the outcome of IVF: modulating neuroendocrinological factors; increasing blood flow to the uterus and ovaries; modulating cytokines; and reducing stress, anxiety, and depression. CONCLUSIONS: More high-quality randomized, controlled trials incorporating placebo acupuncture controls, authentic acupuncture interventions, and a range of outcome measures representative of both clinical outcomes and putative mechanistic processes are required to better assess the efficacy of acupuncture as an adjunct for IVF.

Acupuncture and PCOS

Current evidence of acupuncture on polycystic ovarian syndrome.

Lim CE, Wong WS. *Gynecol Endocrinol*. 2010 Mar 16. [Epub ahead of print]

Faculty of Medicine, South Western Sydney Clinical School, University of New South Wales, Sydney, Australia.

Objective. This paper aims to provide a literature review on evaluating the efficacy of acupuncture therapy in the treatment of polycystic ovarian syndrome (PCOS) by reviewing clinical trials; randomized and non-randomized and observational studies on PCOS. The paper will also determine the possible mechanism of acupuncture treatment in PCOS, limitations of recruited studies and suggest further improvements in future studies. **Design.** A comprehensive literature search was conducted through the databases Medline, PubMed, EMBASE, Cochrane, AMED (Allied and Complementary Medicine), NCCAM (The National Centre for Complementary and Alternative Medicine) to identify relevant monographs. **Results.** Four studies were recruited. Several studies showed that acupuncture significantly increases beta-endorphin levels for periods up to 24 h and may have regulatory effect on FSH, LH and androgen. beta-endorphin increased levels secondary to acupuncture affects the hyperthalamo-pituitary-adrenal (HPA) axis through promoting the release of ACTH through stimulation of its precursor pro-opiomelanocortin synthesis. **Inclusion criteria.** All available acupuncture studies on human subjects with PCOS from June 1970 to June 2009. **Exclusion criteria.** Studies not meeting the inclusion criteria, published in languages other than English or animal studies. **Conclusion.** Acupuncture is a safe and effective treatment to PCOS as the adverse effects of pharmacologic interventions are not expected by women with PCOS. Acupuncture therapy may have a role in PCOS by: increasing of blood flow to the ovaries, reducing of ovarian volume and the number of ovarian cysts, controlling hyperglycemia through increasing insulin sensitivity and decreasing blood glucose and insulin levels, reducing cortisol levels and assisting in weight loss and anorexia. However, well-designed, randomized controlled trials are needed to elucidate the true effect of acupuncture on PCOS.

Influence of Acupuncture on Infertility in Rats with Polycystic Ovarian Syndrome

Zhang Wei Yi et al, *Chinese Jnl Integrated Traditional and Western Med* 2009 Nov (8), 973
Chinese Journal of Integrated Traditional and Western Medicine

This research carried out in Wuhan, China examined the effect of acupuncture administered to rats on various fertility measures including the implantation rate of blastocysts. Acupuncture was used on the abdomen and limbs. This significantly increased ovarian and uterine development and the rate of implantation of embryos compared to the control group of rats which did not have acupuncture.

Abstract

Objective

To observe the effect and mechanism of acupuncture on infertility of rats with polycystic ovarian syndrome (PCOS).

Methods

PCOS rat model was induced by subcutaneous injection of oil solution of dehydroepiandrosterone (DHEA) in immature (24-day-old) female rats for continuous 20 days. Rats in the control group were given the same dose of DHEA oil.

PCOS rats were randomly divided into the control group (untreated) and the acupuncture group treated by needling acupoints of Guanyuan (CV4), Zhongji (CV3), Sanyinjiao (SP6) and Zigong (CX-CA1), 15 min once a day for 5 continuous days, starting from the 80th day after birth.

All rats were sacrificed at termination of the treatment, their uterus and ovaries were dissected for observation and blood levels of sex hormones were measured.

Results

Compared with the control group, the number of implanted blastocysts and the blastocyst implantation rate were higher and the blood levels of testosterone (T) and estradiol (E2) were lower in the acupuncture group ($P < 0.05$); but the difference between groups in serum levels of follicular stimulating hormone, luteinizing hormone and progesterone were of statistical insignificance ($P > 0.05$).

Moreover, the wet weight of the ovaries was lower and the equipotent diameter and area of glandular organ and cavity area ratio of gland and the stroma and mean thickness of endometria were higher in the acupuncture group than those in the control group ($P < 0.05$).

Conclusion

Acupuncture can significantly down-regulate the expressions of serum levels of T and E2, improve the development of ovaries and uterus, promote ovulation, enhance endometrial receptivity, and advance blastocyst implantation.

Electro acupuncture increases ovarian blood flow (PCOS)

Fertility and Sterility

Effect of electro-acupuncture stimulation of different frequencies and intensities on ovarian blood flow in anaesthetized rat with steroid-induced polycystic ovaries

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Abstract

Background

Maintenance of ovarian blood flow (OBF) is suggested to be important for regular ovulation in women with polycystic ovaries (PCO). The purpose of the present study was to investigate whether electro-acupuncture (EA) of different frequencies and intensities can improve the OBF of anaesthetized rat in the animal model of PCO.

Methods

PCO was experimentally induced by a single intramuscular (i.m.) injection of estradiol valerate (EV) in rats. Control rats were given i.m. injection of oil. The involvement of the two ovarian sympathetic nerves; superior ovarian nerve (SON) and plexus ovarian nerve (OPN), in OBF responses was elucidated by severance of SON and OPN in both control and PCO rats. How systemic circulatory changes affect OBF was evaluated by continuous recording of the blood pressure. OBF was measured on the surface of the ovary using laser Doppler flowmetry. Acupuncture needles were inserted bilaterally into the abdominal and hind limb muscles and connected to an electrical stimulator. Two frequencies of 2 Hz (low) and 80 Results

Low-frequency EA at intensities of 3 and 6 mA elicited significant increases in OBF in the Control group compared to baseline. In the PCO group the increases in OBF were significant only when stimulating with low-frequency EA at 6 mA. After severance of the ovarian sympathetic nerves, the increased response of OBF that had been induced by low-frequency EA in both the Control and PCO group was abolished, indicating that the OBF response is mediated via the ovarian sympathetic nerves. High-frequency EA at 6 mA significantly decreased OBF and mean arterial blood pressure (MAP) in the Control group compared to baseline. In the PCO group, the same stimulation produced similar decreases in MAP, but not in OBF.

Conclusion

Low-frequency EA stimulation with a strong intensity (6 mA) increases OBF in rats with steroid-induced PCO whereas less strong intensity (3 mA) induces similar changes in control rats. Severance of the ovarian sympathetic nerves abolishes this OBF increase in both study groups, which suggests that the responses of OBF to EA are mediated via the ovarian sympathetic

nerves. Hz (high) “ with three different intensities “ 1.5, 3, and 6 mA “ were applied for 35 s.

PCOS and Acupuncture: Electro-acupuncture normalizes EV-induced changes in ovarian ARs

Effect of electro-acupuncture on ovarian expression of alpha (1)- and beta (2)-adrenoceptors, and p75 neurotrophin receptors in rats with steroid-induced polycystic ovaries.

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BACKGROUND: Estradiol valerate (EV)-induced polycystic ovaries (PCO) in rats is associated with an increase in ovarian sympathetic outflow. Low-frequency (2 Hz) electro-acupuncture (EA) has been shown to modulate sympathetic markers as well as ovarian blood flow as a reflex response via the ovarian sympathetic nerves, in rats with EV-induced PCO. **METHODS:** In the present study, we further tested the hypothesis that repeated 2 Hz EA treatments modulate ovarian sympathetic outflow in rats with PCO, induced by a single i.m. injection of EV, by investigating the mRNA expression, the amount and distribution of proteins of alpha1a-, alpha1b-, alpha1d-, and beta2-adrenoceptors (ARs), as well as the low-affinity neurotrophin receptor (p75NTR). **RESULTS:** It was found that EV injection results in significantly higher mRNA expression of ovarian alpha1b- and alpha1d-AR in PCO rats compared to control rats. The p75NTR and beta2-ARs mRNA expression were unchanged in the PCO ovary. Low-frequency EA resulted in a significantly lower expression of beta2-ARs mRNA expression in PCO rats. The p75NTR mRNA was unaffected in both PCO and control rats. PCO ovaries displayed significantly higher amount of protein of alpha1a-, alpha1b- and alpha1d-ARs, and of p75NTR, compared to control rats, that were all counteracted by repeated low-frequency EA treatments, except for alpha1b-AR. **CONCLUSION:** The present study shows that EA normalizes most of the EV-induced changes in ovarian ARs. Furthermore, EA was able to prevent the EV-induced up regulation of p75NTR, probably by normalizing the sympathetic ovarian response to NGF action. Our data indicate a possible role of EA in the regulation of ovarian responsiveness to sympathetic inputs and depict a possible complementary therapeutic approach to overcoming sympathetic-related anovulation in women with PCOS.

Effect of electro acupuncture combined with auricular point tapping and pressing on serum insulin and testosterone in the patients of obese women with polycystic ovary syndrome

Xu J, Qu HQ, Fang HLXu J, Qu HQ, Fang HLZhongguo Zhen Jiu. 2009 Jun;29(6):441-3.

OBJECTIVE: To assess the therapeutic effect and mechanism of electro acupuncture combined with auricular point tapping and pressing on the obese women with polycystic ovary syndrome. **METHODS:** Thirty-nine cases of obese women with polycystic ovary syndrome were treated

with electro acupuncture combined with auricular point tapping and pressing, body points as Tianshu (ST 25), Fenglong (ST 40), Guanyuan (CV 4) and Siman (KI 14) etc. were selected, and ear points as Kou (mouth), Wei (stomach) and Pi (spleen) etc. were selected. After 3 courses, the therapeutic effect, the body mass index (BMI), the waist circumference (WC) and the changes of the serum insulin (Ins) and testosterone (T) were compared before and after treatment. RESULTS: Of the 39 cases, 10 cases were cured, 25 cases were effective, 4 cases were ineffective, with a total effective rate of 89.7%; there were significant differences in BMI, WC, Ins and T of the patients compared with that before treatment (all $P < 0.01$). CONCLUSION: Electroacupuncture combined with auricular point tapping and pressing has a good clinical effect on obese women with polycystic ovary syndrome, the treatment mechanism may realized by regulating the serum

Low-frequency electro acupuncture and physical exercise decrease high muscle sympathetic nerve activity in polycystic ovary syndrome.

Stener-Victorin E, Jedel E, Janson PO, Sverrisdottir YB. Institute of Neuroscience and Physiology, Dept. of Physiology, Sahlgrenska Academy, Univ. of Gothenburg, Box 434, SE-405 30 Göteborg, Sweden. elisabet.stener-victorin@neuro.gu.se Am J Physiol Regul Integr Comp Physiol. 2009 Aug;297(2):R387-95. Epub 2009 Jun 3.

We have recently shown that polycystic ovary syndrome (PCOS) is associated with high muscle sympathetic nerve activity (MSNA). Animal studies support the concept that low-frequency electro acupuncture (EA) and physical exercise, via stimulation of ergoreceptors and somatic afferents in the muscles, may modulate the activity of the sympathetic nervous system. The aim of the present study was to investigate the effect of these interventions on sympathetic nerve activity in women with PCOS. In a randomized controlled trial, 20 women with PCOS were randomly allocated to one of three groups: low-frequency EA ($n = 9$), physical exercise ($n = 5$), or untreated control ($n = 6$) during 16 wk. Direct recordings of multiunit efferent postganglionic MSNA in a muscle fascicle of the peroneal nerve before and following 16 wk of treatment. Biometric, hemodynamic, endocrine, and metabolic parameters were measured. Low-frequency EA ($P = 0.036$) and physical exercise ($P = 0.030$) decreased MSNA burst frequency compared with the untreated control group. The low-frequency EA group reduced sagittal diameter ($P = 0.001$), while the physical exercise group reduced body weight ($P = 0.004$) and body mass index ($P = 0.004$) compared with the untreated control group. Sagittal diameter was related to MSNA burst frequency ($R_s = 0.58$, $P < 0.005$) in the EA group. No correlation was found for body mass index and MSNA in the exercise group. There were no differences between the groups in hemodynamic, endocrine, and metabolic variables. For the first time we demonstrate that low-frequency EA and physical exercise lowers high sympathetic nerve activity in women with PCOS. Thus, treatment with low-frequency EA or physical exercise with the aim to reduce MSNA may be of importance for women with PCOS.

Influences of acupuncture on infertility of rats with polycystic ovarian syndrome

[Article in Chinese] Zhang WY, Huang GY, Liu J. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2009 Nov;29(11):997-1000.

Institute of Integrated Traditional Chinese and Western Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan.

OBJECTIVE: To observe the effect and mechanism of acupuncture on infertility of rats with polycystic ovarian syndrome (PCOS). **METHODS:** PCOS rat model was induced by subcutaneous injection of oil solution of dehydroepiandrosterone (DHEA) in immature (24-day-old) female rats for continuous 20 days. Rats for control were given with same dose of oil for instead. PCOS rats were randomly divided into the model group untreated and the acupuncture group treated by needling acupoints of Guanyuan (CV4), Zhongji (CV3), Sanyin-jiao (SP6) and Zigong (CX-CA1), 15 min once a day for 5 continuous days, starting from the 80th day after birth. All rats were sacrificed at terminal of the treatment, their uterus and bilateral ovaries were dissected for observation and blood levels of sex hormones were measured. **RESULTS:** compared with the model group, the number of implanted blastocyst and blastocyst implantation rate were higher and the blood levels of testosterone (T) and estradiol (E2) were lower in the acupuncture group ($P < 0.05$); but the difference between groups in serum levels of follicular stimulating hormone, luteinizing hormone and progesterone were of statistical insignificance ($P > 0.05$). Moreover, the wet weight of ovary was lower and the equipotent diameter and area of glandular organ and cavity, area ratio of gland and the stroma, and mean thickness of endometria were higher in the acupuncture group than those in the control group ($P < 0.05$). **CONCLUSION:** Acupuncture can conspicuously down regulate the expressions of serum levels of T and E2, improve the development of ovaries and uterus, promote ovulation, enhance en

Acupuncture and PCOS anovulation: Electro-Acupuncture induces regular ovulations

Effects of electro-acupuncture on anovulation in women with polycystic ovary syndrome.

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Department of Obstetrics and Gynecology, Goteborg University, Sweden.

BACKGROUND: The present study was designed to evaluate if electro-acupuncture (EA) could affect oligo-/anovulation and related endocrine and neuroendocrine parameters in women with polycystic ovary syndrome (PCOS). **METHODS:** Twenty-four women (between the ages of 24 and 40 years) with PCOS and oligo-/amenorrhea were included in this non-randomized, longitudinal, prospective study. The study period was defined as the period extending from 3 months before the first EA treatment, to 3 months after the last EA treatment (10-14 treatments), in total 8-9 months. The menstrual and ovulation patterns were confirmed by recording of vaginal bleedings and by daily registrations of the basal body temperature (BBT). Blood samples were collected within a week before the first EA, within a week after the last EA and 3 months after EA. **RESULTS:** Nine women (38%) experienced a good effect. They displayed a mean of 0.66 ovulations/woman and month in the period during and after the EA period compared to a mean of 0.15 before the EA period ($p=0.004$). Before EA, women with a good

effect had a significantly lower body-mass index (BMI) ($p<0.001$), waist-to-hip circumference ratio (WHR) ($p=0.0058$), serum testosterone concentration ($p=0.0098$), serum testosterone/sex hormone binding globulin (SHBG) ratio ($p=0.011$) and serum basal insulin concentration ($p=0.0054$), and a significantly higher concentration of serum SHBG ($p=0.040$) than did those women with no effect. **CONCLUSION:** Repeated EA treatments induce regular ovulations in more than one third of the women with PCOS. The group of women with good effect had a less androgenic hormonal profile before treatment and a less pronounced metabolic disturbance compared with the group with no effect. For this selected group EA offers an alternative to pharmacological ovulation induction.

PCOS (polycystic ovaries): Acupuncture reverses PCOS NFG abundance

Electro-acupuncture reverses nerve growth factor abundance in experimental polycystic ovaries in the rat.

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Polycystic ovary syndrome (PCOS) remains one of the most common causes of anovulation in women of reproductive age. There is some evidence that nerve growth factor (NGF) is involved in the pathogenesis of PCOS. Therefore, seeking the pathogenesis of PCOS is important for controlling fertility. In traditional Oriental Medicine, acupuncture has been used for the function of ovaries. The present study was designed to determine whether electro-acupuncture (EA) could affect experimentally induced polycystic ovary (PCO) in the rat. The two acupoints Sp-6 and E-128 were stimulated to test for efficacy in the protein expression of NGF. Polycystic ovaries were induced by a single injection of estradiol valerate (4 mg i.m.). During the experimental period of 8 weeks, some of the rats were treated with EA twice weekly; this group was compared with a vehicle-treated control group and an estradiol-injected group not subjected to EA. At day 60, the protein expression of NGF was examined by immunohistochemistry in the ovaries, the adrenal glands and some parts of the brain. The estradiol treatment induced a clear PCO appearance, and was associated with a robust increase in NGF expression in the ovaries, the adrenal glands and the brain. EA treatment partly reversed the NGF abundance, particularly in the ovaries, but not in the brain. Our data show that EA affects the NGF involvement in ovarian dysfunction. Copyright 2004 S. Karger AG, Basel

Hypothalamic neuroendocrine functions in rats with dihydrotestosterone-induced polycystic ovary syndrome: effects of low-frequency electro-acupuncture.

Feng Y, Johansson J, Shao R, Mannerås L, Fernandez-Rodriguez J, Billig H, Stener-Victorin E. Institute of Neuroscience and Physiology, Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden PLoS ONE 4(8): e6638. doi:10.1371/journal.pone.0006638

Adult female rats continuously exposed to androgens from prepuberty have reproductive and metabolic features of polycystic ovary syndrome (PCOS). We investigated whether such exposure adversely affects estrous cyclicity and the expression and distribution of gonadotropin-releasing hormone (GnRH), GnRH receptors, and corticotrophin-releasing hormone (CRH) in the hypothalamus and whether the effects are mediated by the androgen receptor (AR). We also assessed the effect of low-frequency electro-acupuncture (EA) on those variables. At 21 days of age, rats were randomly divided into three groups (control, PCOS, and PCOS EA; n = 12/group) and implanted subcutaneously with 90-day continuous-release pellets containing vehicle or 5alpha-dihydrotestosterone (DHT). From age 70 days, PCOS EA rats received 2-Hz EA (evoking muscle twitches) five times/week for 4-5 weeks. Hypothalamic protein expression was measured by immunohistochemistry and western blot. DHT-treated rats were acyclic, but controls had regular estrous cycles. In PCOS rats, hypothalamic medial preoptic AR protein expression and the number of AR- and GnRH-immunoreactive cells were increased, but CRH was not affected; however, GnRH receptor expression was decreased in both the pituitary and hypothalamus. Low-frequency EA restored estrous cyclicity within 1 week and reduced the elevated hypothalamic GnRH and AR expression levels. EA did not affect GnRH receptor or CRH expression. Interestingly, nuclear AR co-localized with GnRH in the hypothalamus. Thus, rats with DHT-induced PCOS have disrupted estrous cyclicity and an increased number of hypothalamic cells expressing GnRH, most likely mediated by AR activation. Repeated low-frequency EA normalized estrous cyclicity and restored GnRH and AR protein expression. These results may help explain the beneficial neuroendocrine effects of low-frequency EA in women with PCOS.

Acupuncture and exercise restore adipose tissue expression of sympathetic markers and improve ovarian morphology in rats with dihydrotestosterone-induced PCOS

Manneras L. Cajander S. Lonn M. Stener-Victorin E.

Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden. American Journal of Physiology - Regulatory Integrative and Comparative Physiology. 2009; 296(4)(pp R1124-R1131),

Altered activity of the sympathetic nervous system, which innervates adipose and ovarian tissue, may play a role in polycystic ovary syndrome (PCOS). We hypothesize that electro-acupuncture (EA) and physical exercise reduce sympathetic activity by stimulating ergoreceptors and somatic afferent pathways in muscles. Here we investigated the effects of low-frequency EA and physical exercise on mRNA expression of sympathetic markers in adipose tissue and on ovarian morphology in female rats that received dihydrotestosterone (DHT) continuously, starting before puberty, to induce PCOS. At age 11 wk, rats with DHT-induced PCOS were randomly divided into three groups: PCOS, PCOS plus EA, and PCOS plus exercise. The latter two groups received 2-Hz EA (evoking muscle twitches) three times/week or had free access to a running wheel for 4-5 wk. In mesenteric adipose tissue, expression of beta3-adrenergic receptor (ADRB3), nerve growth factor (NGF), and neuropeptide Y (NPY) mRNA was higher in untreated PCOS rats than in controls. Low-frequency EA and

exercise down regulated mRNA expression of NGF and NPY, and EA also down regulated expression of ADRB3, compared with untreated rats with DHT-induced PCOS. EA and exercise improved ovarian morphology, as reflected in a higher proportion of healthy antral follicles and a thinner theca interna cell layer than in untreated PCOS rats. These findings support the theory that increased sympathetic activity contributes to the development and maintenance of PCOS and that the effects of EA and exercise may be mediated by modulation of sympathetic outflow to the adipose tissue and ovaries

Effects of electro acupuncture on in vitro fertilization and embryo transplantation in the patient of infertility with different syndromes

[Article in Chinese] Cui W, Liu LL, Sun W, Kong W. Second Affiliated Hospital of Shandong University of TCM, Jinan, China. cuiwei9996@sohu.com Zhongguo Zhen Jiu. 2008 Apr;28(4):254-6.

OBJECTIVE: To probe into effects of electro acupuncture (EA) on in vitro fertilization and embryo transplantation (IVF-ET) in the patient of infertility with different syndromes. **METHODS:** Among the 126 patients of infertility who received EA for IVF-ET, 52 cases of kidney deficiency type (group A), 44 cases of the liver-qi stagnation type (group B) and 30 cases of phlegm-dampness type (group C) were selected. All of them in the 3 groups were treated with EA before and during controlled ovarian hyper-stimulation, and the effects of EA on the patients in the 3 groups were investigated. **RESULTS:** The fertility rate, implantation rate and clinical pregnancy rate were 81.3%, 23.5%, 44.1% in group A, 80.5%, 27.8%, 46.5% in group B and 71.9%, 17.1%, 32.7% in group C, respectively, group A and B being better than group C ($P<0.05$); the good quality embryo rate of 70.7% in group B was significantly higher than 57.9% in group C ($P<0.05$); there were no significant differences in patient's basal condition, the dosage and administration time of gonadotropin, and blood level of estradiol on the day of injection of human chorionic gonadotropin, the number of gained oocytes, oocyte cleavage rate and the number of transplantation embryo among the 3 groups. **CONCLUSION:** Clinical effects of EA treatment on IVF-ET in the infertility patients of kidney deficiency type and the patients of the liver-qi stagnation type are better than that in the patients of phlegm-dampness type.

Acupuncture in assisted reproductive technology and PCOS.

Stener-Victorin E. Von Hagens C. Gynakologische Endokrinologie. 6(2)(pp 67-71), 2008

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In controlled trials, acupuncture alleviated pain during oocyte aspiration for in vitro fertilization/embryo transfer (IVF/ET) treatment and regulated uterine and ovarian blood flow. Recent clinical and experimental data on the effect of acupuncture in polycystic ovary syndrome (PCOS) clearly demonstrate that acupuncture affects PCOS via modulation of endocrine, neuroendocrine and endogenous regulatory systems and exerts long-lasting beneficial effects on ovulation and on metabolic and endocrine systems. Some trials even suggest that acupuncture at embryo transfer has a positive impact on pregnancy rates. Results of recent

trials are discussed, as are the difficulties and confounders associated with the interpretation of controlled trials and an attempt to standardize reporting of acupuncture interventions (STRICTA). Acupuncture is a safe intervention in the hands of competent practitioners and is low in cost, but well-designed studies are lacking. Clinicians and scientists are encouraged to conduct large, prospective, randomized trials to demonstrate more precisely the physiological impact of acupuncture on the reproductive system and its possible impact on pregnancy rates.

Acupuncture in polycystic ovary syndrome: Current experimental and clinical evidence.

Stener-Victorin E. Jedel E. Manneras L. Institute of Neuroscience and Physiology, Department of Physiology, Goteborg University, Goteborg, Sweden. *Journal of Neuroendocrinology*. 20(3)(pp 290-298), 2008

This review describes the aetiology and pathogenesis of polycystic ovary syndrome (PCOS) and evaluates the use of acupuncture to prevent and reduce symptoms related with PCOS. PCOS is the most common female endocrine disorder and it is strongly associated with hyperandrogenism, ovulatory dysfunction and obesity. PCOS increases the risk for metabolic disturbances such as hyperinsulinemia and insulin resistance, which can lead to type 2 diabetes, hypertension and an increased likelihood of developing cardiovascular risk factors and impaired mental health later in life. Despite extensive research, little is known about the aetiology of PCOS. The syndrome is associated with peripheral and central factors that influence sympathetic nerve activity. Thus, the sympathetic nervous system may be an important factor in the development and maintenance of PCOS. Many women with PCOS require prolonged treatment. Current pharmacological approaches are effective but have adverse effects. Therefore, nonpharmacological treatment strategies need to be evaluated. Clearly, acupuncture can affect PCOS via modulation of endogenous regulatory systems, including the sympathetic nervous system, the endocrine and the neuroendocrine system. Experimental observations in rat models of steroid-induced polycystic ovaries and clinical data from studies in women with PCOS suggest that acupuncture exerts long-lasting beneficial effects on metabolic and endocrine systems and ovulation.

Clinical study on needle-pricking therapy for treatment of polycystic ovarian syndrome

Chen D. Chen SR. Shi XL. Guo FL. Zhu YK. Li S. Cai MX. Deng LH. Xu H. *Zhongguo Zhenjiu*. 27(2):99-102, 2007 Feb. The First Affiliated Hospital of Jinan University, Guangzhou 510630, China. drchendong@yahoo.com.cn[Chinese]

OBJECTIVE: To probe into the clinical effect of needle-pricking therapy for treatment of polycystic ovarian syndrome. **METHODS:** One hundred and twenty-one cases of polycystic ovarian syndrome were divided into a needle-pricking therapy group of 61 cases and a medication group of 60 cases with randomized and controlled method. The needle-pricking therapy group were treated by needle-pricking therapy at sacral plexus stimulating points on both sides of the spine and lateral points of Dazhui (CV 14), and the medication group by oral

administration of Clomiphene and intramuscular injection of chorionic gonadotropin (HCG). Levels of hormones and symptoms in the patients before treatment, after treatment of 3 cycles and at the sixth cycle after treatment were investigated. RESULTS: After treatment of 3 cycles, the level of hormone and B type ultrasound examination were significantly improved in the two groups ($P < 0.01$). At the sixth cycle after treatment, the conditions of the patients in the medication group were returned to the original levels before treatment, while the conditions in the needle-pricking therapy group still kept at the post-therapeutic level, and their menstruation and ovulation restored to normal state, and the ovulation mucosa and the pregnancy rate were significantly higher than those in the medication group (all $P < 0.01$). CONCLUSION: Needle-pricking therapy has obvious effect on polycystic ovarian syndrome, and has a good long-term therapeutic effect.

Application of acupuncture in intrauterine insemination in patients with polycystic ovary syndrome.

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Journal of Clinical Rehabilitative Tissue Engineering Research. 11(39)(pp 7996-7998), 2007.

Aim: To summarize the influence of acupuncture on intrauterine insemination (IUI) in patients with polycystic ovary syndrome (PCOS) and its application through the study of recent ten-year relevant literatures. Methods: The articles of influence of acupuncture on patients with PCOS were searched for in China Journal Full-text Database (CJFD) published from January 1996 to June 2006 with the key words of "acupuncture, polycystic ovary syndrome, intrauterine insemination" in Chinese. At the same time, Elsevier-SDOL database was undertaken to identify the relevant articles published between January 1996 and June 2006 with the same key words in English. Results: The selected articles should be as follows: the effect of acupuncture on PCOS patients, the application of acupuncture to IUI, the influential factors during IUI and study of acupuncture on this aspect. Totally 200 articles of the effect of acupuncture on PCOS patients, 300 of the influential factors during IUI, 30 of the application of acupuncture to IUI were collected, and 16 of them were accorded with the criteria. Most former study had focused on acupuncture for PCOS and clinical research of acupuncture for improving ovulation. It thought that acupuncture could effectively cure PCOS, improve ovulation by stimulating ovary, and believed that acupuncture for improving ovulation not only had no side effect. but also could get good curative effect, which was stable and unvarying. Besides, German scholars found that if acupuncture therapy was used in insemination externalis or intracytoplasmic sperm injection (ICSI), the successful rate of pregnancy was nearly 50%. However, there was no report of the application of acupuncture to IUI in patients with PCOS at abroad. Conclusion: IUI has been widely used in the treatment of infertilities, and acupuncture has better accelerated effect on ovulation. Therefore, acupuncture therapy can be applied before and after IUI in PCOS patients so as to study the application of acupuncture that induces ovulation to IUI in PCOS patients and observe the successful rate of IUI in PCOS patients due to acupuncture.

The Effect of Acupuncture in Treating Polycystic Ovary Syndrome

Qu F. Zhou J. Zhu H. Nan R International Journal of Clinical Acupuncture 2006;15(4):233-6.

Objective: To explore the effect of acupuncture in treating polycystic ovary syndrome (PCOS).
Method: 25 patients were treated with acupuncture. The menstrual cycle, genital hormone and that were detected. Result: 20 patients recovered regular menstruation, and the level of gonadal hormone was improved, the maximum cross-section areas of ovaries and the number of corpora luteal atresia decreased. 10 of the 16 patients with sterility were able to become pregnant. Conclusion: Acupuncture can safely and effectively treat patients with PCOS, which deserves further clinical application and research.

Chinese medicine/herbs and PCOS

Clinical observation on treatment of 43 women with polycystic ovary syndrome based on syndrome differentiation

Zhong Xi Yi Jie He Xue Bao. 2006 Nov;4(6):585-8.

Jia LN, Wang XJ.

Department of Gynecology of Integrative Medicine, Huashan Hospital, Fudan University, Shanghai 200040, China.

OBJECTIVE: To investigate the therapeutic effect of treatment based on syndrome differentiation and its influence on the serum levels of testosterone and insulin in women with polycystic ovary syndrome (PCOS). **METHODS:** Forty-three women, diagnosed with PCOS as well as syndrome of kidney yin deficiency or syndrome of spleen qi deficiency, were enrolled in the study. Twenty-five PCOS women with syndrome of kidney yin deficiency were treated with traditional Chinese herbs for nourishing yin to reduce fire (nourishing yin group), and 18 PCOS women with syndrome of spleen qi deficiency were treated with herbs for invigorating spleen and replenishing qi (replenishing qi group). Body mass index (BMI), waist-to-hip ratio (WHR), waist circumference (WC), and the serum levels of insulin and testosterone before and after treatment were detected. **RESULTS:** Among the 43 cases, 20 cases had high serum testosterone level, in which 13 cases with syndrome of kidney yin deficiency, 7 cases with syndrome of spleen qi deficiency, but the difference had no statistical significance; 17 cases had high serum insulin level, in which 11 cases with syndrome of spleen qi deficiency, 6 cases with syndrome of kidney yin deficiency, the difference had statistical significance ($P<0.05$). In nourishing yin group, the serum levels of insulin and testosterone declined after treatment ($P<0.05$), and BMI, WHR and WC showed no significant changes. In replenishing qi group, the serum level of insulin declined after treatment ($P<0.01$), and BMI, WHR, WC and the serum level of testosterone showed no significant changes. **CONCLUSION:** Traditional Chinese herbs for nourishing yin to reduce fire can significantly reduce the serum levels of testosterone and insulin in PCOS women with syndrome of kidney yin deficiency, and herbs for invigorating spleen and replenishing qi can significantly reduce the serum level of insulin in PCOS women with syndrome of spleen qi deficiency.

Acupuncture and sperm

A prospective randomized placebo-controlled study of the effect of acupuncture in infertile patients with severe oligoasthenozoospermia.

Fertil Steril. 2009 Oct;92(4):1340-3. Epub 2009 Apr 25.

Dieterle S, Li C, Greb R, Bartsch F, Hatzmann W, Huang D.

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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.

Point- and frequency-specific response of the testicular artery to abdominal electro acupuncture 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 electro acupuncture can improve sperm manufacture in this instance.

Abstract

Objective: To clarify the role of the abdominal acupuncture points and the frequency of short-term electro acupuncture (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.

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

1997, Vol. 39, No. 2 , Pages 155-161

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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 ultra morphological observations. The fertility index increased significantly ($p \leq .05$) following improvement in total functional sperm fraction, percentage of viability, total motile spermatozoa per ejaculate, and integrity of the axonema ($p \leq .05$), which occurred upon treatment. The intactness of axonema and sperm motility were highly correlated ($\text{corr.} = .50, p \leq .05$). Thus, patients exhibiting a low fertility potential due to reduced sperm activity may benefit from acupuncture treatment.

Effects of Electro-Acupuncture on Nerve Growth Factor and Ovarian Morphology in Rats with Experimentally Induced Polycystic Ovaries

Elisabet Stener-Victorin

2,a, Thomas Lundeborgb, Urban Waldenströma, Luigi Mannic, Luigi Aloec, Stefan Gunnarssond, and Per Olof Janssona

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ABSTRACT

Despite extensive research on the pathogenesis of polycystic ovary syndrome (PCOS), there is still disagreement on the underlying mechanisms. The rat model for experimentally induced polycystic ovaries (PCO)—produced by a single injection of estradiol valerate—has similarities with human PCOS, and both are associated with hyperactivity in the sympathetic nervous system. Nerve growth factor (NGF) is known to serve as a neurotrophin for both the sympathetic and the sensory nervous systems and to enhance the activity of catecholaminergic and possibly other neuron types. Electro-acupuncture (EA) is known to reduce hyperactivity in the sympathetic nervous system. For these reasons, the model was used in the present study to investigate the effects of EA (12 treatments, approximately 25 min each, over 30 days) by analyzing NGF in the central nervous system and the endocrine organs, including the ovaries. The main findings in the present study were first, that significantly higher concentrations of NGF were found in the ovaries and the adrenal glands in the rats in the PCO model than in the control rats that were only injected with the vehicle (oil or NaCl). Second, that repeated EA treatments in PCO rats resulted in concentrations of NGF in the ovaries that were significantly lower than those in non-EA-treated PCO rats but were within a normal range that did not differ from those in the untreated oil and NaCl control groups. The results in the present study provide support for the theory that EA inhibits hyperactivity in the sympathetic nervous system.

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

INTERVENTION(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.

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 oligoastenoteratozoospermia without apparent cause.

Influence of acupuncture on idiopathic male infertility in assisted reproductive technology.

Zhang M et al J Huazhong Univ Sci Tech Med Sci.2002;22(3):228-30

Journal of Huazhong University (Abstract in Chinese)

This trial looks at sperm behaviour in an IVF setting. It was a “before and after” study involving 82 infertile men with pathological semen abnormalities and who’s sperm achieved a poor fertilization rate in at least 2 IVF/ICSI cycles. They were given acupuncture twice a week over 8 weeks and the IVF/ICSI cycles were repeated. The fertilization rates after acupuncture (66.2%) were significantly higher than that before treatment (40.2%) ($P < 0.01$).

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 ($p < 0.01$) i.e. 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.

Direct effects of Chinese herbal medicine “hachuekkito” on sperm movement.

“Yamanaka M; Kitamura M; Kishikawa H; Tsuboniwa N; Koga M; Nishimura K; Tsujimura A; Takahara S; Matsumiya K; Okuyama A Department of Urology, Osaka University Medical School

Nippon Hinyokika Gakkai Zasshi, 89(7):641-6 1998 Jul (ISSN: 0021-5287)

BACKGROUND AND PURPOSE: Chinese herbal medicine, “Hochuekkitto” is widely used for male infertility in Japan. There have been many reports concerning its clinical usefulness but very few reports of in vitro experiments studying the mechanism of its effects. In addition to stimulating germ cells, we analyzed its direct effects on sperm using computer assisted semen analyzer (CASA). **MATERIALS AND METHODS:** Motile sperm were prepared using swim up

technique from semen collected from ten healthy volunteers. Sperm movements (motility, velocity, linearity) were analyzed by CASA after adding either serum containing anti-sperm antibody (ASA) or normal serum with or without Hochuekkito. RESULTS: Two hours after adding serum with ASA, the decrease of sperm motility was significantly reduced from 25.1% (92.8%→67.7%) to 12.5% (92.9%→80.6%) by adding Hochuekkito. No significant difference in velocity and linearity was observed between two groups. By adding normal serum, any of three parameters differed significantly with or without Hochuekkito. CONCLUSION: Protective effects of Hochuekkito on sperm was suggested. Although normal sperm with ASA was used in this report, since the sperm of infertile patients are said to be more fragile, this results imply that direct protective effect is one of the mechanism of Hochuekkito for male infertility

Effect of acupuncture on sperm parameters of males suffering from subfertility related to low sperm quality.

Siterman S; Eltes F; Wolfson V; Zabludovsky N; Bartoov B Institute of Chinese Medicine, Tel Aviv, Israel.

Arch Androl, 39(2):155-61 1997 Sep-Oct (ISSN: 0148-5016)

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.

An experimental study on inhibitory effect of Chinese medicine tai-bao on antisperm antibody

Lai AN; Song JF; Liu XJ Xiyuan Hospital, China Academy of TCM, Beijing.

Chung Kuo Chung Hsi I Chieh Ho Tsa Chih, 17(6):360-2 1997 Jun (ISSN: 1003-5370)

OBJECTIVE: To investigate whether Chinese medicine Tai-bao could inhibit antisperm antibody in experimental mice. METHODS: The experimental immunoinfertility mice were due to antisperm antibody induced by injection of human sperm membrane antigens. The experimental immuno-infertile mice used in the present study were divided into four groups including Tai-bao high dose group (46.8 g.kg-1.d-1), Tai-bao low dose group (31.2 g.kg-1.d-1), prednisone group and normal saline group. The enzyme linked immune sorbent assay (ELISA) and microcytotoxic assay were used for detection of antisperm antibody. The change of levels of antisperm antibody before and after treatment, pregnant rate, and the number of implantation were

investigated in tested mice. RESULTS: The pregnant rates in normal saline group, prednisone group, Tai-bao high dose group and low dose were 38.89%, 47.06%, 70.00% and 75.00% respectively. The rate of pregnancy in Tai-bao low dose group was significantly higher as compared with normal saline group ($P < 0.05$). The rate of implantation in Tai-bao low dose group was significantly higher than that in prednisone group ($P < 0.05$). The results of detection of cytotoxic antibody to sperm showed that cytotoxic percentages in Tai-bao high dose group ($63.0 \pm 10.3\%$) and prednisone group ($56.3 \pm 13.7\%$) were significantly lower ($P < 0.05$ and $P < 0.01$) than that in normal saline group ($72.84 \pm 5.05\%$). CONCLUSION: Chinese medicine Tai-bao possesses regulatory effect on reproductive immune function, inhibitory effect on antisperm cytotoxic antibody, and promoting effect on pregnancy.

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.

Male infertility treated by bushen shengjing pill in clinical observation and evaluation on its curative effect

Yue GP; Chen Q; Dai N Institute of Acupuncture and Meridians, Anhui College of TCM, Hefei.

Chung Kuo Chung Hsi I Chieh Ho Tsa Chih, 16(8):463-6 1996 Aug (ISSN: 1003-5370)

Eighty-seven cases of male infertility with semen abnormality were treated and observed by Bushen Shengjing Pill, its curative effect was evaluated with quantitative assessment and analytical comparison comprehensive scoring of semen routine analysis. These patients were treated for one of three courses of treatment, the semen quality was enhanced obviously, the comprehensive semen routine analysis score was enhanced significantly ($P < 0.001$) as compared with that before treatment, the spouse pregnant rate was 56.32% (49/87), and total effective rate was 95.40% (83/87). The result showed that this prescription had bidirectional regulatory function in follicle stimulating hormone, luteotropic hormone, testosterone, corticosterone, and could make the enhanced or reduced hormone level to normal value.

Effects of guizhi-fuling-wan on male infertility with varicocele

Ishikawa H; Ohashi M; Hayakawa K; Kaneko S; Hata M Department of Urology, Ichikawa General Hospital, Tokyo Dental College, Chiba, Japan.

Am J Chin Med, 24(3-4):327-31 1996 (ISSN: 0192-415X)

Thirty-seven infertile patients with varicocele were treated with Guizhi-Fuling-Wan (7.5 g/day) for at least 3 months. Before and after the administration, semen qualities such as sperm concentration and motility were examined, and the varicocele was graded. A varicocele disappearance rate of 80% was obtained with 40 out of 50 varicocele, and improvement of sperm concentration and motility were found in 71.4% and 62.1% of patients, respectively. From these results, Guizhi-Fuling-Wan is considered to be effective for circulation disorders in varicocele as well as semen quality.

Correlation of psychological changes and spermogram improvements following acupuncture (article in German)

Riegler R et al Urologe A. 1984 Nov;23(6):329-33

Der Urologe

This German group were the first to publish studies on the effect of acupuncture on sperm parameters. In this study they not only measured changes in semen analysis after acupuncture but also certain psychological parameters.

Abstract

The purpose of the study was to find the correlation between the effect of acupuncture on fertility and psychological effects. To investigate its influence on male subfertility, 28 patients received acupuncture treatment after informed consent. We evaluated subjective parameters by written psychological tests, while objective parameters consisted of measuring concentration,

volume and motility in the spermiogram before and after acupuncture. There was a significant increase in sperm quality in all parameters but volume. The psychological test showed no change caused by acupuncture. Hence, we believe, that the effect of acupuncture on sperm quality is not caused by placebo-mechanisms.

Acupuncture normalizes dysfunction of hypothalamic-pituitary-ovarian axis

Acupunct Electrother Res. 1997;22(2):97-108.

Acupuncture normalizes dysfunction of hypothalamic-pituitary-ovarian axis.

Chen BY.

Institute of Acupuncture, Shanghai Medical University, P.R. China.

This article summarizes the studies of the mechanism of electro acupuncture (EA) in the regulation of the abnormal function of hypothalamic-pituitary-ovarian axis (HPOA) in our laboratory. Clinical observation showed that EA with the effective acupoints could cure some anovulatory patients in a highly effective rate and the experimental results suggested that EA might regulate the dysfunction of HPOA in several ways, which means EA could influence some gene expression of brain, thereby, normalizing secretion of some hormones, such as GnRH, LH and E2. The effects of EA might possess a relative specificity on acupoints.

Acupuncture and wellbeing of IVF patients

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.

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 lay 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 psycho- logical 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.

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 wellbeing. 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 Fertilization (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 counseling interventions have previously been widely recommended in parallel with infertility treatments but whilst in many jurisdictions counseling 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 analyze 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.<http://www.biomedcentral.com/1472-6882/9/50>

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.

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

Balk J et al, Complementary Therapies in Clinical Practice, Online 24 December 2009

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

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 wellbeing, 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 wellbeing, 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.

Acupuncture and Pregnancy

Acupuncture for Depression During Pregnancy: A Randomized Controlled Trial

Manber R et al, Obst and Gynec 2010, 115 (3) 511 - 520

Obstetrics and Gynecology

Since there is evidence that the use of antidepressants increases the risk of miscarriage there has been much interest in the use of acupuncture to treat depression which occurs in pregnancy.

A number of trials and systematic reviews of the effectiveness of acupuncture in the treatment of depression have been published over the last 5 years and a meta-analysis of these trials concluded that acupuncture is an effective treatment for depression. This trial looked specifically at depression in pregnancy and found that acupuncture was as effective as other standard treatments and worked more quickly.

Abstract

OBJECTIVE: To estimate the efficacy of acupuncture for depression during pregnancy in a randomized controlled trial.

METHODS: A total of 150 pregnant women who met Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) criteria for major depressive disorder were randomized to receive either acupuncture specific for depression or one of two active controls: control acupuncture or massage. Treatments lasted 8 weeks (12 sessions). Junior acupuncturists, who were not told about treatment assignment, needled participants at points prescribed by senior acupuncturists. All treatments were standardized. The primary outcome was the Hamilton Rating Scale for Depression, administered by masked raters at baseline and after 4 and 8 weeks of treatment. Continuous data were analyzed using mixed effects models and by intent to treat.

RESULTS: Fifty-two women were randomized to acupuncture specific for depression, 49 to control acupuncture, and 49 to massage. Women who received acupuncture specific for depression experienced a greater rate of decrease in symptom severity ($P < .05$) compared with the combined controls (Cohen's $d = 0.39$, 95% confidence interval [CI] 0.01–0.77) or control acupuncture alone ($P < .05$; Cohen's $d = 0.46$, 95% CI 0.01–0.92). They also had significantly greater response rate (63.0%) than the combined controls (44.3%; $P < .05$; number needed to treat, 5.3; 95% CI 2.8–75.0) and control acupuncture alone (37.5%; $P < .05$; number needed to treat, 3.9; 95% CI 2.2–19.8). Symptom reduction and response rates did not differ significantly between controls (control acupuncture, 37.5%; massage, 50.0%).

CONCLUSION: The short acupuncture protocol demonstrated symptom reduction and a response rate comparable to those observed in standard depression treatments of similar length and could be a viable treatment option for depression during pregnancy

Acupuncture for breech version: principles, technique, mode of action and utility--a literature review.

J Matern Fetal Neonatal Med. 2010 May;23(5):455-8.

Sananès N, Vayssière C, Helmlinger C, Viville B, Kohler M, Aïssi G, Trieu NT, Langer B, Favre R.

CMCO-SIHCUS, Department of Obstetrics and Gynecology, Schiltigheim, France.
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Abstract

OBJECTIVE: Version to correct breech presentation at term remains important, because feet-first vaginal delivery of a baby is associated with a higher risk of fetal morbidity and mortality.

METHOD: The technique consists of puncture at point B67. This technique is thought to work by increasing the probability of the fetus turning by increasing active fetal movements.

RESULTS: Five randomized studies evaluating the value of acupuncture in cases of siege presentation indicate that this method tended to be effective. However, no placebo-controlled study has been carried out.

CONCLUSION: Acupuncture should be attempted in cases of breech presentation.

Acupuncture For Prebirth Treatment: An Observational Study of Its Use in Midwifery Practice

Betts D and Lennox S, Medical Acupuncture 2006, 17, (3) 16 - 19

Medical Acupuncture

This review conducted in New Zealand revealed that women who had acupuncture in the last 4 weeks of their pregnancy had a third less the number of medical inductions, epidurals and emergency caesarians compare to local population rates.

ABSTRACT

Background Midwives in Wellington, New Zealand, observed that women receiving prebirth acupuncture consistently experienced efficient labors, reporting a reduction in the length of labor and medical intervention, specifically the use of epidurals, medical inductions, and cesarean deliveries.

Objective To undertake a naturalistic observational study of women receiving acupuncture as part of their antenatal care.

Design, Setting, and Patients Practices of 14 midwives recorded their prebirth acupuncture treatments over a 4-month period in 2004 in 169 New Zealand women who received prebirth acupuncture.

Main Outcome Measures Gestation at onset of labor, incidence of medical induction, length of labor, use of analgesia, and type of delivery.

Results When compared with the local population rates, there was an overall 35% reduction in the number of inductions (for primigravida women, this was a 43% reduction); 31% reduction in the epidural rate; 32% reduction in emergency cesarean delivery; and a 9% increase in normal vaginal birth.

Conclusions Prebirth acupuncture appeared to provide some promising therapeutic benefits in assisting women to have a normal vaginal birth. A further randomized controlled study is warranted. **KEY WORDS**

Acupuncture: hormone changes/ blood flow/endometrium/poor responders

Changes in serum cortisol and prolactin associated with acupuncture during controlled ovarian hyperstimulation in women undergoing in vitro fertilization–embryo transfer treatment

Magarelli, PC, D Cridennda, M Cohen. Fertil Steril. 2009 Dec;92(6):1870-9

Fertility and Sterility

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;—:—. ♦ 2008 by American Society for Reproductive Medicine.)

Key Words: IVF, acupuncture, cortisol, prolactin, pregnancy, traditional Chinese medicine, TCM

A randomized double blind comparison of real and placebo acupuncture in IVF treatment.

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

This trial (also included above in the Embryo Transfer trials) examined the effect of acupuncture using real or placebo needles on blood flow to the lining of the uterus and found that when certain acupuncture points were stimulated whether by pricking or by penetration the blood flow increased significantly.

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.

Effects of electro acupuncture on in vitro fertilization-embryo transfer (IVF-ET) of patients with poor ovarian response.

Chen J et al [Chinese] Zhongguo Zhenjiu 2009;29:775-9

A randomized controlled trial to observe the effect of electro acupuncture therapy on oocyte quality and pregnancy outcome of 60 patients with poor ovarian response or decreased reserve in the course of in vitro fertilization (IVF). The levels of serum estradiol, fertilization rate, oocyte maturation rate, good quality embryos rate, and implantation rate in the acupuncture group were superior to those in the control group on the day of human Chorionic Gonadotropin (hCG) injection (all $p < 0.05$). Also, the levels of stem cell factor in follicular fluid and serum in the acupuncture group were significantly higher than those in the control group (both $p < 0.05$). The researchers concluded that electro acupuncture therapy has a good clinical effect for IVF patients with poor ovarian reserve, and can improve oocyte quality and pregnancy outcome.

Electroacupuncture Reduces Uterine Artery Blood Flow Impedance in Infertile Women

Ho M et al. Taiwanese Journal of Obstetrics and Gynecology 2009;48:148-51.

A randomized controlled trial that evaluated the effects of electro acupuncture on pregnancy rate and uterine artery blood flow impedance in patients undergoing in vitro fertilization (IVF). A total of 44 patients were enrolled in the study. Acupuncture was performed four times, twice a week for 2 weeks, from day 2 of the study to the day before oocyte retrieval. Clinical pregnancy and Pulsatility index (PI) of right and left uterine arteries before and after treatment were measured. There was no significant difference in pregnancy rate between the two groups (acupuncture group 30%; non-acupuncture group 28.6%). The mean PI of both uterine arteries was significantly reduced after acupuncture (left uterine artery 2.3 to 2.0; right uterine artery 2.4 to 2.2), but not in the no acupuncture group (left uterine artery 2.5 to 2.3; right uterine artery 2.4 to 2.3). The researchers concluded that electro acupuncture could be useful for reducing uterine artery blood flow impedance, but did not increase the pregnancy rate in patients undergoing IVF.

Clinical observation on acupuncture for treatment of infertility of ovulatory disturbance.

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Zhongguo Zhenjiu. 28(1):21-3, 2008 Jan.

OBJECTIVE: To probe into clinical therapeutic effect of acupuncture on infertility of ovulatory disturbance and the mechanism. **METHODS:** The patients were randomly divided into an acup-moxibustion group and a medication group in the order of visiting, 60 cases in each group. The acup-moxibustion group were treated with acupuncture at Zhongji (CV 3), Guanyuan (CV 4), Zigong (EX-CA 1), Zusanli (ST 36), Sanyinjiao (SP 6) and suspended moxibustion over Shenque (CV 8), Sanyinjiao (SP 6), and the medication group with oral administration of 50 mg Clomiphene. After treatment for 3 menstrual cycles, pregnancy rate, basal body temperature, B-ultrasonic examination and ovulation were assessed. **RESULTS:** Acup-moxibustion and oral administration of Clomiphene had higher ovulating effect, with no significant difference between them ($P > 0.05$); the pregnancy rate in the acup-moxibustion group was significantly higher than that in the medication group ($P < 0.05$). **CONCLUSION:** Acup-moxibustion and Clomiphene have a same ovulating effect, and the pregnancy rate is higher and the abortion rate is lower for the patient of acup-moxibustion treatment than that for oral administration of Clomiphene.

Traditional Chinese medicine and infertility.

Huang S.-T. Chen A.P.-C. Current Opinion in Obstetrics and Gynecology. 20(3)(pp 211-215), 2008

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PURPOSE OF REVIEW: The present review gives an overview of the potential use of traditional Chinese medicine in the treatment of infertility, including an evidence-based evaluation of its efficacy and tolerance. **RECENT FINDINGS:** Recent studies demonstrated that traditional Chinese medicine could regulate the gonadotropin-releasing hormone to induce ovulation and improve the uterus blood flow and menstrual changes of endometrium. In addition, it also has impacts on patients with infertility resulting from polycystic ovarian syndrome, anxiety, stress and immunological disorders. Although study design with adequate sample size and appropriate control for the use of traditional Chinese medicine is not sufficient, the effective studies have already indicated the necessity to explore the possible mechanisms, that is, effective dose, side effect and toxicity of traditional Chinese medicine, in the treatment of infertility by means of prospective randomized control trial. **SUMMARY:** The growing popularity of traditional Chinese medicine used alone or in combination with Western medicine highlights the need to examine the pros and cons of both Western and traditional Chinese medicine approaches. Integrating the principle and knowledge from well characterized approaches and quality control of both traditional Chinese medicine and Western medical approaches should become a trend in existing clinical practice and serve as a better methodology for treating infertility.

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 up regulate 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.

Acupuncture & IVF Poor Responders: A Cure?

Magarelli P, Cridennda D. Fertil Steril, 2004;81(Supplement 3):S20

Fertility and Sterility

This clinical trial combined the acupuncture protocol used on the day of embryo transfer with the acupuncture treatment protocol designed to increase blood flow to the uterus. The authors report that "Significant increases in pregnancy outcomes were confirmed by this study which demonstrated that both acupuncture treatment protocols could be used together with a synergistic effect." They add that "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."

Abstract

The utility of acupuncture in the treatment of infertility has been demonstrated in two controlled studies. The first study determined the effect of reducing the Pulsatility Index (PI) of the uterine artery on reproductive outcomes; the second study described a Pre/Post embryo transfer protocol that enhanced overall pregnancy rates (PR).

There are no studies that have utilized both techniques.

Objective: The purpose of the study was to determine the influence of these 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 Gonadotropin 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

A randomized, controlled, double blind, cross-over study evaluating acupuncture as an adjunct to IVF.

Quintero R et al, Fertil Steril, 2004;81(Supplement 3):S11-12

Fertility and Sterility

This pilot study showed that a significantly lower amount of gonadotropins (IVF drugs) was used when IVF was combined with standard acupuncture, i.e. the acupuncture appeared to make the ovaries more responsive to the drugs possibly due to increased blood supply to the ovaries. Increased ovarian responsiveness could be a useful effect for women who produce small numbers of eggs. This trial needs to be repeated with larger numbers of patients.

Abstract

Objective: The purpose of this study was to determine if there are benefits of standard acupuncture compared to sham acupuncture as an adjunct to IVF.

Materials and Methods: A randomized, controlled, double-blind, cross- over pilot trial was performed using a needle-like device (sham acupuncture) as a control. Approval from GAMC's Investigational Review Board was acquired. Inclusion criteria were women aged 18 to 42 years with a history of failed IVF cycle(s); the presence of both ovaries; and a normal uterine cavity. Exclusion criteria was Kruger morphology <4%.

Results: Seventeen subjects were enrolled and seven subjects completed both arms of the study. The mean age was 36.2 years (range 28-41 years). The mean Day 3 FSH=3D6.8 IU (range 3-13 IU). There were four ongoing pregnancies after the first cycle, equally distributed. Seven subjects were crossed over after the first cycle. Of these, four from the standard acupuncture group and one from the sham acupuncture group attained pregnancy.

Two subjects of the standard acupuncture group were on-going pregnancies and one from the sham group. Only the sham group had two IVF cancellations. An unpaired Mann-Whitney Test using a two-sided p value was performed.

Ovarian blood flow responses to electro-acupuncture stimulation at different frequencies and intensities in anaesthetized rats

Stener-Victorin E et al Autonomic Neuroscience Volume 108, Issues 1-2, 31 October 2003, Pages 50-5

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 hind limb 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 non-significant.

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.

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 studied 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.

herbal

Acupuncture and herbal formulas infertility/IVF Abstracts

Chinese herbal medicine for endometriosis.

Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006568

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Abstract

BACKGROUND: Endometriosis is characterized by the presence of tissue that is morphologically and biologically similar to normal endometrium in locations outside the uterus. Surgical and hormonal treatment of endometriosis have unpleasant side effects and high rates of relapse. In China, treatment of endometriosis using Chinese herbal medicine (CHM) is routine and considerable research into the role of CHM in alleviating pain, promoting fertility, and preventing relapse has taken place.

OBJECTIVES: To review the effectiveness and safety of CHM in alleviating endometriosis-related pain and infertility.

SEARCH STRATEGY: We searched the Menstrual Disorders and Subfertility Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library) and the following English language electronic databases (from their inception to the present): MEDLINE, EMBASE, AMED, CINAHL, NLH on the 30/04/09. We also searched Chinese language electronic databases: Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Sci & Tech Journals (VIP), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and Chinese Medical Current Contents (CMCC).

SELECTION CRITERIA: Randomized controlled trials (RCTs) involving CHM versus placebo, biomedical treatment, another CHM intervention, or CHM plus biomedical treatment versus biomedical treatment were selected. Only trials with confirmed randomization procedures and laparoscopic diagnosis of endometriosis were included.

DATA COLLECTION AND ANALYSIS: Risk of bias assessment, and data extraction and analysis were performed independently by three review authors. Data were combined for meta-analysis using relative risk (RR) for dichotomous data. A fixed-effect statistical model was used, where appropriate. Data not suitable for meta-analysis are presented as descriptive data.

MAIN RESULTS: Two Chinese RCTs involving 158 women were included in this review. Both these trials described adequate methodology. Neither trial compared CHM with placebo treatment. There was no evidence of a significant difference in rates of symptomatic relief between CHM and gestrinone administered subsequent to laparoscopic surgery (95.65% versus 93.87%; risk ratio (RR) 1.02, 95% confidence interval (CI) 0.93 to 1.12, one RCT). The intention-to-treat analysis also showed no significant difference between the groups (RR 1.04, 95% CI 0.91 to 1.18). There was no significant difference between the CHM and gestrinone groups with regard to the total pregnancy rate (69.6% versus 59.1%; RR 1.18, 95% CI 0.87 to 1.59, one RCT). CHM administered orally and then in conjunction with a herbal enema resulted in a greater proportion of women obtaining symptomatic relief than with danazol (RR 5.06, 95% CI 1.28 to 20.05; RR 5.63, 95% CI 1.47 to 21.54, respectively). Overall, 100% of women in all the groups showed some improvement in their symptoms. Oral plus enema administration of CHM showed a greater reduction in average dysmenorrhea pain scores than did danazol (mean difference (MD) -2.90, 95% CI -4.55 to -1.25; $P < 0.01$). Combined oral and enema administration of CHM showed a greater improvement, measured as the disappearance or shrinkage of adnexal masses, than with danazol (RR 1.70, 95% CI 1.04 to 2.78). For lumbosacral pain, rectal discomfort, or vaginal nodules tenderness, there was no significant difference either between CHM and danazol.

AUTHORS' CONCLUSIONS: Post-surgical administration of CHM may have comparable benefits to gestrinone but with fewer side effects. Oral CHM may have a better overall treatment effect than danazol; it may be more effective in relieving dysmenorrhea and shrinking adnexal masses when used in conjunction with a CHM enema. However, more rigorous research is required to accurately assess the potential role of CHM in treating endometriosis.

Effect of Quyu Jiedu Granule () on microenvironment of ova in patients with endometriosis.

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OBJECTIVE: To observe the effect of Quyu Jiedu Granules (, QJG) on the micro-environment of ova in patients with endometriosis (EM). **environment METHODS:** Twenty EM patients who received in vitro fertilization and embryo transfer (IVF-ET) were randomized equally into a treated group and a control group. Further, 20 patients who received IVF-ET due to oviduct factors were enrolled into a non-endometriosis group. The dosage of gonadotrophic hormone used, the number of ova attained, fertilization rate and clinical pregnancy rate were all observed, and the levels of tumor necrosis factor alpha (TNF-right harpoon over left harpoon) and interleukin 6 (IL-6) in follicular fluid as well as their mRNA expressions in ovarian granular cells were detected by RT-PCR on the very day of ovum attainment. **RESULTS:** The ova attainment (13.80 ± 6.87) and fertilization rate (0.69 ± 0.31) in the treated group were all higher than the corresponding values in the control group (9.80 ± 5.32 and 0.47 ± 0.22); the follicular

fluid contents of TNF-alpha and IL-6 in the treated group were 1.38+/-0.21 ng/mL and 130.56+/-12.81 pg/mL, respectively, which were lower than those in the control group (1.98+/-0.34 ng/mL and 146.83+/-17.65 pg/mL, respectively). Further, the treated group showed much lower mRNA expressions of TNF-alpha and IL-6 in ovarian granular cells. CONCLUSIONS: The elevation of TNF-alpha and IL-6 contents in follicular fluid and their mRNA expressions in ovarian granular cells are possibly related to the low quality of ova in EM; QJG might raise the ova quality by reducing TNF-alpha and IL-6 levels to improve the living micro-environment for the ova.

Keywords: ova; endometriosis; tn-alpha; follicularfluid; harpoon; granular cell; granule; ovarian; treatgroup; group; ivfet; follicular; fertilization; microenvironment; pg/ml;

Combined therapy of Chinese medicine with in vitro fertilization and embryo transplantation for treatment of polycystic ovarian syndrome

Zhongguo Zhong Xi Yi Jie He Za Zhi. 2008 Nov ;28 (11):977-80 19213337

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OBJECTIVE: To evaluate the validity of Chinese drugs for reinforcing Shen and regulating Chong channel (RSRCC) on patients with polycystic ovarian syndrome (PCOS) undergoing in vitro fertilization and embryo transplantation (IVF-ET). METHODS: Sixty-four patients with PCOS undergoing IVF-ET were randomly assigned to two groups, the treated group (36 cases) and the control group (28 cases), to the former, Chinese recipe for RSRCC was given additionally. RESULTS: On the human chorionic gonadotropin (HCG) injecting day, the percentage of three-line sign of endometrium (type A) in the treated group was 75.0%(27/36), which was higher than that in the control group (42.9%, 12/28), showing significant difference between the two groups ($P < 0.01$). The rates of mature oocytes, fertilization, high-qualified embryo rate, clinical pregnancy rate and incidence rate of ovary hyper-stimulating syndrome (OHSS) in the treated group were (76.8 +/- 8.2%),(73.5 +/- 8.9%),(89.4 +/- 14.4)%, 36.11%(13/36) and 5.56%(2/36), respectively; whereas those in the control group (64.4 +/- 8.7%),(68.2 +/- 10.0%),(79.5 +/- 15.2)%, 21.43%(6/28) and 10.71%(3/28); the dosage of gonadotropin administered in the treated group was 33.8 +/- 12.5 ampoules, and in the control group 47.6 +/- 18.2 ampoules, statistical significance was shown between groups in comparing all the above-mentioned parameters ($P < 0.05$, $P < 0.01$). However, the number of oocytes obtained in the two groups was insignificantly different ($P > 0.05$). CONCLUSION: Combined use of Chinese drugs for RSRCC in IVF-ET can reduce the dosage of gonadotropin administered and raise the clinical pregnant rate.

Traditional Chinese medicine and infertility.

Curr Opin Obstet Gynecol. 2008 Jun;20(3):211-5.

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Abstract

PURPOSE OF REVIEW: The present review gives an overview of the potential use of traditional Chinese medicine in the treatment of infertility, including an evidence-based evaluation of its efficacy and tolerance.

RECENT FINDINGS: Recent studies demonstrated that traditional Chinese medicine could regulate the gonadotropin-releasing hormone to induce ovulation and improve the uterus blood flow and menstrual changes of endometrium. In addition, it also has impacts on patients with infertility resulting from polycystic ovarian syndrome, anxiety, stress and immunological disorders. Although study design with adequate sample size and appropriate control for the use of traditional Chinese medicine is not sufficient, the effective studies have already indicated the necessity to explore the possible mechanisms, that is, effective dose, side effect and toxicity of traditional Chinese medicine, in the treatment of infertility by means of prospective randomized control trial.

SUMMARY: The growing popularity of traditional Chinese medicine used alone or in combination with Western medicine highlights the need to examine the pros and cons of both Western and traditional Chinese medicine approaches. Integrating the principle and knowledge from well characterized approaches and quality control of both traditional Chinese medicine and Western medical approaches should become a trend in existing clinical practice and serve as a better methodology for treating infertility.

Chinese herbal medicine for primary dysmenorrhea.

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Update in: Cochrane Database Syst Rev. 2008;(2):CD005288.

Abstract

BACKGROUND: Conventional treatment for primary dysmenorrhea (PD) has a failure rate of 20% to 25% and may be contraindicated or not tolerated by some women. Chinese herbal medicine (CHM) may be a suitable alternative.

OBJECTIVES: To determine the efficacy and safety of CHM for PD when compared with placebo, no treatment, and other treatment.

SEARCH STRATEGY: The Cochrane Menstrual Disorders and Subfertility Group Trials Register (to 2006), MEDLINE (1950 to January 2007), EMBASE (1980 to January 2007), CINAHL (1982 to January 2007), AMED (1985 to January 2007), CENTRAL (The Cochrane Library issue 4, 2006), China National Knowledge Infrastructure (CNKI, 1990 to January 2007), Traditional Chinese Medicine Database System (TCMDS, 1990 to Dec 2006), and the Chinese BioMedicine Database (CBM, 1990 to Dec 2006) were searched. Citation lists of included trials were also reviewed.

SELECTION CRITERIA: Any randomized controlled trials (RCTs) involving CHM versus placebo, no treatment, conventional therapy, heat compression, another type of CHM, acupuncture or massage. Exclusion criteria were identifiable pelvic pathology and dysmenorrhea resulting from the use of an intra-uterine contraceptive device (IUD).

DATA COLLECTION AND ANALYSIS: Quality assessment, data extraction and data translation were performed independently by two review authors. Attempts were made to contact study authors for additional information and data. Data were combined for meta-analysis using either Peto odds ratios or relative risk (RR) for dichotomous data or weighted mean difference for continuous data. A fixed-effect statistical model was used, where suitable. If data were not suitable for meta-analysis, any available data from the trial were extracted and presented as descriptive data.

MAIN RESULTS: Thirty-nine RCTs involving a total of 3475 women were included in the review. A number of the trials were of small sample size and poor methodological quality. Results for CHM compared to placebo were unclear as data could not be combined (3 RCTs). CHM resulted in significant improvements in pain relief (14 RCTs; RR 1.99, 95% CI 1.52 to 2.60), overall symptoms (6 RCTs; RR 2.17, 95% CI 1.73 to 2.73) and use of additional medication (2 RCTs; RR 1.58, 95% CI 1.30 to 1.93) when compared to use of pharmaceutical drugs. Self-designed CHM resulted in significant improvements in pain relief (18 RCTs; RR 2.06, 95% CI 1.80 to 2.36), overall symptoms (14 RCTs; RR 1.99, 95% CI 1.65 to 2.40) and use of additional medication (5 RCTs; RR 1.58, 95% CI 1.34 to 1.87) after up to three months follow up when compared to commonly used Chinese herbal health products. CHM also resulted in better pain relief than acupuncture (2 RCTs; RR 1.75, 95% CI 1.09 to 2.82) and heat compression (1 RCT; RR 2.08, 95% CI 2.06 to 499.18).

AUTHORS' CONCLUSIONS: The review found promising evidence supporting the use of CHM for primary dysmenorrhea; however, results are limited by the poor methodological quality of the included trials.

Chinese Herbs increase ATP production and antioxidants

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Enhancement of ATP generation capacity, antioxidant activity and immunomodulatory activities by Chinese Yang and Yin tonifying herbs

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Abstract

Chinese tonifying herbs such as *Herba Cistanche*, *Ganoderma* and *Cordyceps*, which possess antioxidant and/or immunomodulatory activities, can be useful in the prevention and treatment of age-related diseases. Pharmacological studies on Yang and Yin tonifying herbs suggest that Yang tonifying herbs stimulate mitochondrial adenosine triphosphate (ATP) generation, presumably through the intermediacy of reactive oxidant species, leading to the enhancement of cellular/mitochondrial antioxidant status. Yin tonifying herbs, however, apart from possessing antioxidant properties, exert mainly immunomodulatory functions that may boost a weak immune system and may also suppress overactive immune responses. The abilities of Yang and Yin Chinese tonifying herbs to enhance ATP generation and to exhibit antioxidant and/or immunomodulatory actions are the pharmacological basis for their beneficial effects on the retardation of aging.

Background

Aging is a process of bodily change with time, leading to increased susceptibility to disease, and ultimately death. Because reactive oxidant species (ROS) and immune dysfunction are major causes of age-related diseases [1-3], the maintenance of antioxidant and immune fitness is a rational approach to preventive health care. Accumulation of ROS-induced oxidative damage to DNA, proteins, and other macromolecules has been regarded as a major endogenous cause of aging [1]. In addition to ROS-mediated cellular damage, aging was found to be associated with immune senescence, attributable at least partly to the loss of T lymphocyte functions [2,3]. Such loss increases the prevalence of infectious diseases in the elderly. With advances in modern medical research techniques, research on age-related chronic illnesses has become intense, in the quest for valuable preventive and therapeutic measures. Humans have been making continuous efforts to fight aging. As Chinese medicine has always emphasized the prolongation of a healthy lifespan, many Chinese tonifying herbs have long been used to safeguard health and to delay the onset of senility.

Under both normal and pathological conditions, ROS are generated in all cells undergoing aerobic metabolism, particularly from mitochondria. The cell possesses two distinct antioxidant defense systems to counteract damaging ROS: (1) enzymatic antioxidants such as catalase,

superoxide dismutase (SOD), glutathione peroxidase and other related enzymes/molecules, and (2) non-enzymatic antioxidants such as ascorbic acid (vitamin C), α -tocopherol (vitamin E) and β -carotene. To achieve optimal antioxidant fitness, every component of the antioxidant defense system should function optimally because antioxidants must work together in a synergistic manner. Chinese tonifying herbs have been shown to possess both in vitro and in vivo antioxidant activities [4,5].

The immune system fights against 'foreign invaders' such as bacteria, viruses, fungi, yeasts and parasites. The humoral and cell-mediated immune responses show great competence in dealing with intruders. Moreover, the surveillance function of the immune system tends to prevent cancers, particularly in old age. However, an over reactive or imbalanced immune system can cause allergies or autoimmune disorders. A well-constituted and balanced immune system is thus crucial for safeguarding health. Chinese tonifying herbs have been shown to stimulate or suppress the cell-mediated immune response both in vitro and in vivo [6].

The importance of disease prevention has been recognized by Chinese medicine through experience accumulated over centuries. Many Chinese tonifying herbs have long been used for safeguarding health and for delaying the onset of senility. According to Chinese medicine theories, tonifying herbs prescribed for various symptoms of ill-health are generally classified into four categories on the basis of their health-promoting actions, namely 'Yang-invigorating', the 'Qi-invigorating', the 'Yin-nourishing' and the 'Blood-enriching' herbs [7]. The 'Qi-invigorating' and 'Blood-enriching' herbs are of Yang and Yin characteristics respectively. Chinese medicine theories suggest that a balance of Yin and Yang is essential to sustain optimal body function [8]. From a modern medical perspective, the maintenance of Yin and Yang in harmony may be described as the attainment of bodily homeostasis. The long-known antagonistic relationship between parasympathetic and sympathetic neural activities affords an example of both a phenomenon well-recognized by Western medicine and the Yin/Yang balance. A recent psychophysiological investigation in humans revealed an association between decreased parasympathetic or sympathetic activities with deficiencies of Yin or Yang respectively [9].

The theoretical framework of Chinese medicine is based on the Chinese cultural fabrics and clinical experience, while modern Western medicine has been established on the basis of laboratory and clinical investigations [10]. As the two distinct medical systems are complementary, bridging of the knowledge gap between Chinese and Western medicine is essential for their integration, in clinical practice, for disease prevention and treatment. Expounding Chinese medicinal theories in modern scientific terms to a Western audience facilitates communication between practitioners of the two systems.

In our earlier studies, we found that tonifying herbs with Yang or Yin properties were associated with antioxidant and immunostimulatory activities respectively [4]. Recent studies indicated that only Yang tonifying herbs (not Yin tonifying herbs) enhanced mitochondrial ATP generation capacity in mouse hearts [11]. We therefore suggest that Yang tonifying herbs enhance mitochondrial ATP generation, while Yin tonifying herbs are associated with immunomodulatory activities. In this mini-review, we summarize the abilities of Yang and Yin tonifying herbs to

enhance ATP generation capacity, and to potentiate antioxidant and/or immunomodulatory actions, in an effort to characterize their respective pharmacological properties.

Enhancement of ATP generation by Yang tonifying herbs

In Chinese medicinal theories, Yang is a manifestation of body functions supported by various organs. A 'Yang-invigorating' action therefore involves the enhancement of bodily functions in general and cellular activities that consume ATP in particular. The mitochondrion is responsible for the generation of ATP through oxidative metabolism. To establish the pharmacological basis of 'Yang-invigorating' action, we have recently investigated the effect of Yang herbs on ATP generation capacity in heart homogenates prepared from mice that were pretreated with methanolic extracts of herbs [11]. Tonifying herbs from other functional categories were examined for comparison. While Chinese herbs are usually extracted by water for human oral consumption, water was replaced by methanol in our study for convenience in the processing and storage of samples. Yang herbs invariably enhanced myocardial ATP generation, with stimulation ranging from 20–130%. *Herba Cynomorii* and *Semen Cuscutae* were the most potent herbs examined. By contrast, none of the Yin herbs enhanced ATP generation; some Yin herbs even suppressed ATP generation slightly (Table 1). A preliminary mechanistic study indicated that Yang herbs may speed up ATP synthesis by increasing mitochondrial electron transport [11].

Effect of Yang and Yin tonifying herbs on myocardial ATP generation capacity in mice ex vivo

Correlation between enhancement of ATP generation capacity and antioxidative capacity

Mitochondrial oxidative phosphorylation generates ROS as byproducts. Highly reactive chemically, ROS attack cellular structures located near the sites where ROS are generated. Mitochondrial DNA, proteins, and lipids in the inner membrane of mitochondria are thus vulnerable to oxidative damage [12], resulting in generalized organelle dysfunction, defective mitochondrial biosynthesis and poor energy metabolism [13].

Under normal physiological conditions, the mitochondrial antioxidant defense system adequately handles the potentially detrimental effects of ROS derived from energy metabolism [14]. When a functional imbalance between ROS levels and antioxidant concentrations caused by various disease states and/or aging occurs, age-related disorders such as cancer, cardiovascular diseases, brain dysfunction, or cataract may occur [15]. Antioxidant supplementation, particularly from herbal extracts, has become a trend in preventive health care.

Using an oxygen radical absorbance capacity assay, Ou et al. recently compared the free radical scavenging (i.e. antioxidant) activities of Yang and Yin herbs [16]. The results indicated that Yin herbs generally possessed higher antioxidant activities than Yang herbs and that the antioxidant potencies correlated well with the amounts of total phenolic compounds in the herbs. The authors suggested an analogy between Yin/Yang balance and antioxidation/oxidation in energy metabolism. These findings of higher antioxidant activities in Yin herbs as compared with those in Yang herbs do not agree with the findings from one of our earlier studies which

showed that most of the Yang herbs possessed a more potent 1,1-diphenylpicrylhydrazyl radical-scavenging action than other tonifying herbs [4] (Table 2). Although the use of different herbal extraction methods and distinct antioxidant assays precludes direct comparison of the two studies, the discrepancy might be due to the selection of almost completely different sets of Yin and Yang herbs for testing in the two studies. Our study focused on herbs used for safeguarding health (i.e. herbs used for tonifying purposes) (Tables 2, Table 3 of reference [17]). Ou et al. probably used a selection criterion based on the general Yin and Yang properties of the herbs instead of their Yin-tonifying and Yang-tonifying actions [16]. Szeto and Benzie, using the same set of herbs described in Ou et al. to examine possible protective effects on DNA oxidative damage, found that the Yang herbs showed an antioxidant effect superior to that of Yin herbs [5].

Antioxidant activities of Yang tonifying herbs

Several Yang herbs have been shown to possess antioxidant activities both in vitro and in vivo (Table 4). In vitro free radical-scavenging activities were detected in herbal extracts prepared from *Herba Epimedii* [4,18], *Radix Dipsaci* [4,16], *Fructus Psoraleae* [4], *Semen Cuscutae* [16], *Herba Cistanche* [4,16,18], *Cortex Eucommiae* [19] and *Rhizoma Cibotii* [4,16]. Aqueous extracts of *Rhizoma Drynariae* and *Cortex Eucommiae* were found to inhibit oxidant production from rat osteoblasts [20], and also inhibited biomolecular oxidative damage [21]. Active ingredients (bakuchiol, isobavachin and isobavachalcone) from *Fructus Psoraleae* inhibited the NADPH-dependent peroxidation of rat microsomal and mitochondrial lipids in vitro [22]. An ethanolic extract of *Radix Dipsaci* enhanced the antioxidant status of blood and liver in rodents [23] and a *Radix Morindae* extract increased blood antioxidant enzyme activities in diabetic rats [24]. Phenylethanoids isolated from *Herba Cistanche* were found to prevent cell damage induced by in vitro and in vivo exposure to carbon tetrachloride in rats [25]. A recent study from our laboratory indicated that pretreatment with the methanolic extract of *Herba Cistanche* protected against ischemia-reperfusion injury in rat hearts ex vivo and enhanced mitochondrial ATP generation in the rat hearts ex vivo and H9c2 cells in situ. The ATP-stimulating action was possibly due to enhanced oxidative phosphorylation caused by increases in the activities of complexes I and III [26]. As good body function requires a large amount of energy and antioxidant defense is essential in sustaining mitochondrial ATP production [27], the antioxidant activities of Yang herbs may safeguard ATP generation, particularly under conditions of upregulated cellular activities.

Antioxidant activities of Yang tonifying herbs

Methanolic extracts of both *Fructus Ligustri* and *Herba Ecliptae* were found to enhance hepatic glutathione (GSH) regeneration capacity in rats [4,28]. The enhancement of hepatic GSH regeneration capacity by *Fructus Ligustri* was associated with a hepatoprotective action against carbon tetrachloride toxicity [28]. Activity-directed fractionation of *Fructus Ligustri* indicated that the hepatoprotective principle(s) resided mainly in the oleanolic acid-enriched butanol and chloroform fractions [28]. Moreover, our recent studies showed that both short and long term pretreatment with oleanolic acid protected against myocardial ischemia-reperfusion injury in rats [29,30]. It was suggested that the cardioprotection afforded by oleanolic acid pretreatment was

related to the enhancement of mitochondrial antioxidant mechanism mediated by GSH and α -tocopherol [29]. Both experimental and clinical investigations indicated that the antioxidant status influenced immunocompetence, particularly under conditions of stress such as physical exercises or chronic diseases [31]. The antioxidant activities of Yin tonifying herbs may positively influence immunostimulatory activities.

Experimental studies on a 'Yang-invigorating' herbal formula

A 'Yang-invigorating' herbal formula named VI-28 has been shown to produce 'Yang-invigorating' effects [32] and enhance red cell antioxidant status, particularly Cu-Zn-superoxide dismutase (SOD) activity, in elderly male human subjects [33]. This herbal formula is comprised of *Radix Ginseng*, *Cornu Cervi*, *Cordyceps*, *Semen Allii*, *Fructus Cnidii*, *Fructus Evodiae* and *Rhizoma Laemferiae*. Recently we investigated the effects of long-term VI-28 treatment on red cell Cu-Zn-SOD activity, mitochondrial functional ability, and antioxidant levels, in various tissues of rats of both sexes [34]. The results indicated that VI-28 treatment increased red cell Cu-Zn-SOD activity and mitochondrial ATP generation capacity, increased the levels of reduced GSH and α -tocopherol, and reduced Mn-SOD activities. The enhancement of ATP generation by VI-28 increased mitochondrial ROS production, resulting in the upregulation of mitochondrial antioxidant mechanism. The VI-28-induced increase in mitochondrial antioxidant capacity in various tissues was evidenced by a significant reduction in ROS generation. Given that cellular energy status and mitochondrial ROS generation are factors critically involved in aging, the dual effect of 'Yang-invigoration' produced by VI-28 may have clinical implications in the prevention of age-related diseases.

Immunomodulatory activities of Yin tonifying herbs

It was suggested that the proper functioning of the immune system requires dynamic interactions between Yang and Yin. And while the antigen-nonspecific immune response is associated with Yang, the antigen-specific response is related to Yin [35]. One of our earlier studies investigated antioxidant and immunomodulatory activities in different categories of tonifying herbs. The results showed that 6 and 7 of a total of 8 Yin herbs tested potentiated concanavalin A (Con A)-stimulated splenocyte proliferation (an antigen-specific response) in mice in vitro and ex vivo respectively. By contrast, only 3 of 9 Yang herbs tested showed a similar enhancement of the Con A-stimulated immune response [4] (Table 2).

Among the Yin herbs, the methanolic extract of *Fructus Ligustri* yielded the most robust immunostimulatory action in mouse splenocytes [4]. Differential extraction of *Fructus Ligustri* by solvents of increasing polarity indicated that the immunostimulatory activity resided mainly in the petroleum ether fraction [36]. Oleanolic acid, an immunomodulatory triterpenoid commonly found in herbs including *Fructus ligustri* [37,38], was undetectable in this fraction [36]. Currently, activity-directed fractionation of the petroleum ether extract of *Fructus Ligustri* is under way in our laboratory. Various immunomodulatory actions of Yin tonifying herbs, and the active ingredients of the herbs, have been reported in other studies (Table 5). An aqueous extract of *Radix Asparagi* was found to inhibit tissue necrosis factor- α (TNF- α) secretion by suppressing Interleukin (IL)-2 secretion from astrocytes, implicating that the extract might exhibit anti-inflammatory activity in the central nervous system [39]. Both the crude aqueous extract and the

two active ingredients (ruscogenin and ophiopogonin D) of *Radix Ophiopogonis* produced anti-inflammatory effects in rodents [40]. While the aqueous extract inhibited xylene-induced ear swelling and carrageenan-induced paw edema in mice, it also suppressed carrageenan-induced pleural leukocyte migration in rats, and the zymosan-evoked migration of peritoneal total leukocytes and neutrophils in mice. Treatments with ruscogenin and ophiopogonin D decreased zymosan-induced peritoneal leukocyte migration in mice and reduced the phorbol-12-myristate-13 acetate-induced adhesion of HL60 cells to ECV304 cells [40]. Several sesquiterpenes isolated from *Herba Dendrobii* were found to exhibit immunomodulatory activity by exerting comitogenic effects on Con A and lipopolysaccharide-stimulated mouse splenocytes [41,42]. It has recently been reported that an ethanolic extract of black rice (the fruit of *Oryza sativa*) showed anti-asthmatic effects in a mouse model [43]. Treatment with the ethanolic extract of black rice reduced the number of eosinophils in bronchoalveolar lavage fluid, alleviated the airway hyper-response, and decreased the extent of airway inflammation in ovalbumin (OVA)-immunized and -aerolized mice challenged with OVA. Moreover, the ethanolic extract treatment decreased interferon- γ (INF- γ), IL-4, IL-5 and IL-13 levels in the supernatants of cultured splenocytes and suppressed the plasma levels of OVA-specific immunoglobulin (Ig)G, IgG2 α , IgG1 and total IgE in OVA-immunized and -challenged mice [43]. Clinical investigations indicated that intramuscular injection of undiluted *Fructus Ligustri* extract at a dose of 2–4 ml once or twice daily could prevent leucopenia caused by chemotherapy or radiotherapy. *Fructus Ligustri* treatment normalized white blood cell counts, thereby increasing tolerance to chemo/radiotherapy [44]. Oral administration of *Fructus Ligustri* tablets at a daily dose of 50 g equivalence of crude herb was found to ameliorate the symptoms of chronic bronchitis [44]. A herbal formula comprising *Fructus Ligustri*, *Radix Scutellariae*, *Radix Astragalus* and *Eupolyphaga et polyphae* was found to alleviate symptoms and improve immune function in HIV/AIDS patients [45].

Immunomodulatory activities of Yin tonifying herbs

Ganoderma – A 'Fu Zheng' tonifying herb

Ganoderma, another Yin tonifying herb with immunomodulatory effects, is widely consumed by the Chinese people who believe that it promotes health and longevity, lowers the risk of cancer and heart diseases and boosts the immune system [46]. In Chinese medicine, Ganoderma is regarded as a very potent herb for 'Fu Zheng', a Chinese medicine concept comparable to immunotherapy/immunomodulation in Western medicine. While Ganoderma is traditionally used to increase the resistance of the body immune system to pathogens and to restore normal body functions, the herb has now also been used to decrease the side effects of Western medical procedures, such as surgery, radiotherapy and chemotherapy which often weaken the immune system. The anti-cancer/immunomodulatory effects of Ganoderma were associated with triterpenes [47], polysaccharides [48,49] or immunomodulatory proteins [50] through mechanisms involving inhibition of DNA polymerase [51], inhibition of post-translational modification of the Ras oncoprotein [52] or the stimulation of cytokine production [53]. Recent studies on the immunomodulatory activities of Ganoderma indicated that Ganoderma extract stimulated the proliferation of human peripheral blood mononuclear cells and raised the levels of mRNAs encoding Th1 and Th2 cytokines in these cells [54]. Moreover, polysaccharides of

Ganoderma activated mouse splenic B cells and induced these cells to differentiate into IgM-secreting plasma cells. This process was dependent on the polysaccharide-mediated induction of Blimp-1, a master regulator capable of triggering a cascade of gene expression during plasmacytic differentiation [55]. In human peripheral B lymphocytes, the Ganoderma polysaccharide fraction enhanced antibody secretion and induced the production of Blimp-1 mRNA, though it failed to induce lymphocyte differentiation [55].

In addition to immunomodulating activities, Ganoderma possesses in vivo antioxidant potential, another aspect of Yin tonifying action. Treatment with Ganoderma extract was found to enhance the hydroxyl radical scavenging activity of rabbit blood plasma [56,57]. Ganoderma acted by stimulating cellular and mitochondrial SOD activities, thereby enhancing the antioxidant capacity of the body [58]. It was shown that an intraperitoneal injection of Ganoderma extract following a lethal dose of cobalt X-ray radiation caused a marked prolongation of survival time in mice [59]. Pretreatment with Ganoderma extract also markedly protected against carbon tetrachloride-induced hepatic damage and the associated impairment in hepatic antioxidant status [60].

Cordyceps – A Yin/Yang tonifying herb

Cordyceps, a premium Chinese tonifying herb which replenishes the 'kidney' and soothes the 'lung', is prescribed for the treatment of a host of disorders, including hyposexualities, hyperglycemia, hyperlipidemia, asthenia after illness, respiratory diseases, renal disorders, liver and heart diseases [61]. Cordyceps is regarded as a tonifying herb with both 'Yin-nourishing' and 'Yang-invigorating' actions. Pharmacological studies have shown that Cordyceps possesses a wide spectrum of biological activities including antioxidation [61-64], immunopotentiality [65-68], anti-tumorigenesis [68-71], anti-inflammation [72] and stimulation of testosterone biosynthesis [73]. We have recently investigated the effects of wild and cultured Cordyceps on Con A-stimulated splenocytes (an in vitro bioassay for Yin tonifying action) and myocardial ATP generation capacity (an ex vivo bioassay for Yang tonifying action) [74]. The results indicated that methanolic extracts of wild and cultured Cordyceps enhanced both the Con A-stimulated splenocyte proliferation in vitro and myocardial mitochondrial ATP generation ex vivo in mice, with no significant difference in potencies when the two types of Cordyceps were compared. While the immunopotentiating effect was associated with an increase in IL2 production, the stimulation of myocardial ATP generation was paralleled by an enhancement in mitochondrial electron transport. When compared with typical Yin and Yang tonifying herbs (Fructus Ligustri and Herba Cynomorii respectively), Cordyceps was found to possess both Yin and Yang tonifying actions, with a lower potency in both modes of action. The observation of both immunopotentiating and ATP-enhancing activities in Cordyceps extracts further supports the pharmacological basis of Yin and Yang tonifying herbs in Chinese medicine.

Conclusion

Yang tonifying herbs stimulate mitochondrial ATP generation, leading to the enhancement of cellular/mitochondrial antioxidant status, presumably through the intermediacy of ROS. Yin tonifying herbs, which also possess antioxidant properties, are mainly immunomodulatory, thereby boosting weak immune functions and suppressing over reactive or unbalanced immune responses. Cordyceps, highly regarded as a tonifying herb with a dual action of Yin and Yang,

stimulates mitochondrial ATP generation and enhances cellular immune responses. Given that impairment in mitochondrial functional ability and antioxidant status, and a decline in immunocompetence, are believed to be critically involved in the development of age-related diseases and the aging process, the abilities of Yang and Yin tonifying herbs to enhance ATP generation capacity and to produce antioxidant and immunomodulatory actions are beneficial for safeguarding health and delaying the onset of senility (Figure 1). While animal models may be used for testing working hypotheses on Yang and Yin tonifying actions, clinical studies, using Yang and Yin tonifying herbs and/or defined chemicals isolated from the herbs or synthesized in the laboratory, on age-related variations in antioxidant and immune function, would be of considerable value.

Progress of integrative Chinese and Western medicine in treating polycystic ovarian syndrome caused infertility.

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Abstract

Polycystic ovarian syndrome (PCOS) is one of the most popular diseases that cause menstrual dysfunction and infertility in women. The present paper is a brief retrospection on the progress in treatment of PCOS caused infertility with integrative Chinese and Western medicine (ICWM). It can be seen from these materials that using traditional Chinese medicine (TCM) recipes formulated by Shen-replenishing herbs or acupuncture to reinforce Gan-Shen, regulate Chong-Ren Channels in treating PCOS, stable clinical efficacy could be obtained, with less adverse reaction, though the effect initiated somewhat late. Whereas, when Shen-replenishing recipe and acupuncture are combined with hormone or ovulation promoting drugs of Western medicine, the above-mentioned shortcomings would be overcome. So, this combined therapy is frequently used in clinical practice.

Effect of erzhi tiangui recipe on ovarian reactivity in elderly sterile women

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OBJECTIVE: To observe the clinical effect of Erzhi Tiangui Recipe (ETR), a traditional Chinese recipe for strengthening Shen and nourishing Tiangui, in improving the ovarian reactivity in elderly sterile women.

METHODS: Sixty-six elderly sterile women receiving in vitro fertilization pre-embryo transfer (IVF-ET) were randomly divided into two groups: the ETR group treated with ETR plus follicle stimulating hormone (FSH) and the control group treated with FSH alone, 33 cases in each group. Changes of symptoms and the relative parameters were observed, including the dosage of FSH used, the serum hormone levels at different periods, endometrium thickness and arteriopalmus of uterus and ovary on the day of HCG injection, follicle number, follicular oocyte number, mature follicular oocyte rate and fertilization rate, prime embryo rate, and pregnancy rate. Moreover, the correlation of the symptom score of colpoxerosis (CR2) and serum estradiol (E2) level was analyzed after treatment (on the HCG injection day). **RESULTS:** Symptoms of Shen qi-yin deficiency were improved significantly in the ETR group, with the improvement better than that in the control group ($P < 0.05$). The total and daily FSH dosage in the ETR group were lower than those in the control group, showing significant difference between the two groups ($P < 0.05$). The effects were better in the ETR group than those in the control group in increasing serum E2 and endometrium thickness on the HCG injection day, and also in elevating the follicular oocyte number, the mature oocytes rate, the fertilization rate, and the prime embryo rate (all $P < 0.05$). CR2 analysis showed low negative correlation in both groups ($r = -0.369$ in the ETR group and $r = -0.425$ in the control group), suggesting E2 could be one of the factors but not the only factor for influencing colpoxerosis. And the score of colpoxerosis was lower in the ETR group after treatment than that in the control group ($t = 2.422$, $P < 0.05$). **CONCLUSION:** ETR combined with FSH can obviously reduce the dosage of FSH used, improve ovarian reactivity and pregnancy rate, and improve the quality of oocytes, the mechanism is possibly related with its effects in improving ovarian reactivity elevating blood estradiol and regulating the hypothalamus-pituitary-ovary axis (HPOA).

Keywords: etr; fsh; oocyte; sterile women; ovarian; group; recipe; hcg; elderly; reactivity; follicular oocyte; women; sterile; hcg injection; control group;

Experimental study on effect of er'zhi tiangui granule in improving quality of oocyte and its correlation with level of insulin-like growth factor 1R mRNA expression in ovary of mice.

Zhongguo Zhong Xi Yi Jie He Za Zhi. 2006 May ;26 (5):431-4 16883911

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OBJECTIVE: To explore the mechanism of Er'zhi Tiangui Granule (ETG) in improving the quality of oocyte.

METHODS: Ninety mice were randomly divided into 6 groups. The number of high-quality oocytes was comparatively observed in the 1st experimental group and the 1st control group;

the embryonic cleavage rate was observed in the 2nd experimental group and the 2nd control group and the quantity of insulin-like growth factor-1R mRNA (IGF-1R mRNA) expression in ovarian granular cells was determined by using in situ hybridization in the 3rd experimental group and the 3rd control group. RESULTS: The high-quality oocytes rate, the embryonic cleavage rate and the quantity of IGF-1R mRNA expression in the three paired groups was (78 \pm 8)% vs. (71 \pm 5)%, (88 \pm 3)% vs. (83 \pm 5)%, 0.4890 \pm 0.0454 vs. 0.4439 \pm 0.0283, respectively. The difference between the experimental groups to the respective control groups was significant (all $P < 0.05$), and positive correlation was shown between the high-quality oocytes rate and the quantity of IGF-1R mRNA expression. CONCLUSION: The mechanism of ETG in improving the quality of oocyte may be related with the elevation of IGF-1R mRNA level in ovarian granular cells.

Application of traditional Chinese medicine in the treatment of infertility.

Hum Fertil (Camb). 2003 Nov;6(4):161-8.

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Abstract

The philosophy and practice of traditional Chinese medicine (TCM) have been evolving for thousands of years in China, Japan and other Asian countries. TCM is now generating popular interest worldwide for reproductive health care and disease prevention, including applications for treating infertility and improving sexual function. This review focuses on the application of TCM for infertility patients, and provides a critical reflection on the efficacy and safety of selected Chinese herbal formulas. It has been claimed that some formulas produce high clinical pregnancy rates with few or no side effects, as well as improving the general well-being of patients. The need for randomized control trials and research into possible mechanisms of action, effective doses, contra-indications and toxicity is self-evident. However, the task is enormous in view of the number of herbal products currently available on the market; yet among these products are undoubtedly some that will prove to be safe and beneficial

A preliminary immunopharmacological study of an antiendometriotic herbal medicine, Keishi-bukuryo-gan (Gui Zhi Fu Ling Wan).

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Changes in the specific antiendometrial IgM antibodies in an endometriotic patient, who were treated with leuproride acetate and in turn with Keishi-bukuyogan, were investigated by the

flowcytometric analysis which was developed in our laboratory. The oriental therapy decreased the specific IgM antibody titer gradually and kept the patient symptom-free for more than 7 months without any suppression of serum CA125 and estradiol levels. On the other hand, leuproride acetate therapy suppressed both serum CA125 and serum estradiol levels but not the IgM antibody titer. The results suggest that the specific antiendometrial IgM autoantibody could be a pathogenic molecule in endometriosis and it could also serve as a clinical marker for the oriental therapy of endometriosis.

Measuring the Effectiveness of Chinese Herbal Medicine in Improving Female Fertility

Keywords: Infertility, Chinese herbal medicine, ultrasound, hormone levels.

Aim: To determine the relationship between female fertility indicators and the administration of Chinese herbal medicine (CHM).

Design: A prospective cohort clinical study to measure accepted bio-medical

factors that affect female fertility and to determine if CHM can improve these factors as well as pregnancy outcome.

Setting: A private practice specializing in treating infertility with traditional Chinese medicine (TCM). The study took place between November 2003 and December 2004. Patient(s): Fifty women with the Western medical diagnosis of unexplained infertility.

Interventions: One monitored menstrual cycle measuring pre-treatment fertility factors, followed by treatment with Chinese herbal medicine and subsequent measurement of the changes in the same fertility factors.

Results: Significant differences were observed between the two time points for the majority of factors measured. Pregnancies in the sample group recorded 6 months after commencement of the last treatment were 28, with 11 live births and 7 miscarriages.

Conclusion: The study outcome demonstrates that using Chinese herbal medicine results in higher success rates of pregnancy, with no patient side-effects and a reduction in the category of patients conventionally classified as having unexplained infertility.

Preventive and therapeutic effects of Bushen Huoxue Recipe on autoimmune premature ovarian failure in mice

Dong L, Jiang L, Men W, Zhu NS. <http://www.ncbi.nlm.nih.gov/pubmed/18334152>

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Objective: To investigate the preventive effect of Bushen Huoxue Recipe (BSHXR), a compound traditional Chinese herbal medicine, on autoimmune premature ovarian failure (POF) in mice. **Methods:** Ovarian antigen was prepared with the ovarian tissue of female BALB/c mice. A mouse model of POF was established by immunization injection of the ovarian antigen of isotype female mice on multiple subcutaneous sites and two posterior soles. The POF mice were treated with BSHXR after the first and third immunization. The levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) in peripheral blood were detected by enzyme linked immunosorbent assay. **Results:** Lymphocyte infiltration was appeared in ovarian stroma of POF mice. The levels of FSH and LH were evaluated and the E(2) level was decreased significantly ($P<0.05$). BSHXR could reduce the increased levels of FSH and LH, increase the level of E(2) and the number of growing and mature follicles. The efficacy of early treatment was better than that of late treatment. **Conclusion:** BSHXR can recover ovarian function in POF mice mainly by regulating the indiscriminate hormone level, and BSHXR has preventive effect on autoimmune POF in mice.

Protective effect of zuogui pill on ovarian autoimmune injury

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OBJECTIVE: To probe the effect of Zuogui pill (ZGP), a Chinese compound recipe for tonifying Shen, on ovarian function in mice with premature ovarian failure (POF). **METHODS:** BALB/C female mice model of POF was established by multiple sites subcutaneous injection of ovarian antigen elicited with ovarian tissue of SD female rats, and treated with ZGP at different time points in the modeling, with prednisone as positive control. The levels of follicle-stimulating hormone (FSH) and estradiol (E2) in peripheral blood were measured with radioimmunoassay, and ovarian antibody (AoAb) was determined by enzyme linked immunosorbent assay. The mRNA expression of ovarian growth and differentiation factor-9 was detected with in situ hybridization. **RESULTS:** POF model mice manifested such abnormalities as increased FSH, decreased E2, and positive AoAb in peripheral blood, with lymphocytes infiltration in ovarian mesenchyma, reduction of GDF-9 mRNA positive oocytes, and decrease of growing and mature follicles. ZGP could reduce the increase of FSH, increase the level of E2, inhibit the production of AoAb, raise the GDF-9 mRNA positive cells of oocytes, increase the number of growing and mature follicles. The clinical efficacy was more significant in early stage than in advanced stage. **CONCLUSION:** ZGP can improve immune inflammatory injury of ovary, and shows therapeutic effect on POF.

Research into Chinese herbal medicine and ovarian dysfunction

9 separate studies

(1) The effectiveness of a Chinese formula called Tian gui fang in comparison with metformin was tested on patients with polycystic ovarian syndrome [PCOS]. The patients were divided into two groups and either Tian gui fang or metformin was administered for three months. After treatment, 4 out of the 8 patients on metformin had restoration of menstrual cyclicity, and two of them had a double phase BBT. The testosterone levels had decreased. No other measures changed. In the group that received the Chinese medicine, 6 patients out of 8 had a restored cycle as well as a double phase BBT. Testosterone and the body mass index (BMI) decreased significantly. The authors conclude that both therapies can induce ovulation but that Chinese herbal medicine has a higher efficacy in restoring ovulation and normal BBT measures.

Hou J, Yu J, Wei M. [Study on treatment of hyperandrogenism and hyperinsulinism in polycystic ovary syndrome with Chinese herbal formula tian gui fang] . Zhongguo Zhong Xi Jie he Za Zhi. 2000; 20 (8):589.

(2) The effectiveness of a Chinese herbal formula was tested on patients with high LH levels due to polycystic ovary syndrome. Eight weeks of treatment with Chinese herbal medicine significantly reduced plasma LH.

Ushiroyama T, Ikeda A, Sakai M, Hosotani T, Suzuki Y, Tsubokura S, Ueki M. Effects of unkei-to, an herbal medicine, on endocrine function and ovulation in women with high basal levels of luteinizing hormone secretion. J Reprod Med. 2001 May; 46(5):451-6.

(3) In Japan, a Chinese herbal formula was tested on patients with polycystic ovarian disease [PCOD] to find an effective treatment without side effects that could be used instead of clomiphene citrate or gonadotropin therapy. After a course of treatment, the FSH/ LH ratio had significantly decreased, and the ovulatory rate was 70.6%. Serum testosterone did not change during treatment. The authors conclude that the Chinese formula may be useful for the treatment of anovulation in PCOS patients.

Sakai A, Kondo Z, Kamei K, Izumi S, Sumi K. Induction of ovulation by Sairei-to for polycystic ovary syndrome patients. Endocr J. 1999 Feb; 46(1):217-20.

(4) A case study from Taiwan discusses the effective treatment of premature ovarian failure using Chinese herbal medicine. Clomiphene citrate therapy over 8 months had not changed the FSH and LH levels from the postmenopausal range. A course of 4 months treatment with Chinese herbal medicine based on Zuo gui wan induced an ovulation, and the patient fell pregnant. The authors conclude that Chinese herbal medicine can restore ovarian function effectively and promptly and offers another option for treating infertility in patients with premature ovarian failure.

Chao SL, Huang LW, Yen HR. Pregnancy in premature ovarian failure after therapy using Chinese herbal medicine. A case study. *Chang Gung Medical Journal* 2003 Jun; 26(6): 449-52.

(5) At Shanghai medical university, the effectiveness of Chinese medical herbs from the category of yin supplementing were tested on 35 patients with polycystic anovulation. The patients were treated for three months, and a variety of tests were carried out before and after the course of treatment. Testosterone levels lowered significantly. In 59.7% of patients a regular cycle was reestablished. 41.2% of women became pregnant. The authors conclude that Kidney Yin nourishing herbs could provide a good micro circumstance for ovarian follicular growth, which results in ovulation and pregnancy.

Zhou LR, Yu J. [Clinical observation on treatment of hyperinsulinemia and hyperandrogenism anovulatory patient with replenishing kidney-yin drugs] *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 1996 Sep; 16(9): 515-8.

(6) Hachimijiogan, a Chinese herbal formulary (Liu wei dihuang wan + rou gui, yin yang huo, huang qi), was shown in one study to benefit female infertility due to pituitary dysfunction. Two infertile women (one with and one without a pituitary adenoma) who were resistant to medical treatment, were given Hachimijiogan which subsequently reduced the serum prolactin level, and resulted in a normal ovulatory cycle and pregnancy, without side effects.

Usuki S; Kubota S; Usuki Y. Treatment with hachimijiogan, an ergot Chinese herbal medicine, in two hyperprolactinemic infertile women. *Acta Obstet Gynecol Scand* 1989, 68 (5) p475-8.

(7) In another study looking at pituitary dysfunction causing infertility, 27 women were given the same formulae as discussed above. 6 of the women had amenorrhea. In 15 patients, the prolactin levels dropped to a healthy range, and remained low 6 months after the course of treatment. Four patients with amenorrhea ovulated. Eleven patients conceived and delivered a healthy baby. In three women, the prolactin level did not lower. The authors conclude that a modification of Liuwei di huang wan can be a safe and effective treatment for hyperprolactinemic women.

Usuki S, Usuki Y. Hachimijiogan treatment is effective in the management of infertile women with hyperprolactinemia or bromocriptine-resistant hyperprolactinemia. *American Journal of Chinese Medicine* 1989; 17 (3-4):225-41.

(8) In one study of female infertility, 53 patients with luteal phase defect (LPD) were treated with different Chinese medicinal herbs at different phases of menstrual cycle. The patients were treated for three menstrual cycles and there was significant improvement in the luteal phase of endometrium, and a tendency for normalization of the wave forms and its amplitude after the treatment. The findings suggested that Chinese herbal medicines are capable of replenishing the Kidney and regulate the hypothalamus-pituitary-ovarian axis and thus improve the luteal function. Among the 53 cases, 22 (41.5%) conceived but 68.18% of them required other measures to preserve the pregnancy.

Zhang HY; Yu XZ; Wang GL Preliminary report of the treatment of luteal phase defect by replenishing kidney. An analysis of 53 cases. Zhongguo Zhong Xi Yi Jie He Za zhi Aug 1992, 12 (8) p473-4, 452-3.

(9) Women with normal menstrual cycles but low basal body temperature and progesterone levels (luteal insufficiency) were effectively treated with a Chinese herbal formulary called Dang guishao yao tang, with no observed side effects.

Usuki S, Higa TN, Soreya K. The improvement of luteal insufficiency in fecund women by tokishakuyakusan treatment . Am J Chin Med. 2002; 30(2-3):327-38.

Research on Recurrent Miscarriage & Chinese Herbal Medicine

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In 40 women with threatened abortion and a history of miscarriage, blood test showed threatened abortion (TA), compared to the blood test of normal pregnant women (The plasma beta-EP level in TA was significantly higher than that in normal pregnant women, $P < 0.01$. On the contrary, plasma GnRH, HCG and P4 were obviously lower in TA as compared with those of the normal cases, $P < 0.01$.) After treatment with Chinese herbal medicine that supported reproduction and blood circulation and protected the foetus, 36 of the 40 patients continued their pregnancy without symptoms of TA, and the above-mentioned four criteria measured at 10-12th week of gestation were similar to those of normal cases, $P > 0.05$. The authors concluded that Chinese herbal Medicine can regulate plasma beta-EP and placental endocrine function in threatened abortion in women with a history of recurrent miscarriage.

Sun F, Yu J. [Effect of TCM on plasma beta-endorphin and placental endocrine in threatened abortion] *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 1999 Feb; 19 (2):87-9.

(2) A study in Japan showed that recurrent miscarriages with an immunological component (rejection of the foetus as foreign) benefit positively to the treatment with Chinese herbal medicine. Twelve patients with recurrent abortion who had shown positive anti-phospholipid antibodies were treated through the administration of a Japanese modified traditional Chinese herbal medicine Sairei-To (Cai ling Tang). The patients had experienced a total of 27 spontaneous abortions in their previous pregnancies and had no other pregnancy history except for one patient. The patients were treated with 9.0 g of Sairei-To per day before their next pregnancy. The positive value of antiphospholipid antibodies returned to negative in 9 patients out of 12 patients through the treatment. Out of 12 patients, 10 patients continued their new pregnancy uneventfully, and they delivered an offspring (Success rate: 83.3%). Thus, the current treatment was considered to be an effective therapy for patients with recurrent abortion whose miscarriage is immune related (positive anti-phospholipid antibodies).

Takakuwa K, Yasuda M, Hataya I, Sekizuka N, Tamura M, Arakawa M, Higashino M, Hasegawa I, Tanaka K. Treatment for patients with recurrent abortion with positive antiphospholipid antibodies using a traditional Chinese herbal medicine. *J Med*. 1996; 24(5):489-94.

An experimental study on inhibitory effect of Chinese medicine tai-bao on antisperm antibody

OBJECTIVE: To investigate whether Chinese medicine Tai-bao could inhibit antisperm antibody in experimental mice.

METHODS: The experimental immunoinfertility mice were due to antisperm antibody induced by injection of human sperm membrane antigens. The experimental immuno-infertile mice used in the present study were divided into four groups including Tai-bao high dose group (46.8 g.kg-1.d-1), Tai-bao low dose group (31.2 g.kg-1.d-1), prednisone group and normal saline group. The enzyme linked immune sorbent assay (ELISA) and microcytotoxic assay were used for detection of antisperm antibody. The change of levels of antisperm antibody before and after treatment, pregnant rate, and the number of implantation were investigated in tested mice.

RESULTS: The pregnant rates in normal saline group, prednisone group, Tai-bao high dose group and low dose were 38.89%, 47.06%, 70.00% and 75.00% respectively. The rate of pregnancy in Tai-bao low dose group was significantly higher as compared with normal saline group ($P < 0.05$). The rate of implantation in Tai-bao low dose group was significantly higher than that in prednisone group ($P < 0.05$). The results of detection of cytotoxic antibody to sperm showed that cytotoxic percentages in Tai-bao high dose group (63.0 \pm 10.3%) and prednisone group (56.3 \pm 13.7%) were significantly lower ($P < 0.05$ and $P < 0.01$) than that in normal saline group (72.84 \pm 5.05%).

CONCLUSION: Chinese medicine Tai-bao possesses regulatory effect on reproductive immune function, inhibitory effect on antisperm cytotoxic antibody, and promoting effect on pregnancy.

Clinical study on the treatment of male immune infertility by Huzhangdanshenyin

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Chung Kuo Chung Hsi I Chieh Ho Tsa Chih, 17(6):360-2 1997 Jun (ISSN: 1003-5370)

OBJECTIVE: To investigate the efficacy of the Chinese medicine Huzhangdanshenyin on male immune infertility, and provide an effective therapy for this disease. **METHODS:** Ninety men with immune infertility were selected as the research subjects and randomly divided into two groups, 60 in the treatment group, treated by Huzhangdanshenyin, and the other 30 in the control, treated by prednisone, both for 3 months. The improvement of clinical symptoms, immunologic indexes (antisperm antibodies in serum and seminal plasma) and sperm indexes (semen liquefied duration, motility, viability, density and abnormal morphology rate) were observed and the results analyzed. **RESULTS:** The total antisperm antibody reversing ratio of the treatment group was higher than that of the control ($P < 0.01$), especially the serum antisperm antibody reversing ratio. There were significant differences in the clinical cure rate and total validity rate between the treatment group and the control ($P < 0.01$). After the treatment, the markers of the clinical symptoms ($P < 0.01$), especially the serum antisperm antibody reversing ratio. There were significant differences in the clinical cure rate and total validity rate between the treatment group and the control ($P < 0.01$). After the treatment, the markers of the clinical symptoms were lower ($P < 0.01$), and the improvement of the clinical symptoms was better in the treatment group than in the control ($P < 0.01$), especially the symptoms of pain in the back and knees, distending and bearing-down sensation of the perineum and testis, hyper sexuality and topoalgia. Compared with pre-treatment, sperm motility and viability of the treatment group significantly improved ($P < 0.01$), and so did sperm density ($P < 0.05$). However, there were no

significant differences in sperm density, semen liquefied duration, abnormal morphology rate and pH ($P > 0.05$) before and after the treatment.

CONCLUSION: The Chinese medicine Huzhangdanshenyin works more effectively than prednisone in the treatment of male immune infertility. It could improve the antisperm antibody reversing ratio, clinical symptoms and signs and ameliorate sperm indexes with no obvious adverse effects.

Direct effects of Chinese herbal medicine "hachuekkito" on sperm movement

Lu TK, Ouyang HG, Jin GY, Hong YS, Zou Q, Lin ZY, Deng LS, Guo YB.

Zhonghua Nan Ke Xue. 2006 Aug;12(8):750-5.

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BACKGROUND AND PURPOSE: Chinese herbal medicine, "Hochuekkito" is widely used for male infertility in Japan. There have been many reports concerning its clinical usefulness but very few reports of in vitro experiments studying the mechanism of its effects. In addition to stimulating germ cells, we analyzed its direct effects on sperm using computer assisted semen analyzer (CASA).

MATERIALS AND METHODS: Motile sperm were prepared using swim up technique from semen collected from ten healthy volunteers. Sperm movements (motility, velocity, linearity) were analyzed by CASA after adding either serum containing anti-sperm antibody (ASA) or normal serum with or without Hochuekkito.

RESULTS: Two hours after adding serum with ASA, the decrease of sperm motility was significantly reduced from 25.1% (92.8%→67.7%) to 12.5% (92.9%→80.6%) by adding Hochuekkito. No significant difference in velocity and linearity was observed between two groups. By adding normal serum, any of three parameters differed significantly with or without Hochuekkito.

CONCLUSION: Protective effects of Hochuekkito on sperm was suggested. Although normal sperm with ASA was used in this report, since the sperm of infertile patients are said to be more fragile, this results imply that direct protective effect is one of the mechanism of Hochuekkito for male infertility

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21. A substance isolated from *Cornus officinalis* enhances the motility of human sperm

Nippon Hinyokika Gakkai Zasshi, 89(7):641-6 1998 Jul (ISSN: 0021-5287)

The effects of a Chinese herb, *Cornus officinalis*, on the motility of human sperm was studied. An aqueous extract was prepared from the dried fruits of the herb and used in this study. The crude extract at a final concentration of 0.5 microgram/microliter in phosphate buffered saline (pH 7.4) increased sperm motility from 25.8 +/- 7.7% to 42.8 +/- 10.3% (i.e. 68% increase, n = 7), as determined by the computer-aided-sperm-analysis (CASA) method. The crude extract was fractionated by high-performance liquid chromatography (HPLC) into four fractions: C1, C2, C3 and C4. Their effects on sperm motility were further studied by CASA. Only the C4 fraction showed substantial stimulatory effects on sperm motility. At a concentration of 5 ng/microliter, C4 increased the sperm motility from 15.7 +/- 3.8% to 34.5 +/- 6.4% (i.e. 120% increase, n = 6) by CASA and from 14.9 +/- 4.3 to 28.5 +/- 8.1 (i.e. 91% increase, n = 8) by transmembrane migration ratio (TMMR) method. This result suggests that C4 is the active component in *Cornus officinalis* that enhances sperm motility.

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Am J Chin Med 1997;25(3-4):301-6 (ISSN: 0192-415X)

Unexplained infertility treated with acupuncture and herbal medicine in Korea.

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J Altern Complement Med. 2010 Feb;16(2):193-8.

Abstract

AIM: We aim to determine the safety and effectiveness of a standard therapeutic package of Korean medicine for the treatment of unexplained infertility in a cross-section of women who sought treatment at an integrative hospital in Seoul, Korea. **BACKGROUND:** Infertility affects more than 1.2 million women in the United States alone. Treatment options for infertility vary, yet the barriers of invasiveness, cost, and access inhibit treatment use for many women. Alternative medical approaches exist for this indication, and sustain certain popularity. Therefore, we systematically studied a standard therapeutic package of Korean medicine to treat unexplained infertility in women. **METHODS:** Female participants included in this observational study met inclusion criteria before receiving a set of treatments including herbal medicine, acupuncture, and moxibustion. A study physician screened each patient in accordance with inclusion criteria, provided study information, and after the patients consented, performed the baseline assessment. Assessments included age, the history of assisted reproductive technology, and duration of infertility. The key outcome measure included the number who achieved pregnancy and any neo-natal morbidity and mortality at follow-up stage for those who got pregnant. Any other adverse events including aggravation of existing symptoms, and the number of dropouts, were recorded. Treatments were supposed to be completed after 6 menstrual cycles between February 2005 and April 2006. **RESULTS:** One

hundred and four (104) women with unexplained infertility were included in this observational study. Participant mean age was 32 years (SD: 2.7), with a range between 26 and 41 years. The median duration of infertility after diagnosis was 33.5 weeks (interquartile range: 20.8-50.3). In total, 41 participants (39.4%) had undergone a mean number of 1.4 (SD: 2.2) assisted reproductive technology treatments prior to joining the study. The number of patients remaining in or achieving pregnancy throughout the 6-month study period was 23 (14 pregnancies), 22.1%. Six (6) participants (4.8%) reported minor adverse events including rash in the face (n = 1), diarrhea (n = 2), dizziness (n = 1), and heartburn (n = 2). Of the 14 pregnancies, there were 10 normal births, and 4 miscarriages; otherwise, no neonatal morbidity/mortality occurred. According to per protocol analysis, 14 pregnancies out of 23 total were achieved by those who remained for the entire six menstruation cycle treatments, yielding a pregnancy rate of 60.9%.

CONCLUSIONS: The standard therapeutic package for unexplained infertility in women studied here is safe for infants and the treated women, when administered by licensed professionals. While it remains challenging to have the target population complete a 6-month treatment course, during which most patients have to pay out of pocket, the extent of successfully achieved pregnancy in those who received full treatment provides meaningful outcomes, warranting further attention. A future study that includes subsidized treatment costs, encouraging the appropriate compliance rate, is warranted.

Infertility and Chinese Herbal formulas

Active pharmaceutical ingredients and mechanisms underlying phasic myometrial contractions stimulated with the saponin extract from *Paris polyphylla* Sm. var. *yunnanensis* used for abnormal uterine bleeding

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BACKGROUND: Total steroidal saponins of *Paris polyphylla* Sm. var. *yunnanensis* (TSSP) have been widely used in China for the treatment of abnormal uterine bleeding (AUB). But until now, the main active constituents and the mechanisms underlying the pharmacological actions on uterine activity have not been described.

METHODS: Total steroidal saponins were extracted with EtOH and purified by chromatography. In vitro isometric contraction studies were performed using myometrial strips from estrogen-primed or pregnant rats. Intracellular calcium was monitored under a confocal microscope using Fluo-3 AM-loaded myometrial cells.

RESULTS: TSSP dose-dependently induced phasic myometrial contractions in vitro. Experiments with calcium channel blockers or kinase inhibitors demonstrated that the TSSP-stimulated myometrial contraction was mediated by an increase in $[Ca^{2+}]_i$ via influx of extracellular calcium and release of intracellular calcium. Through bioassay-guided separation, it was found that total spirostanol saponins exhibited contractile activity in myometrium and Pennogenin-3-O--L-arabinofuranosyl(14)[-L-rhamnopyranosyl(12)]- β -D-glucopyranoside (PARG) was identified as the active ingredient of TSSP. Furthermore, the contractile response of rat myometrium to PARG was significantly enhanced with advancing pregnancy.

CONCLUSIONS: These data provide evidence that myometrial contractility stimulated by TSSP results from $[Ca^{2+}]_i$ increase and supports the possibility that some spirostanol glycosides may represent a new type of contractile agonist for the uterus.

Key words: steroidal saponins/*Paris polyphylla* Sm. var. *yunnanensis*/myometrial contractility/abnormal uterine bleeding/active pharmaceutical ingredients

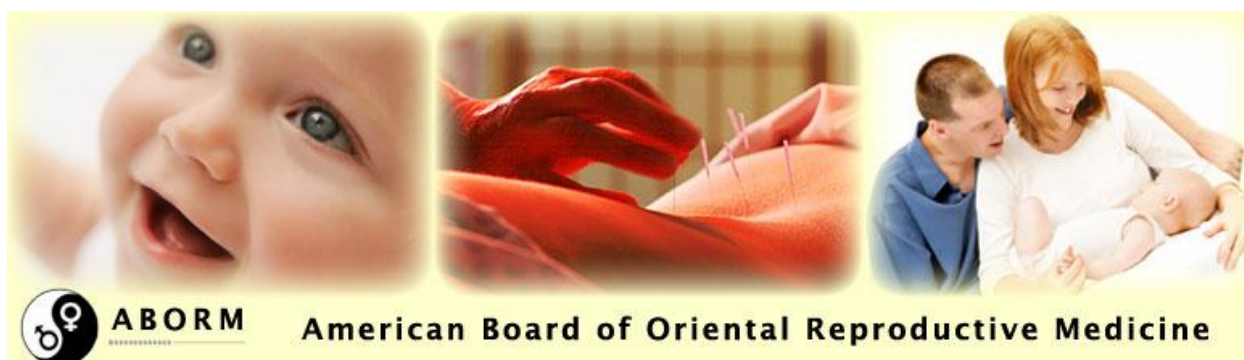
As Dedication and Appreciation

Thanks to the following individuals and to Google and the Internet for the information contained herein. My goal was to provide a handy guide to what research is out there... not in any way to intimate that the work was mine (although some was of course ☺) ... More a gatherer and the organizer.

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- *Paul Magarelli*
- *And the many, many authors that gathered research on the internet*

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Summary of Acupuncture Studies related to Reproductive Medicine

Compiled from Journals, Internet, and Website resources as a tool to aid ABORM members understand the depth and breadth of Western Style research related to our fields.

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