Available online at www.sciencedirect.com

SciVerse ScienceDirect

European Journal of Integrative Medicine 4 (2012) e234–e244

European Journal of INTEGRATIVE MEDICINE

www.elsevier.com/eujim

Review article

Does acupuncture improve the outcome of in vitro fertilization? Guidance for future trials

Fan Qu [a,b,1], Jue Zhou [c,b,1], Mark Bovey [d], Giovanna Franconi [e], Kelvin Chan [f,g], Caroline Smith [f], Dan Jiang [h], Nicola Robinson [i,*]

[a] *Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang 310006, China*
[b] *School of Medicine, King's College London, London SE5 9RJ, UK*
[c] *College of Food Science and Biotechnology, Zhejiang Gongshang University, Hangzhou, Zhejiang 310012, China*
[d] *British Acupuncture Council, London W12 9HQ, UK*
[e] *Department of Systems Medicine, Tor Vergata University, Rome 00133, Italy*
[f] *Centre for Complementary Medicine Research, University of Western Sydney, Sydney, NSW 2751, Australia*
[g] *Faculty of Pharmacy, The University of Sydney, Sydney, NSW 2006, Australia*
[h] *Asante Academy of Chinese Medicine, Middlesex University, London N19 5LW, UK*
[i] *Faculty of Health and Social Care, London South Bank University, London SE1 0AA, UK*

Received 31 May 2012; received in revised form 15 July 2012; accepted 26 July 2012

Abstract

Introduction: The comprehensive review was to appraise the current evidence from both randomized and non-randomized trials by using both Chinese and western databases and to highlight the issues which could guide future trial design. Many infertile couples have chosen acupuncture as an adjunct when they undergo in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment. More than forty trials have emerged since the first clinical research published in 1999 explored the effects of acupuncture on the outcomes of IVF. However, the current evidence makes it difficult for clinical practitioners and patients to make a decision on whether to choose acupuncture as an adjunct when undergoing IVF or ICSI treatment.

Methodology: A total of thirty-three randomized and 5 non-randomized controlled trials were included in the review.

Results: Based on this comprehensive review and analysis of all the relevant trials, the authors identify the factors which have contributed to these inconsistencies, and which should be considered in the design of future studies.

Discussion/conclusions: These items included in the review could provide useful recommendations and guidelines, which will in turn promote better trial design and improve the evidence base for the use of acupuncture for IVF.

Keywords: Acupuncture; In vitro fertilization (IVF); Intracytoplasmic sperm injection (ICSI)

Introduction

In vitro fertilization (IVF) is an effective treatment for various causes of infertility, and has produced over 3,500,000 babies worldwide [1]. In recent years, many infertile couples have chosen acupuncture as an adjunct when they undergo IVF or intracytoplasmic sperm injection (ICSI) [2–8]. However, the current evidence makes it difficult for clinical practitioners and patients to make a decision on whether to choose acupuncture as an adjunct when undergoing IVF or ICSI treatment [9]. Since the first clinical research exploring the effects of acupuncture on the outcomes of IVF was published in 1999 [10], more than forty trials have emerged. However, the conclusions of these trials have been inconsistent. A recent review concluded that acupuncture can improve the outcome of IVF and the mechanisms may be related to the increased uterine blood flow, inhibited uterine motility, and the decreased levels of depression, anxiety and stress [11]. Three systematic reviews or meta-analysis designed

* Corresponding author at: Traditional Chinese Medicine (TCM) and Integrated Health, Faculty of Health and Social Care, London South Bank University, 103 Borough Road, London SE1 0AA, UK. Tel.: +44 0207815 7940; fax: +44 0207815 8490.
E-mail addresses: nicky.robinson@lsbu.ac.uk, syqufan@zju.edu.cn, fan.qu@kcl.ac.uk (N. Robinson).
[1] Both authors contributed equally to the study.

1876-3820
http://dx.doi.org/10.1016/j.eujim.2012.07.978

to explore the effects of acupuncture on IVF outcomes published in 2008 [2–4] also showed that acupuncture improved rates of pregnancy or live birth in women undergoing IVF treatment. A systematic review and meta-analysis reviewed studies that did not include the Streitberger needle as a control and it demonstrated that acupuncture improved clinical pregnancy rate (CPR) and live birth rate (LBR) among women undergoing IVF [8]. However, another meta-analysis [7] together with its updated version [5] did not find any improvement in IVF outcomes following acupuncture, nor did Cheong's updated review in 2010 [6]. Since the publication of these reviews further randomized controlled trials have been published. A large, randomized, multicentre, double-blinded and placebo-controlled trial including 635 women undergoing IVF or ICSI published in 2010 also failed to show that acupuncture administered in relation to embryo transfer (ET) has effects on the outcomes of IVF or ICSI [12]. The investigators achieved complete follow-up of all pregnancies and obtained outcomes relating to the number of live births, which is considered to be the optimal endpoint for assisted reproduction treatment. Another large, prospective, randomized, single-center, single-blinded and placebo-controlled trial including 309 women undergoing IVF or ICSI published in 2011 showed that electro-acupuncture administered before and after ET significantly improved the clinical outcomes of IVF [13]. The primary outcome was CPR, and secondary outcomes were biochemical pregnancy rate (BCPR), implantation rate (IR), miscarriage rate (MR), and LBR. This evidence raises questions regarding how research in this area was conducted and how future research in this area should be carried out. High quality of evidence is needed before any specific intervention is incorporated into routine clinical practice [14] even though practitioners and patients report its success as a supportive treatment. In our systematic review with meta-analysis of 17 randomized controlled trials of acupuncture during IVF or ICSI treatment on the outcomes of IVF or ICSI, found no significant benefits for the use of acupuncture for a variety of outcomes [15]. It is possible a consensus amongst experts on key components of a best practice treatment protocol can be achieved, although there exists a lack of homogeneity in the research and clinical literature on assisted reproductive technology (ART) and acupuncture [16]. The aim of this comprehensive review was to appraise the current evidence from both randomized and non-randomized trials by using both Chinese and western databases which could inform and provide guidance for future trial design.

Methods

To review the existing studies regarding acupuncture as an adjunct therapy for IVF, a systematic literature search was performed using MEDLINE (1966 to January 2012), SCISEARCH (1974 to January 2012), Cumulative Index to Nursing and Allied Health Literature (1982 to January 2012), the Cochrane Menstrual Disorders and Subfertility Group trials register (January 2012), AMED (Allied and Complementary Medicine) (1985 to January 2012), EMBASE (1974 to January 2012), Wanfang Database (1982 to January 2012), China Academic Journal Electronic full text Database in China National Knowledge Infrastructure (1982 to January 2012), Index to Chinese Periodical Literature (1978 to January 2012) and ISI Proceedings for conference abstracts, and ISRCTN Register and meta-register for randomized controlled trials (mRCT). The reference lists of relevant primary and review articles were examined to identify cited articles not captured by electronic searches.

Search terms or key words included "acupuncture", "acupressure", "moxibustion", "electro-acupuncture", "auricular-acupuncture", "laser acupuncture", "auriculotherapy", "acupuncture therapy" "transcutaneous electrical acupoint stimulation", and "Traditional Chinese Medicine" "in vitro fertilization", "fertilization in vitro", "intracytoplasmic-sperm-injection", "assisted reproductive techniques", "assisted reproduction treatment", "oocytes", "egg collection", "embryo transfer" and "embryo implantation".

The acupuncture intervention included any accepted regimen of acupuncture including traditional needling acupuncture, auricular acupuncture, electro-acupuncture and laser acupuncture. Studies using Chinese herbs in conjunction with acupuncture were also included in this review. As the focus of the review was on whether acupuncture improves the outcomes of IVF or not, studies were only included from which exact data could be extracted on at least one of the following outcomes: CPR, BCPR, ongoing pregnancy rate (OPR), IR, LBR and MR. No restrictions of language or publication type were placed in the review. Five trials [17–21] were excluded due to lack of exact data on IVF outcomes or inconsistent data on the number of canceled IVF cycles. Data abstracted from the accepted articles included: details of the participants, countries, intervention, IVF outcomes, randomization, single/multi-center, concealment of allocation, control and placebo intervention, blinding, comparability at baseline, acupuncture practitioner and adherence to standards for reporting interventions in clinical trials of acupuncture (STRICTA) [22].

Results and discussion

A total of thirty-three randomized and 5 non-randomized controlled trials were included. The summary of the characteristics of the included studies identified and the quality evaluation of the studies are shown in Tables 1 and 2 respectively. Compared with our previous systematic review and meta-analysis [15], 16 additional randomized and 5 non-randomized controlled trials were included in this comprehensive review. The objective of the previous systematic review was to explore whether acupuncture can improve the outcomes of IVF or ICSI [15], This comprehensive review was to appraise the current evidence from both randomized and non-randomized trials to inform and provide guidance for future trial design. As our systematic review with meta-analysis was completed in October 2010, the new research published after that date had not been included [15], however, this comprehensive review includes all of these new papers. By investigating the individual studies identified and the differences in these studies, the authors highlight the factors which may have contributed to the variability of the results as seen in previous meta-analyses [2–8], and which should be considered in the design of future studies. The key factors identified which may

Table 1
Summary of the studies.

Study	Participants	Country	Intervention	Control	IVF outcomes
Stener-Victorin et al. [9]	150 randomized—no inclusion criteria	Sweden	EA and PCB	Alfentanil + PCB	CPR, IR, MR
Paulus et al. [27]	160 randomized—only women with good quality embryos included	Germany	TA and AA for 25 min before and after ET	Lying still for 25 min before and after ET	CPR, OPR, LBR
Balk et al. [34]	10 Non-randomized—women undergoing IVF	U.S.A.	TA	No intervention	CPR,
Paulus et al. [28]	200 randomized—only women with good quality embryos included	Germany	TA for 25 min before and after ET	Sham (noninvasive) acupuncture	CPR, OPR, LBR
Stener-Victorin et al. [22]	286 randomized—eligible women aged <38 years, BMI <28 kg/m^2, had four or more follicles of size 18 mm or more and no more than three previous IVF attempts	Sweden	PCB and EA	Alfentanil + PCB	CPR, OPR, IR, MR
Zhang et al. [46]	210 randomized—only women with good quality embryos included	China	TA for 25 min before and after ET	Sham (noninvasive) acupuncture	CPR
Humaidan and Stener-Victorin [23]	200 randomized—no inclusion criteria;	Denmark	PCB and EA	Alfentanil + PCB	CPR, BCP, IR
Gejervall et al. [24]	160 randomized—no inclusion criteria	Sweden	PCB and EA	Premedication + alfentanil + PCB	CPR
Benson et al. [35]	258 randomized—women scheduled to have ET were eligible	U.S.A.	Traditional needle or Laser acupuncture for 25 min before and after ET	Sham laser acupuncture, relaxation or no intervention	CPR, BCPR
Dieterle et al. [29]	225 randomized—no inclusion criteria	Germany	TA for 30 min after ET and 3 days later + Chinese medical herbs	Placebo needling at acupoints designed not to influence fertility	CPR, BCPR, OPR, IR, LBR, MR
Domar et al. [36]	83 randomized—women scheduled to undergo ET from a fresh cycle using their own eggs	U.S.A.	TA and AA for 25 min before and after ET	Lying still for 25 min before and after ET	CPR
Humaidan et al. [26]	152 randomized—women undergoing IVF	Denmark	TA and EA	TA and EA	CPR
Sator-Katzenschlager et al. [25]	94 randomized—women aged <43 years, BMI <28 kg/m^2, had four or more follicles of size >18 mm	Austria	AA with or without electrical stimulation + PCA	PCA + placebo AA	CPR
Smith et al. [32]	228 randomized—women with a planned ET were eligible	Australia	TA	Placebo needling at points close to the real acupuncture acupoints	CPR, OPR
Westergaard et al. [30]	300 randomized—no inclusion criteria	Denmark	TA for 25 min before and after ET with or without a third session for 25 min 2 days after ET	Bed rest for 1 h after ET	CPR, BCPR, OPR, IR, LBR
Xu [47]	57 randomized—no inclusion criteria	China	TA and Chinese medicinal herbs	No intervention	CPR
Craig et al. [37]	107 randomized—women undergoing IVF who have not had acupuncture within 3 months	U.S.A.	TA for 25 min before and after ET	No intervention	CPR, BCPR
Cui et al. [48]	94 randomized—women undergoing IVF who had a normal uterine cavity shown on ultrasound scanning and had no history of COH	China	TA before and during COH	No intervention	CPR,
Cai et al. [38]	126 Non-randomized The women were divided into 3 groups based on the ages Group A: <35 years old Group B: between 35 and 39 years old Group C: >39 years old	U.S.A.	TA, AA and Chinese medicinal herbs	TA, AA and Chinese medicinal herbs	CPR, LBR

Table 1 (*Continued*)

Study	Participants	Country	Intervention	Control	IVF outcomes
Cui et al. [49]	126 Non-randomized—The women were divided into 3 groups based on the diagnosis of the patient's syndrome according to TCM theory: Group A: Kidney deficiency type Group B: Liver-qi stagnation type Group C: Phlegm dampness type	China	EA	EA	CPR, IR
Fratterelli et al. [39]	1000 randomized—women receiving an ET	U.S.A.	Traditional needle or Laser acupuncture	Sham laser acupuncture, relaxation or no intervention	CPR, BCPR, OPR, IR
Chen et al. [50]	60 randomized—women with poor ovarian response or decreased reserve	China	TA around ovulation induction	No intervention	CPR, IR, MR
Chen et al. [51]	100 randomized—women undergoing frozen ET	China	EA from the 5th day of natural menstrual cycle	No intervention	CPR, IR
Domar et al. [40]	150 randomized—women scheduled to have ET using non-donor eggs were eligible	U.S.A.	TA for 25 min before and after ET	Lay quietly for same amounts of time	CPR, BCPR
Ho et al. [52]	44 randomized—women had to consent to be randomly assigned to one of the two groups	China	EA was performed four times, twice a week for 2 weeks, from day 2 of the study to the day before TVOR	No intervention	CPR,
Kong et al. [41]	52 randomized—women between 29 and 45 years old, undergoing IVF	U.S.A.	TA and EA	1. TA 2. EA	CRP
Magarelli et al. [42]	67 Non-randomized—women undergoing IVF, agreeing to have a vial of blood drawn during the normal standard times (7 A.M. to 9 A.M.)	U.S.A.	EA	No intervention	CPR, IR, LBR, MR
Smith et al. [33]	28 randomized—women undergoing an IVF cycle with a planned ET at day 3 or day 5	Australia	TA and AA	No intervention	BCPR
So et al. [53]	370 randomized—women who had a normal uterine cavity shown on ultrasound scanning on the day of TVOR	China	TA for 25 min before and after ET	Placebo needling for 25 min before and after ET	CPR, BCPR, OPR, IR, LBR, MR
Andersen et al. [11]	635 randomized—<37 years of age, treatment with IVF/ICSI and transfer of one or two embryos in the first, second or third stimulated cycle	Denmark	TA accompanying ET	Placebo needling accompanying ET	CPR, BCPR, OPR, LBR
Arnoldi et al. [31]	204 randomized—women for IVF-ICSI with an unfavorable reproductive prognosis were assigned randomly to two groups. Inclusion criteria were as follow: (1) at least two previous poor responses to ovarian stimulation and/or recurrent implantation failure (for ≥2 cycles), (2) ovarian and/or pelvic endometriosis, (3) raised early follicular phase FSH (>10 IU/l)	Italy	TA	No intervention	CPR, IR
Balk et al. [43]	57 Non-randomized—women receiving an ET	U.S.A.	TA and AA for 25 min before and after ET	Lying still for 25 min before and after ET	CPR,
Madaschi et al. [45]	416 randomized—women undergoing ICSI cycles for the first time	Brazil	TA	No intervention	CPR, IR, LBR, MR
So et al. [54]	226 randomized—women undergoing FET treatment	China	TA	Placebo needling at the same acupoints as the real acupuncture group	CPR, OPR, IR, LBR, MR
Yin et al. [55]	60 randomized—no inclusion criteria	China	TA, AA and Chinese medicinal herbs	No intervention	CPR,

Table 1 (*Continued*)

Study	Participants	Country	Intervention	Control	IVF outcomes
Moy et al. [44]	161 randomized—women <38 years old undergoing IVF with or without ICSI	U.S.A.	TA and AA for 25 min before and after ET	Placebo needling in non-qi lines in the predetermined locations. AA was performed at the following acupoints: knee, heel, allergic area, mouth	CPR, BCPR
Cui et al. [56]	66 randomized—women with polycystic ovary syndrome undergoing IVF–ET	China	EA	No intervention	CPR
Zhang et al. [12]	309 randomized—infertile women aged 21–44 years, eligible for ET, no adverse ovarian reserve, no previous acupuncture experience	China	Double EA: 24 h before ET and 30 min after ET	Mock EA: 30 min after ET; single EA: 30 min after ET	CPR, IR, LBR

Note: IVF: in vitro fertilization; ICSI: intracytoplasmic-sperm-injection; ET: embryo transfer; TVOR: time of transvaginal oocyte retrieval; EA: electro-acupuncture; TA: traditional acupuncture; AA: auricular acupuncture; PCB: paracervical block; PCA: patient-controlled analgesia (remifentanil pump); CPR: clinical pregnancy rate; IR: implantation rate; MR: miscarriage rate; BCPR: biochemical pregnancy rate; OPR: ongoing pregnancy rate; LBR: live birth rate; BMI: body mass index; COH: controlled ovarian hyper-stimulation; TCM: traditional Chinese medicine; FET: frozen-thawed embryo transfer.

influence study outcome and need to be considered in future trial design are as follows:

1. *Main aim of the studies*: Six studies were mainly designed to assess the pain-relieving effects of acupuncture used at the time of trans-vaginal oocyte retrieval (TVOR) compared with conventional analgesia [10,23–27], while the other studies were designed to evaluate the effects of acupuncture on the outcomes of IVF.
2. *Country of location*: The studies were performed in Germany [28–30], Denmark [12,24,27,31], Sweden [10,23,25], Italy [32] Austria, [26], Australia [33,34], U.S.A. [35–45], Brazil [46], China [13,47–57]. Inter-country differences in patients' experience, expectations and knowledge of acupuncture may lead to variability in outcomes.
3. *Single vs. multicenter studies and variations in treatment protocol*: Among all the 38 trials reviewed, only four were multi-center trials [10,12,23,38]. Single-center trials may produce more inconsistent conclusions due to differences in the protocols for IVF or ICSI, such as the protocol for controlled ovarian hyperstimulation (COH), the baseline CPR and LBR, which appeared to differ in various centers.
4. *Study size*: The average number of participants in the relevant studies was 190 patients, with a range of 10–1000 patients. In the trials reviewed, thirteen trials provided a power analysis and presented a calculation of sample size [13,23–27,30,33,43,45,46,54,55]. IVF outcomes are affected by many confounders, such as life style, gynecological and IVF associated factors. The higher the absolute value of the correlation between the exposure and the confounder, the larger the sample size required [58]. Many studies to date have not been of sufficient size to demonstrate meaningful results.
5. *Participant characteristics*: Although some of the studies described detailed inclusion criteria of the patients, for most of the studies the inclusion criteria were not clearly stated. The women's age, body mass index (BMI) and other known confounding factors such as number of previous IVF cycles, duration and cause of infertility have been shown important in large prospective studies [59,60]. Lifestyle factors such as smoking and alcohol intake are also important and these should be clearly described in future studies.
6. *Location of acupuncture treatment provision*: The location of the acupuncture provision includes hospital, IVF center, the acupuncturists' offices and the patients' home. Stress, anxiety and depression contribute to lower pregnancy rates among women undergoing IVF [61]. Both anxiety and depression negatively influenced the CPR of IVF treatment in women with tubal factor infertility [62]. When controlling for other factors, a strong negative relationship existed between state anxiety and CPR of women undergoing IVF or ICSI treatment [63].
7. *Choice of controls and placebo*: Control interventions included: no intervention, lying still for a similar time as the intervention group before and after ET, bed rest for 1 h after ET, superficial needling of the true acupoints, placebo needling at acupoints designed not to influence fertility, placebo needling at acupoints close to the real acupuncture acupoints and sham laser acupuncture. According to a recent paper, researchers were advised to carefully weigh the benefits and drawbacks of using sham acupuncture to blind patients in adjuvant acupuncture for IVF trials, and should question, rather than automatically accept, whether "placebo effects" are key risk factors of bias in this context [64]. Moreover, the Streitberger control may not be an inactive control according to a recent meta-analysis [8]. Placebo needling does not make for a placebo control and hence is best avoided [65], especially for fertility where the outcomes are objective [64]. Including so many different controls may have influenced the efficacy of the intervention and caused variability in the measured outcomes.

Table 2
Quality evaluation of the studies.

Study	Randomization	Randomization method	Single-/multi-center	Concealment of allocation	Placebo intervention	Blinding	Comparability at baseline	Acupuncture practitioner	Adherence to STRICTA
Stener-Victorin et al. [9]	Yes	Not mentioned	Multi-center	Adequate	No	No	Unclear	Trained midwives	No
Paulus et al. [27]	Yes	Computerized randomization	Single-center	Adequate	No	Yes	Yes	Trained examiner	No
Balk et al. [34]	No	–	Single-center	None	No	No	Unclear	Not mentioned	No
Paulus et al. [28]	Yes	Not mentioned	Single-center	Adequate	Yes	No	Unclear	Not mentioned	No
Stener-Victorin et al. [22]	Yes	Not mentioned	Multi-center	Adequate	No	No	Unclear	Trained nurses	Yes
Zhang et al. [46]	Yes	Not mentioned	Single-center	Unclear	Yes	Yes	Yes	Not mentioned	No
Humaidan and Stener-Victorin [23]	Yes	Not mentioned	Single-center	Adequate	No	No	Yes	Trained nurses	Yes
Gejervall et al. [24]	Yes	Computerized randomization	Single-center	Unclear	No	No	Unclear	Four midwives	Yes
Benson et al. [35]	Yes	Not mentioned	Single-center	Unclear	No (except laser group)	No (except laser groups)	Yes	Acupuncturist	No
Dieterle et al. [29]	Yes	Not mentioned	Single-center	Adequate	Yes	Yes	Yes	Physician	No
Domar et al. [36]	Yes	Not mentioned	Single-center	Unclear	No	Yes	Yes	Not mentioned	No
Humaidan et al. [26]	Yes	Not mentioned	Single-center	Adequate	No	No	Yes	Trained nurses	Yes
Sator-Katzenschlager et al. [25]	Yes	Computerized randomization	Single-center	Unclear	Yes	Yes	Yes	Trained gynecologist	Yes
Smith et al. [32]	Yes	Block randomization	Single-center	Adequate	Yes	Yes	Yes	Acupuncturist	Yes
Westergaard et al. [30]	Yes	Unclear	Single-center	Adequate	No	No	Yes	Nurse	Yes
Xu [47]	Yes	Not mentioned	Single-center	None	No	No	Unclear	Not mentioned	No
Craig et al. [37]	Yes	Computerized randomization	Multi-center	Adequate	No	Yes	Yes	Acupuncturist	No
Cui et al. [48]	Yes	Not mentioned	Single-center	Unclear	No	No	Yes	Not mentioned	No
Cai et al. [38]	No	–	Single-center	None	No	No	Unclear	Not mentioned	No
Cui et al. [49]	No	–	Single-center	None	No	No	Yes	Acupuncturist	No
Fratterelli et al. [39]	Yes	Not mentioned	Single-center	Adequate	Yes	Yes	Yes	Acupuncturist	No
Chen et al. [50]	Yes	Computerized randomization	Single-center	Unclear	No	No	Yes	Unclear	No
Chen et al. [51]	Yes	Not mentioned	Single-center	Unclear	No	No	Yes	Not mentioned	No
Domar et al. [40]	Yes	Computerized randomization	Single-center	Adequate	No	Yes	Yes	Acupuncturist	No
Ho et al. [52]	Yes	By selection of a sealed envelope	Single-center	Unclear	No	No	Yes	Not mentioned	No
Kong et al. [41]	Yes	Not mentioned	Single-center	None	No	No	Unclear	Not mentioned	No
Magarelli et al. [42]	No	–	Single-center	None	No	No	Yes	Acupuncturist	No
Smith et al. [33]	Yes	Computerized randomization	Single-center	Adequate	No	No	Yes	Acupuncturist	Yes
So et al. [53]	Yes	Computerized randomization	Single-center	Adequate	Yes	Yes	Yes	Acupuncturist	Yes

Table 2 (*Continued*)

Study	Randomization	Randomization method	Single-/multi-center	Concealment of allocation	Placebo intervention	Blinding	Comparability at baseline	Acupuncture practitioner	Adherence to STRICTA
Andersen et al. [11]	Yes	Computerized randomization	Multi-center	Adequate	Yes	Yes	Yes	Nurses who were authorized professional acupuncturists	Yes
Arnoldi et al. [31]	Yes	Not mentioned	Single-center	Unclear	No	No	Yes	Not mentioned	No
Balk et al. [43]	No	–	Single-center	None	No	No	No	Acupuncturist	No
Madaschi et al. [45]	Yes	Computerized randomization	Single-center	Adequate	No	Yes	Yes	Acupuncturist	Yes
So et al. [54]	Yes	Computerized randomization	Single-center	Adequate	Yes	Yes	Yes	Acupuncturist	Yes
Yin et al. [55]	Yes	Not mentioned	Single-center	Unclear	No	No	Yes	Not mentioned	No
Moy et al. [44]	Yes	Computerized randomization	Single-center	Adequate	Yes	Yes	Yes	Acupuncturist	Yes
Cui et al. [56]	Yes	Not mentioned	Single-center	Unclear	No	No	Yes	Not mentioned	No
Zhang et al. [12]	Yes	Computerized randomization	Single-center	Unclear	Yes	Yes	Unclear	Not mentioned	No

Note: STRICTA: standards for reporting interventions in clinical trials of acupuncture.

Comparisons with no acupuncture intervention or with other promising adjuvant treatments should be encouraged.

8. *Blinding*: In an acupuncture clinical trial theoretically blinding can include the patient, acupuncturist, assessor, analyst and clinician. In all the studies reviewed, blinding was only applied in fifteen studies [12,13,26,28,30,33,37,38,40,41,45–47,54,55]. Although blinding is problematic for the physicians or the acupuncturists administering the acupuncture treatment, it is not impossible, and elaborate methods are available. The blinding should be assessed early in the study to avoid being influenced by the outcomes of treatment, and patients blinding should be preserved by careful attention to verbal and non-verbal communication [66,67].
9. *Acupuncture dose and mode of delivery*: Acupuncture used in these studies included traditional acupuncture needling, auricular acupuncture, electro-acupuncture and laser acupuncture. Variation in the delivery, frequency and intensity of the acupuncture may affect the results, but in some cases there was insufficient recording of these details. According to STRICTA criteria [22], these details include number of needle insertions per subject per session (mean and range where relevant), names (or location if no standard name) of acupoints used (uni/bilateral), depth of insertion based on a specified unit of measurement or on a particular tissue level, response sought (e.g. *de qi* or muscle twitch response), needle stimulation (e.g. manual, electrical), needle retention time, needle type (diameter, length, and manufacturer or material), number of treatment sessions, frequency and duration of treatment sessions and details of other interventions administered to the acupuncture group (e.g. moxibustion, cupping, herbs, exercises, lifestyle advice) [22]. Among the 38 included trials, acupuncture was applied along with Chinese medicinal herbs in four trials [30,39,48,56], and the combined use of acupuncture and Chinese medicinal herbs led to better IVF outcomes.
10. *Acupoints selected and use of diagnostic patterns*: In most studies, the acupuncture protocol was developed based on the clinical experience in practice, traditional literature and consultation with experts in traditional Chinese medicine (TCM). Neiguan (PC6), Diji (SP8), Taichong (LR3), Guilai (ST29), Zusanli (ST36), Sanyinjiao (SP6), and Xuehai (SP10) were the most frequently used acupoints. Most of the acupoint protocols have overlapped considerably, with a common root in one seminal RCT [28], though there was some variation from study to study. In clinical practice of acupuncture, the acupoints are usually selected based on the diagnosis of the patient's syndrome according to TCM theory. Among the 38 trials reviewed, only one trial [50] used this method, with patients being divided into three groups, each with a different selection of acupoints.
11. *Timing of acupuncture delivery*: In some of the studies, acupuncture was applied around the time of TVOR to assess the pain-relieving effects. In most trials, acupuncture was applied around the time of ET. Different timing in the provision of the acupuncture intervention during IVF may

account for variations in outcome and research is needed to define the appropriate time to provide acupuncture to maximize its effects.

12. *The acupuncture practitioners*: The education, training and practice of acupuncture practitioners may influence the nature of the acupuncture treatment given and is therefore a variable that may significantly affect the IVF outcome. The acupuncture practitioners in these studies included: TCM doctors or practitioners, trained midwives, trained examiners, trained nurses, physicians, traditional acupuncturists and trained gynecologists. The duration of relevant training, length of clinical experience, and details of expertise in treating the specific condition being evaluated, as well as practical experience that may be relevant to the trial should be clearly described in future studies.
13. *Definition of indicators of IVF outcome*: The IVF outcomes include the indicators of CPR, BCPR, OPR, IR, LBR and MR. For most studies, the authors failed to give the exact definition of these outcome indicators, and in the other studies the definition of the outcome indicators was often different: for example, in some studies, OPR was defined as pregnancy beyond 10 weeks of gestation, and in other studies it was defined as pregnancy beyond 16 or 18 weeks of gestation. The variation in the definition of IVF outcome indicators may produce inconsistent results.

Despite the recent systematic review and meta-analysis in this area, this is a more comprehensive review which adds new information and is critical to direct future research. This is illustrated as follows:

(1) STRICTA criteria [22] were used to appraise all the included trials. However, only thirteen trials [12,23–27,31,33,34,45,46,54,55] adhered to STRICTA.
(2) To provide a more comprehensive review, five non-randomized trials were also included [35,39,43,44,50].
(3) Nine trials published in Chinese were included [39,47–52,56,57], which had been omitted in the previous reviews and meta-analysis. Among these seven were randomized controlled trials [47–49,51,52,56,57] and two were non-randomized controlled trials [39,50]
(4) Four trials which combined the use of acupuncture and Chinese medicinal herbs were included [30,39,48,56].
(5) One trial [50], in which, the women were divided into three groups based on the diagnosis of the patient's syndrome according to TCM theories was also included.

Recommendations for the design of future studies

The limitations identified due to this clinical trial heterogeneity suggest a more rigorous approach is required in future studies and this may be achieved by:

1. Conducting multi-center studies: As early as in 2006, there was a recommendation to establish an international multicenter study group to evaluate the effects of acupuncture on IVF and ICSI outcomes [68]. Multi-center trials using the same study design may reduce the variation caused by the different protocols for IVF or ICSI and differences in baseline CPR and LBR observed between different centers.
2. Taking into account or stratifying according to the different confounders which have been shown to influence IVF outcome, which include: life style factors (maternal and paternal age, weight, vitamin and iodine intake, alcohol and caffeine consumption, smoking, substance misuse, stress, environmental pollutants, oxidative stress, etc.), gynecological factors (duration and cause of infertility, presence and characteristics of uterine fibroids etc.), number of previous IVF cycles, presence of male factor, race and ethnicity [60,69–71]. Some of the IVF-associated factors including the serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (TT) and estradiol (E_2) on the 3rd day of spontaneous menstrual cycle, the cycle length, the dosage of recombinant FSH administered, induction length, number of follicles, number of follicles with diameters of more than 14 mm, number of embryos transferred per cycle, embryo cleavage rate, good-quality embryo rate and fertilization rate have been shown to have important influence on IVF outcomes in large prospective studies [59,60,72].
3. Using the STRICTA criteria to make protocols reproducible [22]. The revised STRICTA includes 6 items and 17 subitems, which set the reporting guidelines for the acupuncture rationale, the details of needling, the treatment regimen, other components of treatment, the practitioner background, and the control or comparator intervention [73]. STRICTA has provided authors a way to structure their reports of interventions with a minimum set of items within a checklist and should be used as the gold standard not only in reporting the trials, but in designing the whole study. One area that is often inadequately reported is a precise description of the control intervention, including needling details and regimen if these are different from those used in the acupuncture group. Some potential factors may influence the applicability of "placebo" needling, amongst which the patient's knowledge, expectation and experience of acupuncture, acupuncture point selection and the visual impact of needling are the most important [74].
4. Establishing detailed fixed protocols based on the correct diagnosis of the patient's syndrome according to TCM theories and expert opinion. As an important part of TCM, acupuncture is based on the classical theories of TCM. The effects of acupuncture on IVF or ICSI outcomes would be predicted to improve with the correct diagnosis of the patient's syndrome based on TCM theories; also the outcomes may vary according to which syndromes are predominant. Some key factors of acupuncture treatment including the angle/direction of insertion, the manipulation method (thrusting, lifting, and rotating techniques) and intensity of these manipulation methods are based on the TCM diagnosis, and hence may vary for different IVF patients. Consequently, the detailed fixed protocols should be based on the correct diagnosis of the patient's syndrome [75,76].

5. Providing a sufficient dose of treatment over the most appropriate time period. Most trials to date have given only two acupuncture treatments, one either side of ET. Only a few have been around TVOR but their primary aim has been analgesia rather than fertility treatment [27,53]. Some have also provided adjunctive acupuncture before or during the earlier ovarian hyper-stimulation phase [49,51,52]. This last approach would appear to be more comparable to TCM theory and practice, though there is currently no research information to inform this aspect of the protocol.
6. Calculating adequate sample sizes. As with any clinical trial, the sample size should be calculated based on previous research and take into account the effect of confounders.
7. Using all the relevant indicators of IVF outcome in future studies. Although over forty clinical trials have been published, due to the complexity of acupuncture and the unknown mechanism, more indicators should be explored. Besides the commonly used indicators for IVF outcomes, such as CPR, BCPR, OPR, IR, LBR and MR, some further relevant indicators should also be considered, such as fertilization rate, embryo cleavage rate, good-quality embryo rate and incidence of birth defects. Also the general wellbeing of the mother and the birth of a healthy baby are important indicators.

It is hoped that these recommendations will provide useful guidelines for promoting better trial design and hence improve the evidence base for the use of acupuncture for IVF.

Author's contribution

Fan Qu contributed to conception and design of the study, acquisition of data, analysis and interpretation of data; contributed to draft the article and revise it critically for important intellectual content; and approved the version to be published. *Jue Zhou* contributed to conception and design of the study, acquisition of data, analysis and interpretation of data; contributed to draft the article and revise it critically for important intellectual content; and approved the version to be published. *Mark Bovey* contributed to acquisition of data, analysis and interpretation of data; contributed to draft the article and revise it critically for important intellectual content; and approved the version to be published. *Giovanna Franconi* contributed to analysis and interpretation of data; contributed to revise the manuscript critically for important intellectual content; and approved the version to be published. *Kelvin Chan* contributed to analysis and interpretation of data; contributed to revise the manuscript critically for important intellectual content; and approved the version to be published. *Caroline Smith* contributed to analysis and interpretation of data; contributed to revise the manuscript critically for important intellectual content; and approved the version to be published. *Dan Jiang* contributed to analysis and interpretation of data; contributed to revise the manuscript critically for important intellectual content; and approved the version to be published. *Nicola Robinson* contributed to conception and design of the study, acquisition of data, analysis and interpretation of data; contributed to draft the article and revise it critically for important intellectual content; and approved the version to be published.

Funding

This work was supported by Good Practice in Traditional Chinese Medicine Research in the Post-genomic Era (GP-TCM), a Coordination Action funded by the European Union's 7th Framework Program under the grant agreement No. 223154.

Conflict of interest

No competing financial interests exist.

References

[1] Embryology ESoHRa. Focus on reproduction. Grimbergen, Belgium: ESHRE; 2008.
[2] Cheong YC, Hung Yu, Ng E, Ledger WL. Acupuncture and assisted conception. Cochrane Database of Systematic Reviews 2008. CD006920.
[3] Manheimer E, Zhang G, Udoff L, Haramati A, Langenberg P, Berman BM, et al. Effects of acupuncture on rates of pregnancy and live birth among women undergoing in vitro fertilisation: systematic review and meta-analysis. BMJ 2008;336:545–9.
[4] Ng EH, So WS, Gao J, Wong YY, Ho PC. The role of acupuncture in the management of subfertility. Fertility and Sterility 2008;90:1–13.
[5] Sunkara SK, Coomarasamy A, Khalaf Y, El-Toukhy T. Acupuncture and in vitro fertilization: updated meta-analysis. Human Reproduction 2009;24:2047–8.
[6] Cheong Y, Nardo LG, Rutherford T, Ledger W. Acupuncture and herbal medicine in in vitro fertilisation: a review of the evidence for clinical practice. Human Fertility (Cambridge) 2010;13:3–12.
[7] El-Toukhy T, Sunkara SK, Khairy M, Dyer R, Khalaf Y, Coomarasamy A. A systematic review and meta-analysis of acupuncture in in vitro fertilisation. BJOG 2008;115:1203–13.
[8] Zheng CH, Huang GY, Zhang MM, Wang W. Effects of acupuncture on pregnancy rates in women undergoing in vitro fertilization: a systematic review and meta-analysis. Fertility and Sterility 2012;97:599–611.
[9] Myers E. Acupuncture as adjunctive therapy in assisted reproduction: remaining uncertainties. Fertility and Sterility 2006;85:1362–3.
[10] Stener-Victorin E, Waldenstrom U, Nilsson L, Wikland M, Janson PO. A prospective randomized study of electro-acupuncture versus alfentanil as anaesthesia during oocyte aspiration in in vitro fertilization. Human Reproduction 1999;14:2480–4.
[11] Huang DM, Huang GY, Lu FE, Stefan D, Andreas N, Robert G. Acupuncture for infertility: is it an effective therapy? Chinese Journal of Integrative Medicine 2011;17:386–95.
[12] Andersen D, Lossl K, Nyboe Andersen A, Furbringer J, Bach H, Simonsen J, et al. Acupuncture on the day of embryo transfer: a randomized controlled trial of 635 patients. Reproductive Biomedicine Online 2010;21:366–72.
[13] Zhang R, Feng XJ, Guan Q, Cui W, Zheng Y, Sun W, et al. Increase of success rate for women undergoing embryo transfer by transcutaneous electrical acupoint stimulation: a prospective randomized placebo-controlled study. Fertility and Sterility 2011;96:912–6.
[14] El-Toukhy T, Khalaf Y. A new study of acupuncture in IVF: pointing in the right direction. Reproductive Biomedicine Online 2010;21:278–9.
[15] Qu F, Zhou J, Ren RX. Effects of acupuncture on the outcomes of in vitro fertilization: a systematic review and meta-analysis. Journal of Alternative and Complementary Medicine 2012;18:429–39.
[16] Smith CA, Grant S, Lyttleton J, Cochrane S. Development of an acupuncture treatment protocol by consensus for women undergoing Assisted Reproductive Technology (ART) treatment. BMC Complementary and Alternative Medicine 2012;12:88.

[17] Quintero R. A randomized controlled, double-blind cross-over study evaluating acupuncture as an adjunct to IVF. Fertility and Sterility 2004;81:S11–2.
[18] Udoff L, Zhang G, Patwardhan S, Wei Z, McClamrock H. The effect of acupuncture on outcomes in in vitro fertilization (IVF). Fertility and Sterility 2006;86:S145.
[19] Li J, Cui W, Sun W. Effects of electroacupuncture on in vitro fertilization–embryo transfer (IVF–ET) of patients with polycystic ovary syndrome. Chinese Journal of Human Sexuality 2009;18:28–30.
[20] Omodei U, Piccioni G, Tombesi S, Dordoni D, Fallo L, Ghilardi F. Effect of acupuncture on rates of pregnancy among women undergoing in vitro fertilization. Fertility and Sterility 2010;94:S170.
[21] Moy I, Milad M, Kazer R, Confino E, Barnes R, Zhang J. RCT: effects of acupuncture in pregnancy rates in women undergoing assisted reproductive technologies. Fertility and Sterility 2008;90:S106.
[22] MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, et al. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. PLoS Medicine 2010;7:e1000261.
[23] Stener-Victorin E, Waldenstrom U, Wikland M, Nilsson L, Hagglund L, Lundeberg T. Electro-acupuncture as a perioperative analgesic method and its effects on implantation rate and neuropeptide Y concentrations in follicular fluid. Human Reproduction 2003;18:1454–60.
[24] Humaidan P, Stener-Victorin E. Pain relief during oocyte retrieval with a new short duration electro-acupuncture technique—an alternative to conventional analgesic methods. Human Reproduction 2004;19:1367–72.
[25] Gejervall AL, Stener-Victorin E, Moller A, Janson PO, Werner C, Bergh C. Electro-acupuncture versus conventional analgesia: a comparison of pain levels during oocyte aspiration and patients' experiences of well-being after surgery. Human Reproduction 2005;20:728–35.
[26] Sator-Katzenschlager SM, Wolfler MM, Kozek-Langenecker SA, Sator K, Sator PG, Li B, et al. Auricular electro-acupuncture as an additional perioperative analgesic method during oocyte aspiration in IVF treatment. Human Reproduction 2006;21:2114–20.
[27] Humaidan P, Brock K, Bungum L, Stener-Victorin E. Pain relief during oocyte retrieval—exploring the role of different frequencies of electro-acupuncture. Reproductive Biomedicine Online 2006;13:120–5.
[28] Paulus WE, Zhang M, Strehler E, El-Danasouri I, Sterzik K. Influence of acupuncture on the pregnancy rate in patients who undergo assisted reproduction therapy. Fertility and Sterility 2002;77:721–4.
[29] Paulus W, Zhang M, Strehler E, Seybold BKS. Placebo-controlled trial of acupuncture effects in assisted reproductive therapy. Human Reproduction 2003;18:xviii18–9.
[30] Dieterle S, Ying G, Hatzmann W, Neuer A. Effect of acupuncture on the outcome of in vitro fertilization and intracytoplasmic sperm injection: a randomized, prospective, controlled clinical study. Fertility and Sterility 2006;85:1347–51.
[31] Westergaard LG, Mao Q, Krogslund M, Sandrini S, Lenz S, Grinsted J. Acupuncture on the day of embryo transfer significantly improves the reproductive outcome in infertile women: a prospective, randomized trial. Fertility and Sterility 2006;85:1341–6.
[32] Arnoldi M, Diaferial D, Corbucci MG, Lauretisl LD. The role of acupuncture in patients at unfavourable reproductive prognosis in IVF: a prospective randomised study. Human Reproduction 2010;25:i257.
[33] Smith C, Coyle M, Norman RJ. Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer. Fertility and Sterility 2006;85:1352–8.
[34] Smith C, Coyle M, Norman RJ. Does acupuncture improve the endometrium for women undergoing an embryo transfer: a pilot randomised controlled trial. Australian Journal of Acupuncture and Chinese Medicine 2009;4:7–13.
[35] Balk J, Roberts BKJM. Electroacupuncture in infertile patients receiving in vitro fertilization and embryo transfer: a pilot study. Medical Acupuncture Online Journal 2003;14:12–4.
[36] Benson M, E-HK, Theall A, Fong K, Hogan R, Scott R. Impact of acupuncture before and after embryo transfer on the outcome of in vitro fertilization cycles: a prospective single blind randomised study. Fertility and Sterility 2006;86:1.
[37] Domar A, Kelliher MI, Wang J, Alper SM. The impact of acupuncture on IVF outcome. Fertility and Sterility 2006;86:2.
[38] Craig L, Hansen CA, Marshall K, Soules LM. Acupuncture lowers pregnancy rates when performed before and after embryo transfer. Fertility and Sterility 2007;88:S40.
[39] Cai HY, Lashi BCS, Kalayun ZLY, Feng XX, Huang YL. The effects of acupuncture and Chinese medicinal herbs on the clinical pregnancy rate of IVF women. Journal of New Traditional Chinese Medicine 2008;40:66–7.
[40] Fratterelli JL, Leondires MR, Fong K, Theall A, Locatelli S, Scott RT. Laser acupuncture before and after embryo transfer improves art delivery rates: results of a prospective randomized double-blinded placebo controlled five-armed trial involving 1000 patients. Fertility and Sterility 2008;90:S105.
[41] Domar AD, Meshay I, Kelliher J, Alper M, Powers RD. The impact of acupuncture on in vitro fertilization outcome. Fertility and Sterility 2009;91:723–6.
[42] Kong S, Ann H. Acupuncture as an adjunct to in vitro fertilization: a randomized trial. Medical Acupuncture Online Journal 2009;21:179–82.
[43] Magarelli PC, Cridennda DK, Cohen M. Changes in serum cortisol and prolactin associated with acupuncture during controlled ovarian hyperstimulation in women undergoing in vitro fertilization–embryo transfer treatment. Fertility and Sterility 2009;92:1870–9.
[44] Balk J, Catov J, Horn B, Gecsi K, Wakim A. The relationship between perceived stress, acupuncture, and pregnancy rates among IVF patients: a pilot study. Complementary Therapies in Clinical Practice 2010;16:154–7.
[45] Moy I, Milad MP, Barnes R, Confino E, Kazer RR, Zhang X. Randomized controlled trial: effects of acupuncture on pregnancy rates in women undergoing in vitro fertilization. Fertility and Sterility 2011;95:583–7.
[46] Madaschi C, Braga DP, Figueira Rde C, Iaconelli Jr A, Borges Jr E. Effect of acupuncture on assisted reproduction treatment outcomes. Acupuncture in Medicine 2010;28:180–4.
[47] Zhang M, Huang G, Lu F, Paulus W, Sterzik K. Effect of acupuncture on the pregnancy rate in embryo transfer and mechanisms: a randomized and control study. Zhongguo Zhen Jiu 2003;23:3–5.
[48] Xu GN. The combination of acupuncture and Chinese medicinal herbs in improving outcomes of IVF. Tianjin Journal of Traditional Chinese Medicine 2006;23:341–2.
[49] Cui W, Sun W, Liu LL, Wen J. Effects of electroacupuncture on the patients undergoing in vitro fertilization and embryo transplantation. Zhongguo Fuyou Baojian 2007;24:3403–5.
[50] Cui W, Liu LL, Sun W, Kong W. Effects of electroacupuncture on in vitro fertilization and embryo transplantation in the patient of infertility with different syndromes. Zhongguo Zhen Jiu 2008;28:254–6.
[51] Chen J, Liu LL, Cui W, Sun W. Effects of electroacupuncture on in vitro fertilization–embryo transfer (IVF–ET) of patients with poor ovarian response. Zhongguo Zhen Jiu 2009;29:775–9.
[52] Chen J, Zhao Y, Sun W. Effect of electroacupuncture treatment on the patients undergoing the natural cycle of frozen embryo transfer. Chinese Journal of Human Sexuality 2009;18:33–5.
[53] Ho M, Huang LC, Chang YY, Chen HY, Chang WC, Yang TC, et al. Electroacupuncture reduces uterine artery blood flow impedance in infertile women. Taiwanese Journal of Obstetrics and Gynecology 2009;48:148–51.
[54] So EW, Ng EH, Wong YY, Lau EY, Yeung WS, Ho PC. A randomized double blind comparison of real and placebo acupuncture in IVF treatment. Human Reproduction 2009;24:341–8.
[55] So EW, Ng EH, Wong YY, Yeung WS, Ho PC. Acupuncture for frozen-thawed embryo transfer cycles: a double-blind randomized controlled trial. Reproductive Biomedicine Online 2010;20:814–21.
[56] Yin XH, Qin GX, You ZL. The effects of acupuncture and Chinese medicinal herbs on the outcomes of IVF–ET. Chinese Journal of Information on Traditional Chinese Medicine 2010;17:81–2.
[57] Cui W, Li J, Sun W, Wen J. Effect of electroacupuncture on oocyte quality and pregnancy for patients with PCOS undergoing in vitro fertilization and embryo transfer vitro fertilization and embryo transfer. Zhongguo Zhen Jiu 2011;31:687–91.
[58] Lui KJ. Sample size determination for case-control studies: the influence of the joint distribution of exposure and confounder. Statistics in Medicine 1990;9:1485–93.

[59] Templeton A, Morris JK, Parslow W. Factors that affect outcome of in-vitro fertilisation treatment. Lancet 1996;348:1402–6.
[60] Lintsen AM, Eijkemans MJ, Hunault CC, Bouwmans CA, Hakkaart L, Habbema JD, et al. Predicting ongoing pregnancy chances after IVF and ICSI: a national prospective study. Human Reproduction 2007;22:2455–62.
[61] Klonoff-Cohen H, Natarajan L. The concerns during assisted reproductive technologies (CART) scale and pregnancy outcomes. Fertility and Sterility 2004;81:982–8.
[62] Li XH, Ma YG, Geng LH, Qin L, Hu H, Li SW. Baseline psychological stress and ovarian norepinephrine levels negatively affect the outcome of in vitro fertilisation. Gynecological Endocrinology 2011;27:139–43.
[63] Smeenk JM, Verhaak CM, Eugster A, van Minnen A, Zielhuis GA, Braat DD. The effect of anxiety and depression on the outcome of in vitro fertilization. Human Reproduction 2001;16:1420–3.
[64] Manheimer E. Selecting a control for in vitro fertilization and acupuncture randomized controlled trials (RCTs): how sham controls may unnecessarily complicate the RCT evidence base. Fertility and Sterility 2011;95:2456–61.
[65] Lundeberg T, Kurosawa M. Acupuncture from a physiological and clinical perspective. Autonomic Neuroscience 2010;157:1.
[66] White AR, Filshie J, Cummings TM. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. Complementary Therapies in Medicine 2001;9:237–45.
[67] Hopton AK, Macpherson H. Assessing blinding in randomised controlled trials of acupuncture: challenges and recommendations. Chinese Journal of Integrative Medicine 2011;17:173–6.
[68] Dieterle S. Invitation to an international multicenter study of the effect of acupuncture on the outcome of in vitro fertilization and intracytoplasmic sperm injection. Fertility and Sterility 2006:85.
[69] Younglai EV, Holloway AC, Foster WG. Environmental and occupational factors affecting fertility and IVF success. Human Reproduction Update 2005;11:43–57.
[70] Cai QF, Wan F, Huang R, Zhang HW. Factors predicting the cumulative outcome of IVF/ICSI treatment: a multivariable analysis of 2450 patients. Human Reproduction 2011;26:2532–40.
[71] Elizur SE, Lerner-Geva L, Levron J, Shulman A, Bider D, Dor J. Factors predicting IVF treatment outcome: a multivariate analysis of 5310 cycles. Reproductive Biomedicine Online 2005;10:645–9.
[72] Scholtes MC, Hop WC, Alberda AT, Janssen-Caspers HA, Leerentveld RA, van Os HC, et al. Factors influencing the outcome of successive IVF treatment cycles in attaining a follicular puncture. Human Reproduction 1988;3:755–9.
[73] Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Medicine 2010;7:e1000251.
[74] Kaptchuk TJ. Placebo needle for acupuncture. Lancet 1998;352:992.
[75] Yu WY, Lu AP, Han XJ. Exploration on syndrome differentiation standardization of Chinese medicine diagnosis and treatment. Zhongguo Zhong Xi Yi Jie He Za Zhi 2011;31:1419–21.
[76] Mei MF. A systematic analysis of the theory and practice of syndrome differentiation. Chinese Journal of Integrative Medicine 2011;17:803–10.