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The role of acupuncture in the management of subfertility

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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. (Fertil Steril® 2008;90:1–13. ©2008 by American Society for Reproductive Medicine.)

Key Words: Acupuncture, anovulation, male subfertility, pain relief, pregnancy rate

Acupuncture is an integral part of traditional Chinese medicine (TCM), which dates back about 3,000 years. Its use has gained increasing popularity in the Western world. In the United Kingdom, 7% of the adult population was estimated to have visited an acupuncture practitioner within their lifetime, and 1.6% had done so within the previous year (1). In the 2002 National Institutes of Health interview-survey conducted in the United States, 4.1% of the respondents reported lifetime use, and 1.1% (representing 2.13 million Americans) reported recent use of acupuncture (2).

A survey of acupuncture released by a National Institutes of Health consensus development panel indicated that promising data exist for the use of acupuncture in postoperative dental pain and treatment of adult postoperative and chemotherapy nausea and vomiting (3). The indications for acupuncture are expanding, in addition to its longstanding role in pain relief. A recent search in the Cochrane library revealed 24 reviews on the use of acupuncture in clinical conditions including pain relief, smoking cessation, stroke, Bell's palsy, depression, epilepsy, schizophrenia, irritable bowel syndrome, cocaine dependence, chronic asthma, nocturnal enuresis in children, postoperative and chemotherapy nausea and vomiting, induction of labor, and the like.

Acupuncture has recently been used in the management of subfertility problems. Numerous investigations on the use of acupuncture in assisted reproduction are booming worldwide, especially in the United Kingdom, Sweden, Austria, Germany, and Denmark (4). The World Heath Organization emphasizes the necessity of "… clinical studies as a way of validating acupuncture, improving its acceptability to modern medicine and thus extending its use as a simple, inexpensive and effective therapeutic option" (5). However, there are inherent problems in the design, sample size, and appropriate controls used in the acupuncture literature (3). Therefore, the effectiveness of acupuncture for the management of subfertility still remains elusive and controversial (6). In this regard, a systematic review on the use of acupuncture in the management of subfertility was conducted.

We searched MEDLINE (1966 to August 2006), EMBASE (1980 to August 2006), the Cochrane Menstrual Disorders and Subfertility Group trials register (August 2006), AMED

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(Allied and Complementary Medicine) (1985 to August 2006), Cumulative Index to Nursing and Allied Health Literature (1982 to August 2006), and reference lists of articles. Chinese studies were also searched from the China Academic Journal Electronic full text Database in China National Knowledge Infrastructure (1979 to August 2006), and Index to Chinese Periodical Literature (1970 to August 2006).

This review summarizes the short history of acupuncture, the physiologic basis of acupuncture in treating subfertility, and the risks of acupuncture. The evidence of the role of acupuncture in anovulatory subfertility, male subfertility, pain relief during transvaginal ultrasound-guided oocyte retrieval (TUGOR), and improving the pregnancy rate of in vitro fertilization/embryo transfer (IVF/ET) treatment was then presented.

HISTORY OF ACUPUNCTURE

Acupuncture is said to have originated in China about 3,000 years ago. During the Stone Age, acupuncture needle-like instruments such as sharpened stones and bones were used as surgical instruments for drawing blood and opening abscesses (7). A primitive system of meridian was found in the Ma Wang Dui tomb in China in 198 BCE (8), and a more organized system of acupuncture was first documented in *The Yellow Emperor's Classic of Internal Medicine (Huang Dei Nei Ching)* by 100 BCE (8, 9). TCM was greatly influenced by Chinese philosophic systems such as Confucianism and Taoism. The concepts of Channels (meridians) in which the Qi (the vital energy) flows through it to regulate the harmony of the body status were well established at that time (7). The basis of modern acupuncture was published in *The Great Compendium of Acupuncture and Moxibustion* during the Ming Dynasty (1368–1644). A full set of 365 acupoints was described in relation to the corresponsive channels (8, 10) (Fig. 1).

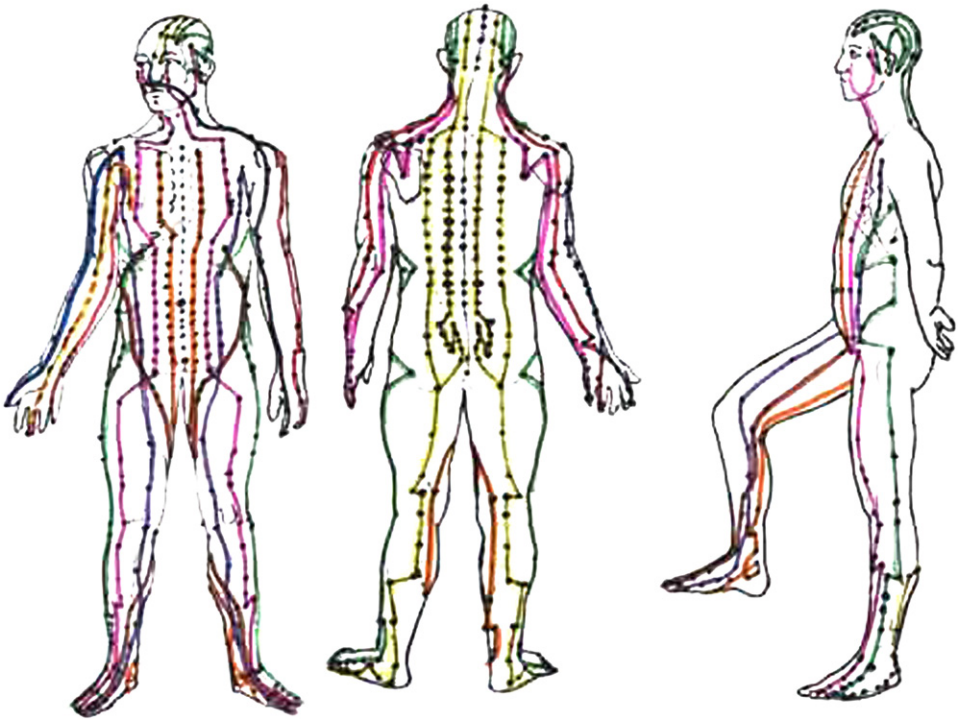
In the sixth century, acupuncture spread to neighboring countries like Japan and Korea (8). The term acupuncture was coined from the Latin word *acus* (needle) and *punctura* (pricking) by Jesuit missionaries (11). In the West, France was the first country to adopt acupuncture as a therapeutic modality. It became more popular in Western countries after James Reston, a member of the US press corps, shared his experience in treating the postoperative complications of an appendectomy with acupuncture and described more details in the uses of acupuncture in the *New York Times* in 1972 (12, 13).

PHYSIOLOGIC BASIS OF ACUPUNCTURE IN TREATING SUBFERTILITY

With recent advancements in modern Western scientific principles, the underlying physiologic mechanisms of acupuncture became better understood (14). 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.

FIGURE 1

Meridians and acupoints in acupuncture.



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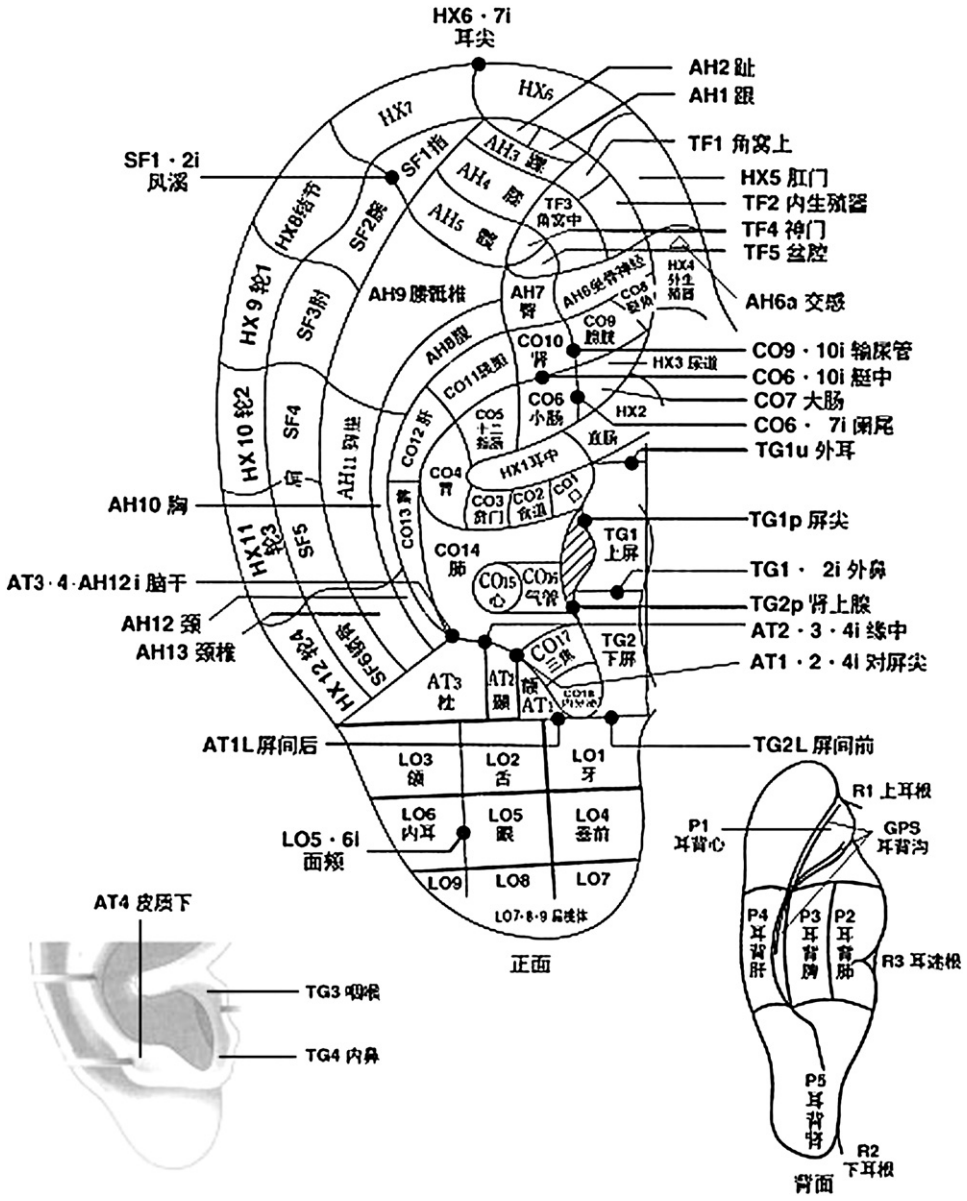
Acupuncture may regulate the function of the hypothalamic–pituitary–ovarian axis by changing the concentration of central opioids (15–21). Acupuncture might also change the charge and potential of neurons and the concentrations of electrolytes and neuropeptides, such as β-endorphin (22, 23). The electric stimulation of acupoints is considered to increase the analgesic effect of acupuncutre (24); electric stimulation involves the biologic activation of endogenous pain inhibiting systems by releasing endogenous opioids and oxytocin, which seem to be essential to the induction of functional changes in different organ systems (25, 26). Both low- and high-frequency stimulations have been found to induce analgesia, but different types of endorphins are released depending on the stimulation pattern (27, 28). Moreover, cumulative analgesic effects may be achieved by longer electric stimulation periods (29).

In addition to conventional body acupuncture, auricular acupuncture is commonly used in IVF patients to improve pregnancy outcomes and to relieve pain during oocyte retrieval. Nevertheless, the underlying mechanism of body acupuncture is still elusive (Fig. 2). Most studies conducted on it suggest that body acupuncture may mediate effects through the activation of descending inhibitory pain control systems and the propriospinal heterosegmental antinociceptive system, which may lead to the slow regulation of pain-induced

FIGURE 2

Auricular acupuncture.



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changes in signal transduction in the spinal cord (30–33). Body acupuncture may also induce the release of various neurotransmitters such as β-endorphin, serotonin, encephalin, dynorphins, and substance P (28, 29, 34) in the central nervous system of both animals and humans. These may result in a similar regulation pathway of acupuncture.

Acupuncture has been reported to affect uterine blood flow. This may improve the endometrial environment for embryo implantation. Stener-Victorin et al. (35) demonstrated that the mean pulsatility index (PI) of uterine vessels was significantly reduced shortly after electroacupuncture given twice a week for eight times to subfertile women with PI $\geq$3.0, when compared with the baseline values. Moreover, acupuncture over the acupoint LI4 was reported to inhibit uterine motility (20). High-frequency uterine contractions on the day of embryo transfer may reduce the pregnancy rate of IVF treatment, possibly by expelling embryos out of the uterine cavity (36).

Many subfertile patients, especially those undergoing IVF treatment, are under great stress. In contrast, stress can reduce fertility (37). In fact, this study (38) found that the psychosocial intervention before the IVF treatment was effective in the reduction of anxiety of these patients, and that there was a nonsignificant trend of a higher pregnancy rate in the intervention group. Acupuncture has both physiologic and psychologic effects, and may provide an excellent alternative for stress reduction in women undergoing subfertility treatment (14, 39–41). Feelings of relaxation were reported by as many as 86% of patients following acupuncture (42).

RISKS OF ACUPUNCTURE

Acupuncture is safe, but also has risks. A systematic review (42) of nine surveys revealed that the common adverse effects of acupuncture were needle pain (1%–45%) from treatments, tiredness (2%–41%), and bleeding (0.03%–38%). Feelings of faintness and syncope were uncommon, with an incidence of 0%–0.3%. Several large prospective studies (43, 44) have also shown that these mild, transient adverse effects occur in about 7% to 11% of all cases.

Serious adverse events, in particular, trauma to internal organs leading to pneumothorax or cardiac tamponade and infections (e.g., hepatitis C or HIV), are extreme rarities, provided that acupuncture is carried out by well-trained practitioners (45) and that the acupuncture needles are disposable.

ROLE OF ACUPUNCTURE IN ANOVULATORY SUBFERTILITY

Chen and Yu (17) reported that 6 of 13 anovulatory cycles responded to acupuncture treatment. Acupuncture has been used to replace human chorionic gonadotrophin as a trigger of ovulation in ovulation induction (46).

Stener-Victorin et al. (47) showed an improvement of ovulation after electroacupuncture in 24 anovulatory women with polycystic ovary syndrome. The percentage of ovulatory cycles increased from 15% 3 months before treatment to 66% up to 3 months after acupuncture. The same group demonstrated that in animal studies, acupuncture modulated sympathetic markers as well as ovarian blood flow as a reflex response via the ovarian sympathetic nerves (48, 49).

However, there are still no randomized studies on the use of acupuncture in the treatment of anovulation.

ROLE OF ACUPUNCTURE IN MALE SUBFERTILITY

Male factors may be found in 30% to 50% of subfertility, and are the dominant causes of subfertility in one-third of subfertile couples (50). Very few effective treatments are available for those with idiopathic causes (51). Oldereid et al. (52) reported that about 20% of men involved in subfertility investigations seek help from alternative medicine including acupuncture.

Siterman et al. (53) assessed the effect of acupuncture on 16 subfertile men with abnormal sperm parameters. Acupuncture was administered for 25 minutes per session, twice a week, for 5 weeks. Semen analysis done 1 month after the acupuncture session demonstrated a significant improvement in total functional sperm fraction, percentage of viability, total motile sperm per ejaculation, and the integrity of the axonema with an increased fertility index, when compared with those before acupuncture.

Siterman et al. (54) also studied acupuncture in patients with a very low sperm count. The treatment group consisted of 5 oligozoospermic and 15 azoospermic men diagnosed by both light microscope and scanning electron microscope. The study also recruited a match control group. One month after the acupuncture treatment, semen analysis revealed a significant increase in sperm count per ejaculation in 10 (67%) of the 15 azoospermic patients. In 3 of the 15, >20 sperm cells were found by scanning electron microscope, and in the remaining patients, the sperm count increased significantly from zero to an average of 1.5×10^6 ($P \leq .01$), which could even be identified by light microscope. In this study, two underwent intracytoplasmic sperm injection (ICSI) following the acupuncture treatment and both achieved pregnancies.

Zhang et al. (55) applied acupuncture to 22 men who had idiopathic semen abnormalities and who had at least two unsuccessful cycles of ICSI treatment. Female factors were excluded. The subjects were treated twice a week for 8 weeks, with each session lasting for 25 minutes with acupoints selected for individuals. The study found significant increases 3 months after acupuncture in the semen parameter of quick progressive motility (from 11.0%–18.3%, $P<.01$) and normal-form sperm ratio (from 16.2%–21.1%, $P<.01$). The partners underwent ICSI treatment again, and there was a significant improvement in fertilization rate when compared with that of the previous cycle (66.2% vs. 41.4%, $P<.01$).

Pei et al. (56) observed an improvement of sperm quality after acupuncture, specifically in the ultrastructural integrity of spermatozoa as shown by transmission electron microscopy, despite the inability to identify specific sperm pathologies that could be particularly sensitive to this therapy.

The effect of acupuncture/electroacupuncture combined with moxibustion in patients with abnormal semen analysis was also investigated. Gurfinkel et al. (57) performed a randomized blinded controlled study involving 19 patients with abnormal semen parameters shown in two semen samples. Those with a sperm concentration of $<5 \times 10^6$/mL or the presence of leukospermia were excluded. Each session of treatment consisted of a 25-minute acupuncture followed by a 20-minute moxibustion. Each session was done twice a week for 10 weeks. In the control group, acupuncture and moxibustion were applied at "nontherapeutic indifferent points." This study revealed a significant increase in the normal-form sperm ratio.

Gerhard et al. (58) reported the effect of a 10-day course of acupuncture combined with moxibustion after the seventh treatment. Improvement in sperm motility was mild but significant from the 1st to the 12th week after treatment. Forward progressive motility increased from 21% to 26%, and total motility increased from 42% to 50%. Serum concentrations of FSH, LH, and testosterone were found to have increased significantly, and the increase in serum testosterone was correlated with improvement of sperm motility.

In addition to the traditional treatments of acupuncture and moxibustion, needling picking therapy, as well as a combined treatment of acupuncture, Chinese material medica, and acupoint injection, were also proven to improve semen quality, hormone profile, and pregnancy rate (59, 60). However, most of the studies are uncontrolled case reports or case series in which the sample sizes were small, and the selection of acupoints was not standardized. In this light, well-designed studies are needed to provide reliable and valid scientific evidence of the possible positive effect of acupuncture on semen parameters and sperm function tests.

A possible benefit of acupuncture in men with erectile dysfunction (ED) has been investigated. In a case report of 16 patients with ED, 15% reported an improvement in the quality of erection, and 31% reported an increase in intercourse frequency after electroacupuncture (61). Nevertheless, there are no definite conclusions that can be drawn from this pilot study; hence, a controlled and blinded study that will include more patients is needed before any definitive conclusion is reached.

In a randomized placebo-controlled study, 3 Hz direct current electroacupuncture was used to treat patients with nonorganic ED (62). The treatment lasted for 20 minutes, twice a week for 6 weeks. The success rate was 60% in the acupuncture group, 75% in the hypnotic suggestion group, 43% in the needle placebo group, and 47% in the oral placebo group with vitamin pills. The difference was not significant.

Engelhardt et al. (63) reported another randomized placebo-controlled trial among 21 patients with psychogenic ED. Acupoints that are conventionally used to treat headache were applied in the control group. A total of 5 to 20 acupuncture treatments were administered with 20 minutes per session, once or twice per week. After 4 to 10 treatments, 10 nonresponders in the control group were crossed over to the treatment group. In the treatment group, 68% achieved erections sufficient for intercourse, and 21% found intercourse possible with an additional therapy. The proportion of patients with improvement was significantly higher than that in the control group. There was also a significant increase in the International Index of Erectile Function score in the domain of erectile function, intercourse satisfaction, and overall satisfaction after the treatment.

ROLE OF ACUPUNCTURE IN PAIN RELIEF DURING TUGOR

IVF is a well-established treatment for various causes of subfertility. It involves ovarian stimulation, which induces the development of multiple follicles, egg collection through the transvaginal route, and embryo transfer after fertilization. During transvaginal ultrasound-guided oocyte retrieval, the needle passes through the vaginal wall to puncture the follicles in the ovary. The procedures are generally short, lasting about 20 to 30 minutes, but can still be painful without adequate anesthesia or analgesia.

Conscious sedation is the most widely used method for the pain relief during TUGOR (64). Randomized studies on the effects of acupuncture on the pain level during TUGOR are summarized in Table 1. Stener-Victorin et al. (65) were the first to investigate the pain-relieving effect of acupuncture during TUGOR and randomized 150 patients to receive either acupuncture or conventional analgesia in addition to the paracervical block given to all patients. The study showed that acupuncture had comparable analgesic effect as conventional analgesia. Similar results on the analgesic effect of acupuncture were subsequently reported by the same group (48).

Humaidan and Stener-Victorin (66) applied a new short duration of acupuncture technique. Two hundred patients were randomly assigned into either the acupuncture or conventional analgesia group. A significantly higher pain level was noted in the acupuncture group than in the conventional analgesia group. The conventional analgesia group received premedication, whereas the acupuncture group did not receive any premedication.

Gejervall et al. (24) subjected 160 patients to electroacupuncture or conventional analgesia. Electroacupuncture was administered 30 to 45 minutes before TUGOR, and was stopped immediately after the procedure. Premedication was used in the conventional analgesia group alone. The use of acupoints with manual and high- or low-frequency electric stimulation was aimed to increase relaxation and activate the gate control system to achieve the analgesic effect (65, 48). The study demonstrated that the pain levels were significantly higher in the acupuncture group than in the conventional analgesia group.

Sator-Katzenschlager et al. (67) conducted a randomized double blind study of 94 IVF patients comparing the pain-relieving effect between auricular acupuncture with or without electric stimulation and the control groups without needles and without electric stimulation. Interestingly, the study showed that auricular electroacupuncture was significantly

TABLE 1

Summary of randomized studies of the effects of acupuncture on the pain level during oocyte retrieval.

Studies	Blindness	Mean pain during oocyte retrieval		Maximum pain during oocyte retrieval	
		Acupuncture	Control	Acupuncture	Control
Stener-Victorin et al. (65)	No	30.1 ± 19.4	26.6 ± 22.0	48.6 ± 23.1	43.6 ± 28.5
Stener-Victorin et al. (48)	No	29.6 ± 17.7	26.4 ± 18.3	45.9 ± 23.6	44.8 ± 23.8
Humaidan and Stener-Victorin (66)	No	2.6 ± 1.8*	1.8 ± 1.7*	4.6 ± 2.5*	3.2 ± 2.3*
Gejervall et al. (24)	No	48.5 ± 26.8*	29.8 ± 23.4*	—	—
Sator-Katzenschlager et al. (67)	Double blind	2.9 ± 1.5*	5.9 ± 1.6*	6.7*	10.0*

Note: Data given as mean ± standard deviation.
* Statistically significant difference.

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superior in reducing the pain levels during TUGOR to both auricular acupuncture alone and the control group.

Two systematic reviews (68, 69) evaluated the analgesic effect of acupuncture during TUGOR in three studies only (65, 66). There was a significant difference in pain score between the two groups in these three trials, favoring conventional analgesia with paracervical block over acupuncture. The reviews concluded that there is no consensus on the use of analgesic method in TUGOR. Acupuncture can be recommended as one of the effective analgesic methods for patients who are unable to comply with the conventional analgesia because of adverse effects during and after TUGOR.

ROLE OF ACUPUNCTURE IN IMPROVING IVF OUTCOMES

Studies on the effect of acupuncture on IVF outcomes are summarized in Table 2. In these studies that evaluated the pain relief effect of acupuncture during TUGOR, acupuncture was administered on the day of TUGOR only. Except for the study by Sator-Katzenschlager et al. (68), other studies (24, 65, 66) failed to demonstrate any significant difference in the pregnancy rate between the acupuncture group and the control group receiving conscious sedation for pain relief. Live birth rate was significantly higher in the acupuncture group than in the control group (65).

Paulas et al. (70) were the first to study the effect of acupuncture that was administered on the day of ET in 160 patients selected randomly to the acupuncture and control groups. The acupuncture group received body acupuncture with manual stimulation and auricular acupuncture, whereas the control group received no acupuncture. The acupoints were selected according to TCM theories. Acupuncture was performed 25 minutes before and after ET, together with auricular acupuncture. The details of the acupoints can be found in Table 3. Pregnancy rate was significantly higher in the acupuncture group than in the control group (42.5% vs. 26.3%; $P=.03$). There was no significant difference in uterine PI before and after ET. However, this is not a double-blind study and the power is only 0.512.

The same group (71) presented in an abstract another randomized study using placebo needling in the controls. The acupoints used were the same as in the previous study (70), but auricular acupuncture was no longer used. In that trial, the pregnancy rates of the acupuncture and placebo groups were comparable (43.0% vs. 37.0%; $P=.39$). The authors considered that the acupressure induced by the placebo needling in the placebo group resulted in a higher pregnancy rate when compared with the previous control group without any acupuncture treatment.

Last year, three more randomized studies (72–74) on the effect of acupuncture on the IVF outcomes were published. Dieterle et al. (72) randomized 225 infertile patients into verum and sham acupuncture groups with different sets of acupoints. The study used an acupuncture protocol that was different from the one used in the study of Paulus et al. (70) (Table 3). Two sessions of acupuncture were given to patients, immediately after ET and 3 days later, together with auricular acupuncture at the same time. The study showed that the clinical and ongoing pregnancy rates of the verum acupuncture group were significantly higher than those of the control group (33.6% vs. 15.6% and 28.4% vs. 13.8%; $P<.01$). However, this was also not a double-blind study.

Smith et al. (73) performed a single-blind trial using retractable needles over placebo acupoints among 228 infertile patients. In addition to the two real or placebo acupuncture treatments immediately before and after ET, one additional session was given to patients on day 9 of ovarian stimulation. The acupuncture protocol before and after ET was similar to that of Paulus et al. (70) with some minor modifications, but the details of acupuncture on day 9 of ovarian stimulation were not given. The pregnancy rates of the acupuncture and control groups were similar (30.9% vs. 22.0%, not statistically significant). In this study, the acupuncture settings in

TABLE 2

Summary of randomized studies of the effect of acupuncture on IVF outcomes.

(a) Acupuncture given on the day of oocyte retrieval only

		Pregnancy rate		Ongoing pregnancy rate		Live birth rate		Miscarriage rate	
Studies	**Blindness**	**Acupuncture**	**Control**	**Acupuncture**	**Control**	**Acupuncture**	**Control**	**Acupuncture**	**Control**
Stener-Victorin et al. (65)	No	37.3% (28/75)	25.3% (19/75)	—	—	33.3%* (25/75)	17.3%* (13/75)	10.7% (3/28)	31.6% (6/19)
Stener-Victorin et al. (48)	No	31.6% (43/141)	35.5% (49/145)	26.2% (37/141)	29.7% (43/145)	—	—	14.0% (6/43)	12.2% (6/49)
Humaidan and Stener-Victorin (66)	No	46.0% (46/100)	50.0% (50/100)	—	—	—	—	—	—
Gejervall et al. (24)	No	28.8% (23/80)	32.5% (26/80)	—	—	—	—	—	—
Sator-Katzenschlager et al. (67)	Double blind	46.9%* (30/64)	23.3%* (7/30)	—	—	—	—	—	—

(b) Acupuncture given on the day of embryo transfer

Paulus et al. (70)	No	42.5%* (34/80)	26.3%* (21/80)	—	—	—	—	—	—
Paulus et al. (71)	Not mentioned	43.0% (43/100)	37.0% (37/100)	—	—	—	—	—	—
Dieterle et al. (72)	Not mentioned	33.6%* (39/116)	15.6%* (17/109)	28.4%* (33/116)	13.8%* (15/109)	—	—	15.4% (6/39)	11.8% (2/17)
Smith et al. (73)	Single blinded	30.9% (34/110)	22.9% (27/118)	28.2% (31/110)	18.6% (22/118)	—	—	—	—
Westergaard et al. (74)	No	35.0%* (70/200)	21.0%* (21/100)	29.0% (58/200)	19.0% (19/100)	—	—	25.7% (18/70)	23.8% (5/21)

* Statistically significant difference.

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TABLE 3

Summary of acupoints used in different randomized studies.

(a) Acupuncture given on the day of oocyte retrieval

Studies	Acupoints
Stener-Victorin et al. (65, 48)	LI4 (Hegu) TE 5 (Waiguan) ST29 (Guilai) GV20 (Baihui) ST36 (Zusanli)
Humaidan and Stener-Victorin (66)	Two points in lower abdomen LI4 (Hegu) GV20 (Baihui) SP6 (Sanyinjiao)
Gejervall et al. (24)	KI11 (Henggu) LI10 (Shousanli) LI4 (Hegu) ST36 (Zusanli) GV20 (Baihui) ST29 (Guilai)
Sator-Katzenschlager et al. (67)	29 (Cushion) 55 (Shenmen) 57 (Uterus)

(b) Acupuncture given on the day of embryo transfer (ET)

Studies	Acupoints before ET	Acupoints after ET		Additional acupuncture	
Paulus et al. (70, 71)	PC6 (Neiguan) SP8 (Diji) LR3 (Taichong) GV20 (Baihui) ST29 (Guilai)	ST36 (Zusanli) SP6 (Sanyinjiao) SP10 (Xuehai) LI4 (Hegu)		Auricular acupuncture	
Dieterle et al. (72)	Nil	*Group1*: RN4 (Guanyuan) RN6 (Qihai) ST29 (Guilai)	*Group2:* SJ9 (Sidu) SJ12 (Xiaoluo) GB31 (Fengshi)	Another session 3 days after ET and auricular acupuncture *Group1*: LI4 (Hegu) ST36 (Zusanli) SP6 (Sanyinjiao)	 *Group2:* SJ9 (Sidu) SJ12 (Xiaoluo) GB31 (Fengshi)

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TABLE 3

Continued.

(b) Acupuncture given on the day of embryo transfer (ET)

Studies	Acupoints before ET	Acupoints after ET	Additional acupuncture
		PC6 (Neiguan) SP10 (Xuehai) SP8 (Diji) GB32 (Zhongdu) GB34 (Yanglingqua)	KI3 (Taixi) LR3 (Taichong) GB32 (Zhongdu) GB34 (Yanglingqua)
Smith et al. (73)	PC6 (Neiguan) SP8 (Diji) ST29 (Guilai)	Same as Paulus et al. (70, 71)	One additional session was performed on day 9 of ovarian stimulation (details not given).
Westergaard et al. (74)	Paulus et al. (70, 71)	Paulus et al. (70, 71)	Third session 2 days after ET CV3 (Zhongji) GV20 (Baihui) ST29 (Guilai) ST36 (Zusanli) SP6 (Sanyinjiao) SP10 (Xuehai) LI4 (Hegu)

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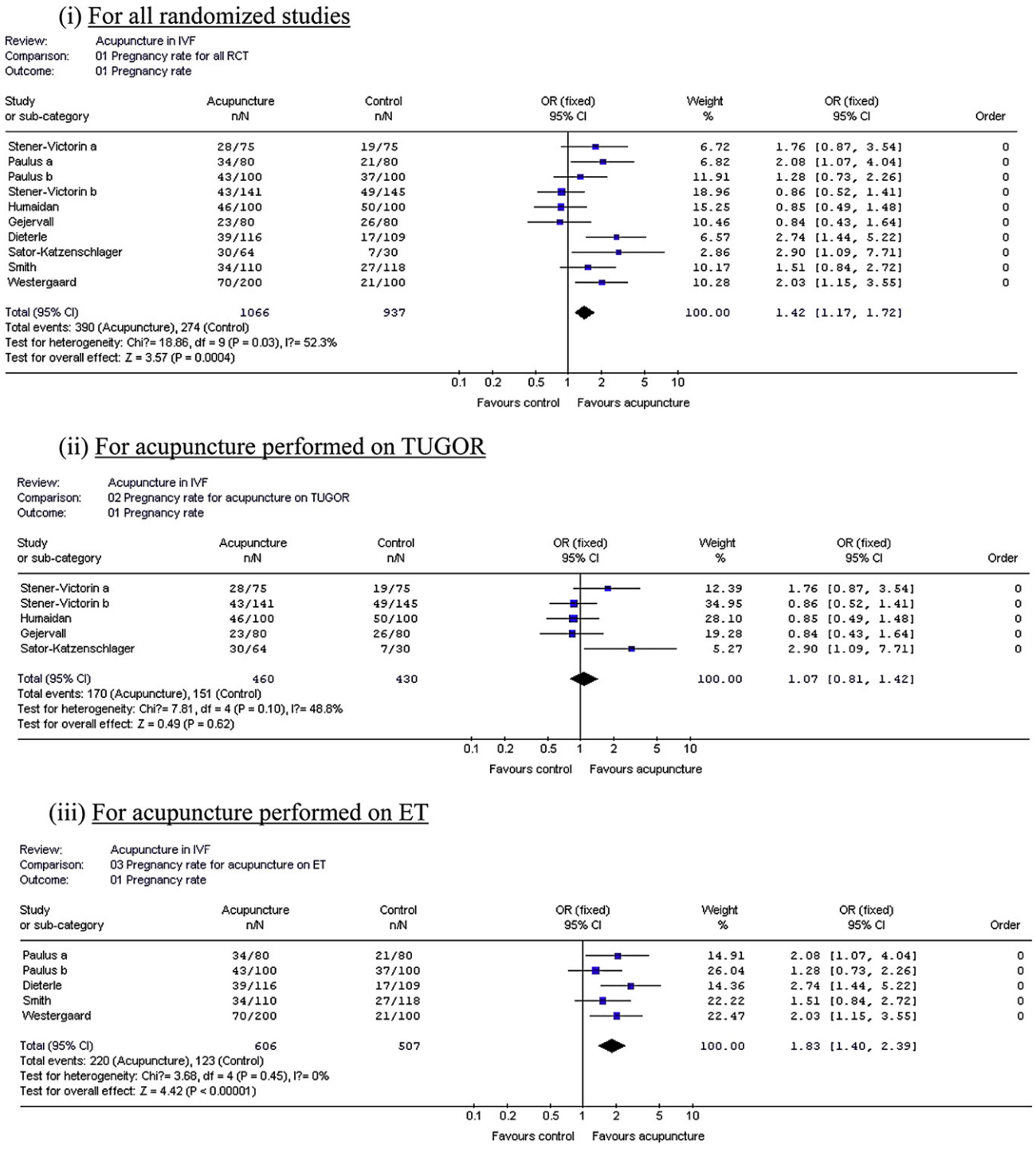
two groups were not identical. For example, the gauge of needles, the method of manual stimulation, and the locations of acupoints were different between the verum and the placebo groups. Acupuncture was performed by two different acupuncturists.

Westergaard et al. (74) randomized 300 patients into three groups: group I receiving acupuncture shortly before and after ET; group II receiving acupuncture on the ET day and again 2 days later, and group III as controls without acupuncture. The acupoints used were the same as those of Paulus

FIGURE 3

Meta-analysis of randomized studies of acupuncture in IVF treatment.



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et al. (70). Similar acupoints were used repeatedly 2 days after ET. The pregnancy rate of group I was significantly higher than that of group III (39% vs. 26.0%; P=.04). As the pregnancy rates of group I and group II were comparable, it seemed that there was no additional benefit of offering acupuncture 2 days after ET in Group II. However, placebo or sham acupuncture was not used in such a study, and the patients were not blinded to the treatment assignment. In addition, the acupuncture treatment was administered by nine nurse practitioners, and thus introducing great variation in the administration of acupuncture.

There are other retrospective or crossover studies published in the abstract format only. In three retrospective studies (75–77) on the IVF outcome following acupuncture treatment, the investigators found a significant increase in pregnancy rate after acupuncture treatment (76, 77) and suggested that patients with good prognosis would benefit from acupuncture treatment. Quintero et al. (78) conducted a randomized double-blind but crossover study using a needle-like device as the sham acupuncture. In such study, only 17 patients were recruited, and 7 of them completed both arms of the study. There was no difference in pregnancy rate between the two groups, but the amount of gonadotropins used was significantly reduced following acupuncture treatment.

A meta-analysis of the 10 randomized studies (Fig. 3) revealed a significant improvement in the pregnancy rate for acupuncture treatment (odds ratio [OR] 1.42, 95% confidence interval [CI] 1.17–1.72). Subgroup analysis based on the day of acupuncture detected a significant improvement in pregnancy rate for acupuncture treatment when acupuncture was administered on the day of ET (OR 1.83, 95% CI 1.40–2.39). However, there was no improvement in pregnancy rate when acupuncture was given on the day of TUGOR only (OR 1.07, 95% CI 0.81–1.42). These data suggest that acupuncture should be offered to patients on the day of ET if the aim is to improve the pregnancy rate of IVF treatment.

There are also variations in the acupoints used among the above randomized studies (Table 3), although it is claimed the selection of these acupoints is based on TCM principles. As the underlying mechanisms for improving the pregnancy rate of IVF treatment following acupuncture remain elusive, it is impossible to conclude which acupoints or combinations of acupoints are essential for the acupuncture treatment.

CONCLUSION

Acupuncture may restore ovulation among patients with polycystic ovary syndrome, but there is not a sufficient number of randomized studies to validate this. Evidence supporting the role of acupuncture in male subfertility is also insufficient, because most of the studies are uncontrolled case reports or case series in which the sample sizes were small. Acupuncture can be considered as an alternative for pain relief during TUGOR in patients who cannot tolerate the conventional conscious sedation because of its associated adverse effects. The pregnancy rate of IVF treatment is significantly increased when acupuncture is administered on the day of ET. Flaws in the study design of the studies reviewed point out the difficulties encountered in evaluating the efficacy of acupuncture in subfertility.

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