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ORIGINAL ARTICLE

Male fertilit

The effectiveness and safety of acupuncture for poor semen quality in infertile males: a systematic review and meta-analysis

Ui Min Jerng^{1*}, Jun-Young Jo^{2,3,*}, Seunghoon Lee⁴, Jin-Moo Lee², Ohmin Kwon⁵

The aim of this review is to evaluate the effectiveness and safety of acupuncture for poor semen quality in infertile men. We searched for relevant trials registered up to May 2013 in 14 databases. We selected randomized controlled trials (RCTs) that compared acupuncture, with or without additional treatment, against placebo, sham, no treatment, or the same additional treatment. Two reviewers independently performed the study selection, data extraction, risk of bias and reporting quality appraisal. Risk of bias and reporting quality were appraised by the Cochrane risk of bias tool, the consolidated standards of reporting trials and Standards for Reporting Interventions in Clinical Trials of Acupuncture. The outcomes were sperm motility, sperm concentration, pregnancy rate, and adverse events. Pregnancy was defined as a positive pregnancy test. Four RCTs met the eligibility criteria. Acupuncture increased the percentage of sperm with rapid progression (mean difference - 6.35, 95% confidence interval (CI): 4.38–8.32, P < 0.00001) and sperm concentration (mean difference - 6.42, 95% CI: 4.91–7.92, P < 0.00001), but these two outcomes were substantially heterogeneous among the studies (P = 72% and 58%, respectively). No differences in pregnancy rate were found between acupuncture and control groups (odds ratio 1.60, 95% CI: 0.70–3.69, P = 0.27, P = 0%). No participants experienced adverse events. The current evidence showing that acupuncture might improve poor semen quality is insufficient because of the small number of studies, inadequacy of procedures and/or insufficient information for semen analysis, high levels of heterogeneity, high risk of bias, and poor quality of reporting. Further large, well-designed RCTs are required.

Asian Journal of Andrology (2014) 16, 884-891; doi: 10.4103/1008-682X.129130; published online: 27 June 2014

Keywords: acupuncture; asthenozoospermia; male infertility; oligozoospermia; sperm quality

INTRODUCTION

Parenthood is one of the most prevalent desires among humans. However, many couples suffer from infertility despite regular unprotected intercourse. Male factors account for about half of all causes of infertility.¹⁻³ Poor semen quality is the main male factor.¹⁻³ Idiopathic oligoasthenoteratozoospermia is the most common medical diagnosis of abnormal semen quality.²

Various empirical drugs have been used to improve abnormal semen quality in infertile men. Androgens, gonadotropins, and corticosteroids are not effective, but follicle-stimulating hormone might be effective in some patients.⁴ Systematic reviews have shown that antioxidants such as vitamin E and L-carnitine could be effective for improving semen quality and the pregnancy rate of couples.^{5,6}

Acupuncture also has been used to improve semen quality. A Norwegian study reported that approximately 20% of infertile men preferred an alternative treatment like acupuncture. However, the therapeutic effects of acupuncture on poor semen quality remain uncertain. Therefore, systematic review on the effects of acupuncture on poor semen quality is required.

This systematic review evaluated current evidence from available randomized controlled trials (RCTs) on the effectiveness and safety of acupuncture with regard to semen parameters and the pregnancy rate of couples with male factor infertility.

MATERIALS AND METHODS

The protocol describing the methods for this review was registered prospectively (CRD 42013004930; http://www.crd.york.ac.uk/PROSPERO).

Literature search

The following digital databases were searched for relevant studies in May 2013: the Cochrane Central Register of Controlled Trials (up to the Cochrane Library Issue 5, 2013), Medline (from 1946 to May 15 2013), Embase (from 1974 to May 15 2013), the Cumulative Index to Nursing Allied Health Literature, the Allied Complementary Medicine Database, eight Korean databases (KoreaMed, Korean Medical Database, Korean Studies Information Service System, Korea Education and Research Information Service, National Discovery for Science Leaders, Database Periodical Information Academic, Korea

¹Class of Oncology, ²Class of Gynecology, Department of Clinical Korean Medicine, Kyung Hee University Graduate School, Seoul, Korea; ³Conmaul Hospital, Seoul, Korea; ⁴Class of Acupuncture and Moxibustion, Department of Clinical Korean Medicine, Kyung Hee University Graduate School, Seoul, Korea; ⁵Medical History and Literature Group. Korea Institute of Oriental Medicine, Daejeon, Korea

^{*}These authors contributed equally to this work.

National Assembly Digital Library, and Oriental Medicine Advanced Searching Integrated System) and one Chinese database (China National Knowledge Infrastructure). We established search terms related to three areas (male infertility, semen, and acupuncture). The detailed search strategies used for each database are shown in **Supplement** 1. Reference texts (e.g. andrology/gynecology textbooks, integrative/complementary and alternative medicine textbooks, clinical guidelines, and other review articles) in the relevant publications were manually checked to find missing eligible trials.

Study selection and data extraction

This study scrutinized all RCTs evaluating the effects of acupuncture on semen parameters in infertile males. In randomized cross-over trials, we only analyzed the data measured before cross-over to remove the carryover effect. Non-randomized trials, quasi-experimental studies, and all observational studies were excluded. We selected trials using manual acupuncture and/or electrically stimulated acupuncture in which needles were inserted in classical acupuncture points. We excluded trials of other treatments using acupuncture points without needle insertion, such as moxibustion, acupressure, laser acupuncture, and electrical acupuncture point stimulation. The control group could have received placebo/sham acupuncture, conventional therapy, or no treatment. Trials that evaluated the effect of acupuncture combined with other treatments, in comparison with the same other treatments alone, were also included. We included these studies because the additional therapeutic effects of acupuncture could be estimated in these trials. Trials without a clear description of at least one of the semen parameters, including semen ejaculate volume, sperm concentration, sperm motility, or sperm morphology, were excluded.

The titles and abstracts retrieved from the electronic databases or relevant publications were examined closely, and the whole content of articles that were considered to meet the eligibility criteria was analyzed. We selected relevant studies only after the close examination of full manuscripts.

Two independent reviewers (UMJ and JYJ) performed a literature search, study selection, and data extraction using a standard form. All disagreements were resolved by consensus between the two reviewers or arbitration by another reviewer (SL). If the data in an article were insufficient or ambiguous, one reviewer (UMJ) contacted the corresponding author by E-mail to request additional information.

Data assessment and synthesis

Two reviewers (UMJ and JYJ) independently assessed the risk of bias and the reporting quality of the included studies. The risk of bias was evaluated using the "risk of bias" tool developed by the Cochrane collaboration. The Consolidated Standards of Reporting Trials (CONSORT), and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA)^{8,9} were used to evaluate reporting quality.

Statistical analyses were performed with RevMan 5.0 (Cochrane collaboration, Oxford, UK). We calculated odds ratios (ORs) for the dichotomous variable (number of pregnancies), and mean differences for the continuous variables (sperm motility and sperm concentration) using a random-effects model with 95% confidence intervals (CI). We utilized a random-effects model because of the clinical and/or methodological heterogeneity of the included trials. Based on the Cochrane guidelines, Cochrane's Q test results with P < 0.01 and $P \ge 75\%$ indicated considerable heterogeneity. If the considerable heterogeneity could be explained by differences in study features, we conducted subgroup analysis.

RESULTS

The searches yielded 801 articles, 700 of which were excluded based on the title and abstract. Ninety-seven studies were excluded after full contents of these studies had been analyzed or the corresponding authors had been contacted: 75 were non-RCTs, three were review articles, 17 used inadequate interventions, one lacked semen analysis¹⁰ and the other¹¹ was the same trial in a study¹² that had already been included. Four eligible RCTs¹²⁻¹⁵ including a total of 500 male participants were chosen (**Figure 1**). The characteristics of the included studies are presented in **Table 1**.

Population

The trials were performed in two different countries; one was conducted in Germany, ¹³ and the others were conducted in China. ^{12,14,15} Two trials ^{14,15} recruited patients with oligozoospermia or asthenozoospermia that had been diagnosed according to the World Health Organization (WHO) criteria. One trial ¹² recruited only patients with asthenozoospermia that had been diagnosed according to the WHO criteria. The remaining trial ¹³ reported that severe oligoasthenozoospermia patients were recruited, but in actuality, only oligozoospermia patients were recruited (<10⁶ sperm per ml). No studies recruited teratozoospermia patients. Three trials ^{12,14,15} excluded men who could not have children due to female factors. Three trials ^{13–15} also excluded men who were infertile due to organic diseases.

Interventions

One trial¹³ used one manual acupuncture treatment group and one control group, which received a nonpenetrating placebo acupuncture, to evaluate the efficacy of acupuncture. The others^{12,14,15} established three treatment groups: the first group received acupuncture therapy combined with an oral herb mixture, the second group were only administered the herb mixture, and the third group received the acupuncture therapy alone. We considered the first group to be the treatment group and the second group to be the control group in these trials^{12,14,15} to evaluate the additional effects of acupuncture.

The selected acupuncture points, administrative procedures, and treatment regimens were highly variable among the studies. Only two trials^{14,15} used the same acupuncture points and treatment regimens, and they used similar procedures (except for acupuncture style). All of the trials induced *De qi* sensation, which is a type of sensation following acupuncture placement and manipulation. ¹⁶ The duration of therapy ranged from 27 days^{14,15} to 3 months. ¹² Each acupuncture regimen is summarized in **Table 2**.

Outcomes

Semen samples were evaluated according to the WHO standard in all the trials. Three trials^{12,14,15} measured abnormal semen quality determined according to the WHO criteria published in 1999, while the other trial¹³ did not report the year when the adopted WHO criteria was published. The frequency and time of semen analysis are described in **Table 1**.

All of the trials assessed sperm motility but reported different reference points according to the WHO classification of the grades of motility: one trial reported the percentage of progressively motile sperm (grade A + B), and the other three trials $^{13-15}$ reported the percentage of sperm with rapid progression (grade A). One trial so reported the percentage of sperm with slow or sluggish progression (grade B), the percentage of nonprogressively motile sperm (grade C), and the percentage of motile (grade A + B + C) sperm. Three trials $^{13-15}$ assessed sperm concentration and only one 13 trial assessed semen volume. None of the studies assessed sperm morphology.

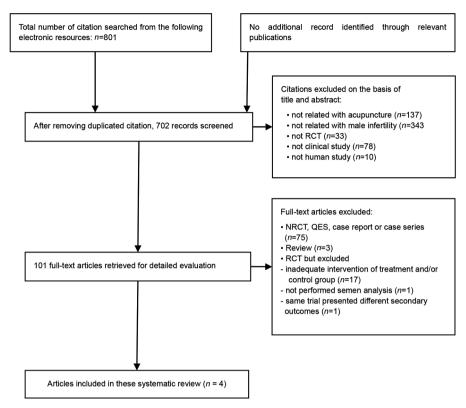


Figure 1: Study selection flow chart. NRCT: non-randomized controlled trial; QES: quasi-experimental study; RCT: randomized controlled trial.

The diagnostic criterion for pregnancy was a positive pregnancy test. None of the studies documented the pregnancy rate using this criterion. Although two trials^{14,15} reported the pregnancy rate of couples with male factor infertility, the diagnostic criterion for pregnancy was not clearly documented. We attempted to contact the authors of the two trials to determine which diagnostic criterion for pregnancy they had used. The author of one study¹⁴ only replied that the diagnostic criterion for pregnancy was a positive pregnancy test. All of the included trials reported that none of the participants experienced adverse events.

Risk of bias

Among the four RCTs, three^{12,14,15} adopted poor randomization procedures with an allocation concealment method based on hospital visitation order, while only one¹³ described adequate methods of random sequence generation and allocation concealment. One trial¹³ blinded patients and outcome assessors. The other three trials^{12,14,15} did not report any information on blinding. Although all the trials reported how many participants dropped out or withdrew, three trials^{12,14,15} were estimated to have a high risk of bias because they did not include any information on whether drop-outs or withdrawals occurred before or after randomization. Risk of bias from selective outcome reporting or from other sources was unclear in all of the included trials (**Figure 2**).

Reporting quality

Even though the CONSORT statement and STRICTA recommendations were updated in 2010, the 2001 versions were used to assess reporting quality because all four trials were conducted before 2010. Based on the CONSORT statement, all the RCTs described the eligibility criteria, sequence generation, adverse events, and a general interpretation of the results. Three RCTs¹²⁻¹⁴ documented the statistical methods used to compare outcomes between groups. Two RCTs^{14,15} presented the baseline demographic and clinical characteristics of the participants.

All of the RCTs either improperly reported or did not report items such as specific objectives and hypothesis, clearly defined outcome measures, methods of random allocation concealment, the precision of each outcome, ancillary analysis, and generalizability. The detailed results are presented in **Supplement 2**.

One study¹³ mentioned that it had been conducted in accordance with STRICTA, but it did not report the rationale for treatment, needle type, practitioner's training duration, or practitioner's years of clinical experience. Three RCTs^{12,14,15} were evaluated as having equal reporting quality based on STRICTA. They had good reporting quality in 11 sub-items (style of acupuncture, rationale for treatment, acupuncture response elicited, type of needle stimulation, needle retention time, number of treatment sessions, frequency of treatment, co-interventions, intended effect of control intervention, precise description of control intervention, and sources that justified the choice of control). The detailed results are presented in **Supplement 3**.

Effects of interventions

Sperm motility

The percentages of grade A and grade A + B motile sperm were pooled because these outcomes were used to diagnose asthenozoospermia. 17,18 Three trials $^{13-15}$ measured the percentage of grade A sperm motility, and the other trial measured the percentage of grade A + B sperm motility. Overall, the pooled data indicated considerable heterogeneity (χ^2 = 122.19, P < 0.00001, I^2 = 98.0%), so subgroup analysis was conducted. The pooled data for the percentage of grade A sperm motility showed large differences between acupuncture and control groups (mean difference 6.35, 95% CI: 4.38–8.32, P < 0.00001), but the results across the trials were substantially heterogeneous (χ^2 = 7.09, P = 0.03, I^2 = 72%). Subgroup analysis was not performed for the percentage of grade A + B sperm motility because it was only evaluated in one trial (**Figure 3**).



Sperm concentration

Three trials¹³⁻¹⁵ evaluated sperm concentration. The pooled results showed a significant difference between acupuncture and control groups (mean difference 6.42, 95% CI: 4.91–7.92, P < 0.00001), but substantial heterogeneity among the trials was observed ($\chi^2 = 4.71$, P = 0.09, $I^2 = 58\%$) (**Figure 4**).

Pregnancy rate (positive pregnancy test rate)

We determined that one trial¹⁴ reported the rate of having a female partner with a positive pregnancy test from contacting the author. No significant difference was found between the acupuncture and control groups in the study (OR: 1.52, 95% CI: 0.46–5.00). Another trial, which reported pregnancy without clear diagnostic criteria, also showed no significant difference between the two groups (OR: 1.69,

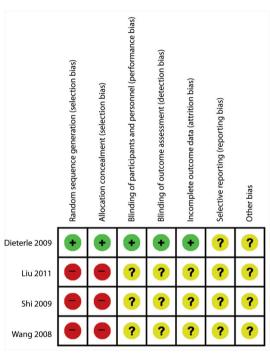


Figure 2: "Risk of bias" summary: review of authors' judgments about each risk of bias item for each included study.

95% CI: 0.52–5.44). Despite an unconfirmed definition of pregnancy in one study, we attempted to pool the results. The results showed no significant differences between the acupuncture and control groups (OR: 1.60, 95% CI: 0.70–3.69, P = 0.27). There was also no significant heterogeneity between these trials ($\chi^2 = 0.02$, P = 0.90, P = 0.90) (**Figure 5**).

Adverse events

All the RCTs reported that no participants experienced adverse events.

DISCUSSION

This systematic review included a total of four RCTs that evaluated acupuncture with or without an additional oral herb mixture, in comparison with placebo or the herb mixture alone. We found that acupuncture might significantly improve sperm motility and sperm concentration, but has no significant additional impact on the pregnancy rate of couples with male infertility. No adverse events were reported in all the trials.

The pooled data on sperm motility and concentration suggest that acupuncture could be applied to oligozoospermia and/or asthenozoospermia patients. Various mechanisms could explain the effectiveness of acupuncture. Pei *et al.*¹⁹ have reported that acupuncture could be beneficial for acrosome position and shape, nuclear shape, axonemal pattern and shape, and accessory fibers. Gurfinkel *et al.*²⁰ suggested that neural stimulation by acupuncture might affect testicle and epididymis vasodilation. Siterman *et al.*^{21,22} proposed that acupuncture might reduce lipid peroxidation in human spermatozoa or genital inflammatory reaction by enhancing immune responses. Future studies confirming these mechanisms are needed.

Although acupuncture might seem beneficial for improving semen quality, the evidence in favor of acupuncture is not compelling. Discrepancy in the effectiveness of acupuncture among the studies is one of the factors that make it difficult to draw definite conclusions. Three studies^{12,14,15} in our meta-analysis reported positive results on semen quality, while one study¹³ did not. Different studies that were excluded in this review also indicate mixed results.^{20–24} We suggest that the following factors possibly caused these discrepant results. First, the outcomes could be affected by whether placebo acupuncture was applied in the control groups. Placebo acupuncture can evoke therapeutic effects^{25,26} or expectancy effects.^{27,28} Thus, the differences which were found between the treatment and control groups in one

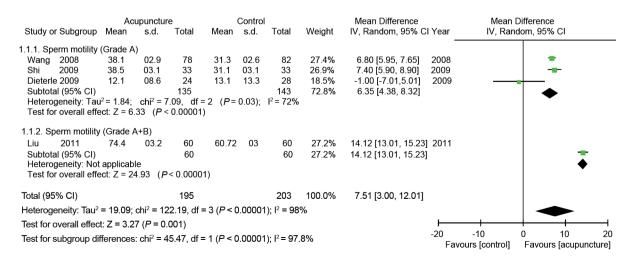


Figure 3: Forest plot for comparison: acupuncture with/without additional treatment versus placebo or same additional treatment. Outcome: sperm motility.

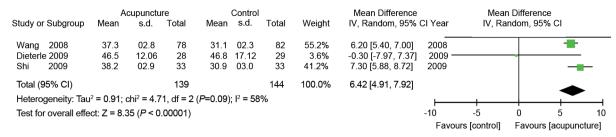


Figure 4: Forest plot for comparison: acupuncture with/without additional treatment versus placebo or same additional treatment. Outcome: sperm concentration.

	Acupuncture	Control		Odds Ratio		Odds Ratio
Study or Subgroup	Events Total	Events Total	Weight	IV, Random, 95% CI	YearIV,	Random, 95% CI
Wang 2008	7 78	5 82	49.1%	1.52 [0.46, 5.00]	2008 —	-
Shi 2009	9 33	6 33	50.9%	1.69 [0.52, 5.44]	2009 –	
Total (95% CI)	111	115	100.0%	1.60 [0.70, 3.69]		
Total events	16	11				
Heterogeneity: Tau ² = 0	0.00; chi ² = 0.02 , df = 1	(P=0.09); I ² = 0%				
Test for overall effect: Z	<i>I</i> = 1.11 (<i>P</i> < 0.27)				0.1 0.2 0.5	1 2 5 10
					Favours [contre	ol] Favours [acupuncture]

Figure 5: Forest plot for comparison: acupuncture with/without additional treatment versus placebo or same additional treatment. Outcome: pregnancy rate.

study¹³ might be underestimated, while the differences in the other three studies^{12,14,15} might be overestimated. Second, inadequate procedures and/or insufficient information for semen analysis could affect outcomes. The WHO states that two semen samples should be collected after a minimum of 2 days to a maximum of 7 days of sexual abstinence and that the interval between the two collections should range from 7 days to 3 weeks to ensure reliable results. 17,29 Although semen samples were collected after a sufficient period of abstinence in the three RCTs, semen sample collection was only conducted once before and once after treatment. 12,14,15 Although the remaining RCT¹³ collected two samples at every assessment, the shortest interval between semen collections was 1 month, and there was no report of whether semen collections were conducted after abstinence. These inadequate procedures and the insufficient information provided for semen analysis made it difficult to validate these results. Finally, high risk of bias and poor reporting quality could cause inconsistent effects. Three RCTs^{12,14,15} used inadequate methods for sequence generation and allocation concealment, which could have caused selection bias. In addition, most items in CONSORT and STRICTA were not described in the three studies. 12,14,15 This means that the studies might not have been conducted according to a predefined plan; therefore, outcomes could have been biased. Furthermore, it is known that there can be an inherent tendency for the treatment group to show more positive results than its control group in a study with poor reporting quality.³⁰

Substantial heterogeneity among the three included studies^{13–15}, which reported the percentage of sperm with rapid progression and sperm concentration, is another factor that makes it difficult to draw definite conclusions. Feature differences among the three studies could have led to substantial heterogeneity. First, different treatment protocols might have induced heterogeneity. The participants in two RCTs^{14,15} received two different acupuncture regimens. After receiving one regimen daily for 10 days, the participants had a rest for 7 days, and then another regimen was also applied daily for 10 days (**Table 2**). The participants in another study¹³ received one acupuncture regimen twice a week for 6 weeks without a resting period. Second, differences in the objectives among the studies might have caused heterogeneity. Two RCTs^{14,15} evaluated the combined effects of acupuncture and

herbs compared with herbs alone, while another study¹³ evaluated the effects of acupuncture compared with placebo acupuncture. Third, different target populations among infertile men could have resulted in heterogeneity. Two RCTs^{14,15} recruited oligozoospermia and/or asthenozoospermia patients, whereas one study¹³ recruited only severe oligozoospermia patients. Finally, inconsistency regarding the risk of bias and reporting quality could have led to heterogeneity. Two^{14,15} of the three studies were identical in all items related to the risk of bias. The other study¹³ and the above two studies^{14,15} were identical in only two items related to the risk of bias. A similar tendency was observed in our assessment of reporting quality. Two studies^{14,15} had similar results for each item on STRICTA and CONSORT, but the other study¹³ differed from the above two studies in more than 50% of the items.

The pooled result for pregnancy rate of couples with male infertility showed no significant difference between the treatment and control groups. However, we could not conclude that acupuncture in infertile men has no effect on the pregnancy rate from this result. The herbal co-intervention could have contributed to the nonsignificant differences in pregnancy outcomes. Two studies^{14,15} used the Wuzi Yanzong herb mixture, which is often administered to improve semen quality in traditional Chinese medicine, as a co-intervention in the treatment and control groups. This medication might have enhanced semen quality in both groups and thus resulted in the lack of a difference in pregnancy rate. Insufficient treatment sessions and short duration of the intervention could also have caused the lack of significant difference between the groups. Acupuncture in two included studies14,15 was performed only 20 times over 27 days, whereas other therapies to improve semen quality and spontaneous pregnancy, including clomiphene citrate and antioxidants, were taken daily for 56 days to 6 months.³¹⁻³⁴ Therefore, the treatment period might have been too short to significantly enhance the pregnancy rate of couples. Other factors associated with spontaneous pregnancy might also have led to the nonsignificant pregnancy results. Age of the spouse and duration of infertility are associated with pregnancy rate. 35,36 The proportion of sperm with normal morphology is also strongly associated with time to pregnancy.³⁷ Two included studies^{14,15} did not report any information on these factors and hence there could have been an imbalance in these factors between groups.



Table 1: Summary of the results of the randomized controlled trials of acupuncture for male infertility

Study, year,	Sample	Interve	Intervention	Time of semen analysis			Outcome		Main results
country		Treatment group	Control group		Sperm motility	Sperm concentration	Sperm Semen No. of p	Semen No. of pregnant Others volume spouse	ı
	(1) Size; (2) Type of abnormal semen findings	(1) Type; (2) Co-interventi-on	(1) Regimen						
Wang <i>et al.</i> 2008, China ¹⁴	(1) T. 78, C: 82; (2) Oligozoo-spermia and/or (2) Wuzi Yanzong asthenozoo-spermia Pill, twice daily, dose=9 g		(1) Wuzi Yanzong Pill, twice daily, dose=9 g	$1^{\rm st}$: Before treatment, $2^{\rm red}$: 3 months after treatment	o (Grade A)	0	° ×	Acrosome enzyme activity	Each electroacupuncture and Wuzi Yanzong pill can improve the semen quality and increase the pregnancy rate for males with infertility due to oligozoospermia and asthenozoospermia. The combined effect of both is the best
Shi, 2009, China ¹⁵	(1) T: 33, C: 33; (1) MA; (2) Oligozoo-spermia and/or (2) Wuzi Yanzong asthenozoo-spermia Pill, twice daily, dose=9 g	(1) MA; (2) Wuzi Yanzong Pill, twice daily, dose=9 g	(1) Wuzi Yanzong Pill, twice daily, dose=9 g	1^{st} : Before treatment, 2^{nd} : 6 months after treatment	o (Grade A)	0	° ×		Same as Wang 2008
Dieterle <i>et al.</i> 2009, Ger-many ¹³	Dieterle <i>et al.</i> (1) T. 24, C: 29, 2009, (2) Severe Ger-many ¹³ oligoasthenozoo-spermia	(1) MA; (2) None	acupuncture	(1) Non-penetrating 1st: Less than 5 months of acupuncture before treatment, (Control 2nd: Less than 3 months before treatment, 3nd: Less than 2 months after treatment, 4th: Less than 3 months after treatment after treatment.	Grade A, Grade B, Grade C, Grade C, to C, Grade D	0	× •		A significantly higher total sperm motility, but no effect on sperm concentration was found after acupuncture compared with placebo acupuncture
Liu 2011b, China ¹²	(1) T. 60, C. 60; (2) Asthenozoo-spermia	(1) EA; (2) <i>Yuzi tang</i> , three times a day		(1) Yuzi tang, three 1^{st} : Before treatment, times a day 2^{nd} : After treatment	o (Grade from A to B)	×	×	Seminal plasma neutral alpha-1, 4 glycosidase level, Seminal plasma zinc level*	The Yuzi tang combined with electroacupuncture can also increase the motility of sperm

No.: number, T: treatment group; C: control group; EA: electroacupuncture; MA: manual acupuncture; o: the study which measured this outcome; x: the study which did not measured this outcome

Table 2: Summary of the acupuncture points and techniques used in the randomized controls trials

Author, year	Style of acupuncture	Treatment acupuncture points	Reasoning for treatment	Details of needling
Wang et al., 2008 ¹⁴	EA	(A) CV6, CV4, CV3, KI3(nr), ST36(nr) (B) GV4, BL23(nr), BL32(nr), SP6(nr)	TCM theory	All participants alternately received (A) and (B) daily for 10 days. After the needles were inserted, the practitioner evoked the <i>Deqi</i> sensation using the tonifying method. After the <i>Deqi</i> sensation had been evoked, an electrostimulator was connected to the acupuncture points. The frequency was 14–26 Hz with an irregular wave. The intensity of the current was enough for patients to feel tolerable pain, numbness, or tingling. Electrostimulation lasted 30 min. A week later, the same treatment was continued for 10 days
Shi, 2009 ¹⁵	MA	(A) CV6, CV4, CV3, KI3(nr), ST36(nr) (B) GV4, BL23(nr), BL32(nr), SP6(nr)	TCM theory	All participants alternately received (A) and (B) daily for 10 days. After the needles were inserted, the practitioner evoked the $Deqi$ sensation using the tonifying method. The needles were left in 30 min. A week later, the same treatment was continued for 10 days
Dieterle et al., 2009 ¹³	MA	ST29(bi), ST36(bi), SP6(bi), SP10(bi), Kl3(bi), LR3(bi), BL23(bi), BL32(bi), CV4, GV20	Past research	Acupuncture needles (0.30 mm×3.0 mm) were inserted to a depth of 15–30 mm. They were rotated manually to evoke the <i>Deqi</i> sensation. A 10 min later, all needles were manipulated again for the <i>Deqi</i> sensation
Liu <i>et al.</i> , 2011 ¹²	EA	(A) GV20, CV6, CV4, KI3(nr), ST36(nr), SP6(nr) (B) BL23(nr), BL24(nr), GV4, SP9(nr), KI7(nr)	TCM theory	All participants alternately received (A) and (B) every other day for three months. After the needles were inserted, an electrostimulator was connected to the acupuncture points. The frequency was 14–26 Hz with an irregular wave. The intensity of the current was enough for patients to feel tolerable pain, numbness, or tingling. Electrostimulation lasted 30 min

EA: electroacupunture; MA: manual acupuncture; bi: bilateral; un: unilateral; nr: not reported whether acupuncture is unilateral or bilateral; TCM: traditional Chinese medicine

All the studies reported no adverse events, but it is uncertain whether acupuncture is a safe treatment for poor semen quality. To reduce publication bias, Ioannidis and Lau³8 recommend that authors describe the information on patients who withdrew because of adverse effects. One included study¹³ mentioned that five patients in the total population discontinued the intervention because of a lack of time. However, the other three studies¹².¹⁴.¹⁵ did not describe why participants withdrew or discontinued during the study. Therefore, there is a possibility of missing data on adverse events. Future clinical trials are required to understand why and when participants withdraw or discontinue.

CONCLUSIONS

This review suggests that current evidence regarding whether acupuncture in infertile men improves sperm motility, sperm concentration, and the pregnancy rate of couples is insufficient. The poor quality of the evidence is attributable to the small number of studies, inadequate procedures and/or insufficient information for semen analysis, high risk of bias, methodological heterogeneity, and poor reporting quality. Large-scale RCTs with elaborate designs are needed to rigorously test the effectiveness and safety of acupuncture on semen quality. Appropriate target populations and sufficient treatment periods should also be considered in future studies.

AUTHOR CONTRIBUTIONS

UMJ and JYJ planned and designed the study, searched for articles from the databases, selected relevant studies, extracted the data, analyzed the data, and drafted the manuscript. SL and JML made substantial contributions to the study design. SL arbitrated contradictory assessments. SL helped to draft the manuscript. SL and OK participated in the critical revision of the manuscript. OK had the final responsibility for the submission decision for publication. All of the authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no conflict of interest.

ACKNOWLEDGMENTS

This study was supported by the "New Donguibogam" Compilation Project for the expansion of Korean Medical Knowledge (No. K13380) of the Korea Institute of Oriental Medicine.

Supplementary Information is linked to the online version of the paper on the *Asian Journal of Andrology* website.

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How to cite this article: Jerng UM, Jo JY, Lee S, Lee JM, Kwon O. The effectiveness and safety of acupuncture for poor semen quality in infertile males: a systematic review and meta-analysis. *Asian J Androl* 27 June 2014. doi: 10.4103/1008-682X.129130. [Epub ahead of print]