Original Article

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Acupuncture for Treatment of Erectile Dysfunction: A Systematic Review and Meta-Analysis

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Purpose: To assess the effectiveness and safety of acupuncture for erectile dysfunction (ED).

Materials and Methods: We searched six major English and Chinese databases included randomized controlled trials (RCTs) testing acupuncture alone or in combination for ED. Dichotomous data were presented as risk ratio (RR) and continuous data were presented as mean difference (MD) both with 95% confidence interval (CI). The Revman (v.5.3) was used for data analyses. Quality of evidence across studies was assessed by the online GRADEpro tool.

Results: We identified 22 RCTs, fourteen of them involving psychogenic ED. Most of the included RCTs had high or unclear risk of bias. There was no difference between electro-acupuncture and sham acupuncture with electrical stimulation on the rate of satisfaction and self-assessment (RR, 1.50; 95% CI, 0.71–3.16; 1 trial). Acupuncture combined with tadalafil appeared to have better effect on increasing cure rate (RR, 1.31; 95% CI, 1.00–1.71; 2 trials), and International Index of Erectile Function-5 scores (MD, 5.38; 95% CI, 4.46–6.29; 2 trials). When acupuncture plus herbal medicine compared with herbal medicine alone, the combination therapy showed significant better improvement in erectile function (RR, 1.68; 95% CI, 1.31–2.15; 7 trials). Only two trials reported facial red and dizziness cases, and needle sticking and pruritus cases in acupuncture group.

Conclusions: Low quality evidence shows beneficial effect of acupuncture as adjunctive treatment for people mainly with psychogenic ED. Safety of acupuncture was insufficiently reported. The findings should be confirmed in large, rigorously designed and well-reported trials.

Keywords: Acupuncture; Erectile dysfunction; Meta-analysis; Randomized controlled trial; Systematic review

INTRODUCTION

Erectile dysfunction (ED), also called impotence, is defined as an inability to obtain or maintain a penile erection sufficient for satisfactory sexual intercourse [1]. ED is a common clinical condition, affecting men of all ages, particularly the elderly. ED affects around 52% in men aged 40 to 70 years, with more than 320 million men predicted to suffer from ED by 2025 years worldwide [2]. ED can result in considerable distress

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and lowered quality of life. As it is associated with a wide variety of underlying conditions such as diabetes and cardiovascular co-morbidities, treatment options depend upon the associated factors and diverse approaches in different settings [3]. Current treatment for ED included oral drugs, intrapenile therapies and penile prosthesis implantation, but with uncertain effect [4]. Alternative options such as non-pharmaceutical therapies are needed and expected.

Acupuncture, part of traditional Chinese medicine (TCM), is increasingly used for the treatment of ED. There are different ways for its use, including stimulation of acupoints with needling, heating (moxibustion), electrical current, or injecting drugs into acupoints [5]. TCM theory states that ED is usually caused by the decline of fire from the life gate (*Ming men*), sexual indulgence or frequent masturbation, and emotional disturbances. Thus, the principle of acupuncture treatment is to invigorate the kidney *qi* and nourish the heart and spleen. As such, and selecting acupoints from the Kidney Meridian of *Foot-Shaoyin* and the *Ren* Meridian and *back-shu* points is commonly used for treating ED, and moxibustion can be used as well during the treatment [6,7].

The potential mechanism of action by how acupuncture may have an effect on ED is unclear. However, there is some indication that acupuncture may stimulate nerve endings, and induce nerve impulses which then impact on levels of norepinephrine, acetylcholine, and their biological enzymes in the central nervous system [8]. Some clinical trials have been conducted to investigate the effect of acupuncture in the treatment of ED. A systematic review published in 2016 concluded with insufficient results about the effect of acupuncture when comparing with sham acupuncture and psychological therapy [9]. Another recent systematic review summarized evidence of acupuncture for ED [10]. However, this review searched literature mainly from Chinese databases, and its control groups were only Chinese herbal medicine. As a result, the interpretation of the findings may be limited. Our review aims to comprehensively review the current evidence of acupuncture for ED.

MATERIALS AND METHODS

1. Inclusion/exclusion criteria

We included both parallel, cross-over, randomized clinical trials, regardless of blinding and publication status. Types of participants included men who were diagnosed as ED by any recognized national or international criteria, regardless of psychogenic and organic origin of impotence. Interventions included as verum acupuncture (defined as needling stimulation of acupuncture points or trigger points by manual acupuncture with or without heating [moxibustion]), electro-stimulating, acupoint injection, acupressure and laser acupuncture [5,6]. Controls included no treatment, sham acupuncture, herbal medicine, or conventional medicine. Co-interventions were allowed as long as they were given equally to all randomized arms.

1) Primary outcomes

(1) Patient erectile function and partner satisfaction measured by International Index of Erectile Function-5 (IIEF-5) score and its components [11]; (2) The effect and quality of sexual intercourse presented as "cure", or "markedly improved on erectile function" based on validated measurement tools or scales. "Cure" was defined as symptom disappearance with successful sexual activity and/or with IIEF-5 score ≥22 [11]. "Markedly improved on erectile function" referred to that all the three below items were met: the self-report disappearance of clinical symptoms, the erection angle of penis is more than 90 degrees in sexual activity, and the success rate of sexual intercourse is over 75%.

2) Secondary outcomes

(1) The quality of sexual activity measured by "satisfaction and self-assessment", which defined as the self-reported satisfaction by patients or their partners. They reported that the symptoms disappeared, at same time, erectile function and sexual life returned to normal; (2) Angle of penile erection measured by self-assessment tools or scales; (3) Adverse events.

2. Search strategy

We searched for published studies in two English and four Chinese electronic databases from their inception to August 31st, 2018, including PubMed, the Cochrane Library, Sinomed Database, China National Knowledge Infrastructure, *Wanfang* Database, and China Science Technology Journal Database. The search terms included acupuncture-related terms (*i.e.*, "acupuncture", "electro-acupuncture", "auricular therapy", "warm needling", "fire needling", "shark hook

needling", "magnet needle", "acupoint injection", "point injection", "moxibustion", "acupressure"), combined with erectile dysfunction related terms (*i.e.*, "erectile dysfunction [Mesh terms]", "impotence", "*yang wei*"). Search term strategies were adapted for each specific database.

3. Study selection and data extraction

Two authors (Lai BY and Jia LY) independently selected the trials included in the review according to the inclusion/exclusion criteria. Any disagreement was resolved by discussion. We performed data extraction using a self-developed data extraction form. If the necessary data were not available in the trial reports, further information was sought by contacting corresponding author.

4. Assessment of methodological quality

The risk of bias of the included trials was assessed independently according to the criteria from the Cochrane Handbook for Systematic Reviews of Interventions [12]. Criteria included adequacy of generation of the allocation sequence, allocation concealment, blinding (blinding of participants and personnel, blinding of outcome assessors), incomplete outcome data or not, whether selected reporting the results and other bias (*e.g.*, imbalance of the baseline information). Risk of bias for each trial was assessed as low, high, or unclear. A trial was considered as having low risk of bias when all the items met the criteria; a trial was considered at high risk of bias when at least one of the items was not met; and a trial was considered unclear risk of bias where insufficient information was available to make the judgment. Any difference in the quality assessment of trials was resolved by discussion in order to reach consensus. Quality of evidence across studies for each important outcome was assessed using the online GRADE approach to support the recommendations using the online GRADEpro tool (https://gradepro.org/).

5. Data analysis

Meta-analysis was performed within comparisons of the same type of acupuncture *versus* the similar control. Dichotomous data were presented as risk ratio (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI). We used *I*-square value to detect statistical heterogeneity and to measure the percentage of the variability in effect sizes between studies that is due to heterogeneity rather than to sampling error. We used random effects model to combine the results in this review due to potential sources of clinical heterogeneity [12]. If the I^2>75%, we did not pool the data and results from each individual trial were presented respectively. The statistical analysis was carried out using Revman 5.3 software. If a sufficient numbers of randomized trials were identified and data available, subgroup analysis would be performed according to the comparisons.

RESULTS

1. Study selection

We identified 300 studies, of which 68 duplicates were removed. After screening the abstracts, 190 trials

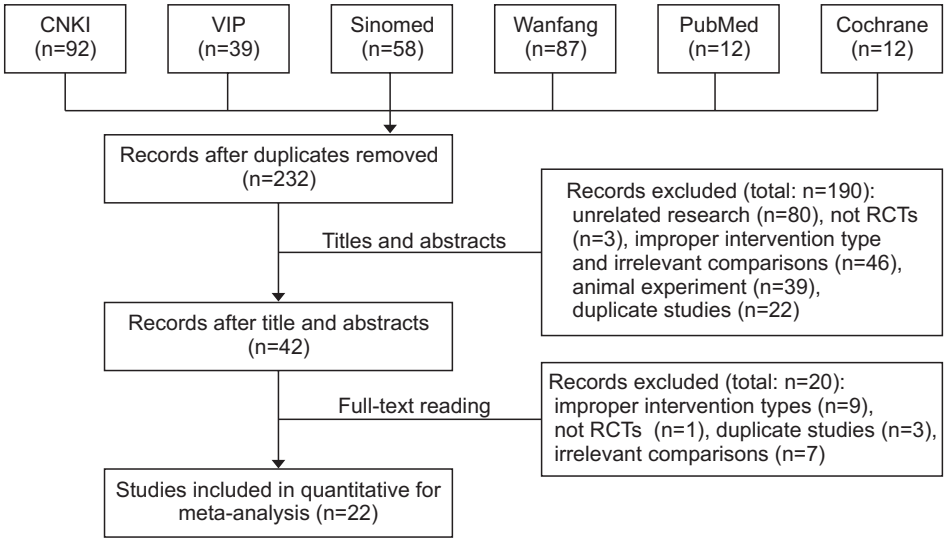

Fig. 1. Study selection flow diagram. CNKI: China National Knowledge Infrastructure, VIP: Chinese Science Journal Database, RCT: randomized controlled trial.

were excluded with reasons. Full-texts of the remaining 42 trials were retrieved and assessed for eligibility. A total of 22 randomized controlled trial (RCT) met the inclusion criteria. Fig. 1 illustrates a PRISMA flow diagram.

2. Description of studies

Twenty-two RCTs involving 1,751 participants were enrolled in this review. All of them were conducted in China, and 2 of them published in English. All trials had parallel comparisons, except one [13] that used a crossover design. The sample size varied from 21 to 176 participants, with an average of 35 patients per group. The participants were male adults aged from 20 to 69 years old. The interventions included manual acupuncture with or without moxibustion, electro-acupuncture, and acupuncture point injection. Type of controls included sham acupuncture, herbal medicine, Western medicine, psychological therapy, and hypnosis therapy. The types of ED of twenty-two trials included 2 trials [14,15] were involving ED participants with type-2 diabetes, two trials [16,17] were involving ED participants with psychogenic or arterial supply insufficiency, fourteen trials [13,18-30] were ED participants with psychogenic, and four trials [31-34] not reported ED information. The characteristics of included studies are shown in Table 1.

3. Description of therapeutic regimen

A summary of acupuncture regimen is provided in Appendix, which contains a list of acupoints, treatment frequency and duration for each trial (Appendix). Participants of included trials accepted acupuncture one session daily for 30 minutes at most of the occasions. The principle of acupuncture treatment was to improve the erectile function and the most common used acupoints and involving meridian were *Guan Yuan* (CV4, the *Ren* Meridian, 15 trials), *San Yin Jiao* (SP6, the Splenic Meridian of *Foot-taiyin*, 15 trials), *Shen Shu* (BL23, the Bladder Meridian *Foot-taiyang*, 13 trials), *Zu San Li* (ST36, the Stomach Meridian of *Foot-yangming*, 12 trials), *Ming Men* (DU4, the *Du* Meridian of *Foot-shaoyin*, 8 trials), *Tai Chong* (LR3, the Liver Meridian of *Foot-jueyin*, 7 trials), *Tai Xi* (KI3, the Kidney Meridian of *Foot-shaoyin*, 7 trials) and *Ci Liao* (BL32, the Bladder Meridian *Foot-taiyang*, 5 trials).

4. Assessment of risk of bias

According to the pre-defined approach, 22 trials were found to be either unclear (n=19) or high risk of bias (n=3) due to insufficient or inadequate reporting of the information. Only 6 trials [14,16,19,25,27,30] described that random number table was used to generate the random allocation, thus assessed as having low risk of bias. However, none of the trials reported the allocation concealment. Due to special characteristics of acupuncture, it is difficult for blinding to practitioners, so only two trials [13,18] used sham acupuncture as control and were assessed as low risk of performance bias regarding to the potential adequate blinding method of participants. Risk of detective bias was assessed to be unclear since none of them reported the method of blinding to outcome assessors or statistician. One trial [18] reported number and reasons for drop-out participants, which was regarded low risk of attrition bias. The other 21 trials did not specify the drop-out, and were all evaluated as unclear risk of attrition bias. Twenty trials were assessed as having unclear risk of selective reporting bias due to the absence of protocol; the remaining three trials [22,25,26] were assessed as high risk of selective reporting bias since they all had obvious problems on primary outcome reporting. Other bias was assessed by comparability between groups on baseline data such as age and duration of ED. Only six trials [16,18,21,24,31,32] reported baseline data including age and duration of dysfunction. There is no statistical description of details, so the risk of bias was assessed as unclear. The methodological quality of all the included trials is shown in the Fig. 2.

5. Effect estimates

Data analysis was conducted according to the type of comparisons. Table 2 illustrates the details of effect estimates of acupuncture for ED.

1) Acupuncture *versus* sham acupuncture

One trial [18] compared electro-acupuncture with sham acupuncture (needles inserted into non acupoints), the results showed no difference on the rates of satisfaction and self-assessment between groups (RR, 1.50; 95% CI, 0.71–3.16; 60 participants). Another crossover trial [13] compared manual acupuncture with sham acupuncture (needle insert into irreverent points) showed significant better effect on the rates of satisfaction and self-assessment (RR, 7.53; 95% CI, 1.13–50.00;

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Table 1. Characteristics of 22 the included randomized trials

Study ID	Sample[a]	Age (y)[b]	Type of ED	Intervention	Control	Duration of treatment (wk)[c]	Outcome measure
Aydin et al (1997) [18]	T: 15, C1: 15, C2: 15, C3: 15	T: 36.75±10.43, C1: 38.4±10.75, C2: 35.1±10.46, C3: 37.1±11.32	Psychogenic	EA, 3 Hz direct-current (dc), 20 minutes, twice a week	C1: hypnotic therapy, (3 times a week, later once a month) C2: oral placebo (vitamin pills) C3: sham acupuncture (non-acupuncture points) 3 Hz dc, 20 minutes, twice a week	T: 6, C1: 6, C2: 6, C3: 6	Satisfaction of self-assessment rate, adverse effects
Cao et al (2007) [31]	T: 36, C: 18	T: 25–58, C: 26–59	NR	MA plus control, 30 minutes, once daily	CHM (self-prescribed herbal decoction), twice daily	8	Markedly improved on erectile function rate
Cheng and Cao (2009) [32]	T: 32, C: 32	T: 20–56, C: 21–54	NR	MA plus control, 30 minutes, once daily	CHM (self-prescribed herbal decoction), twice daily	4	Markedly improved on erectile function rate
Chen et al (2011) [19]	T: 61, C: 62	T: 27.62, C: 27.58	Psychogenic	EA plus control, with density wave, 30 minutes, once daily	CHM (compound Xuan Ju), 3 capsules, 3 times daily	4	Satisfaction of self-assessment rate, IIEF-5 scores
Cui et al (2007) [16]	T: 50, C1: 50, C2: 50	T: 20–69, C1: 20–69, C2: 20–69	Psychogenic or arterial supply insufficiency	Salvia miltiorrhiza injection and bupleurum injection once every 2 days	C1: acupoint injection with saline, once every 2 days C2: CHM (Chun Yi capsule), 0.5 g/times, 3 times daily	3	Markedly improved on erectile function rate, IIEF-5 scores
Dai et al (2003) [20]	T: 44, C: 41	T: 35.75±3.17, C: 36.24±4.12	Psychogenic	MA plus control, 30 minutes, once daily	CHM (Kang Wei Ling decoction), 2.5–4.5 g/times, twice daily	4	Markedly improved on erectile function rate
Ding et al (2012) [33]	T1: 88, C: 44	T: 41.3±8.1, C: 39.1±6.7	Psychogenic	MA plus control, 30 minutes, once daily	CHM (Si Ni decoction), 3 times daily	4–8	Markedly improved on erectile function rate, penile erection angle
	T2: 44, C: 44	T: 38.3±7.4, C: 39.1±6.7	Psychogenic	MA, 30 minutes, once daily	CHM (modified herbal decoction), 3 times daily	4–8	Markedly improved on erectile function rate, penile erection angle
Duan (2007) [17]	T: 30, C: 30	T: 27–55, C: 29–52	Psychogenic or arterial supply insufficiency	MA, 30 minutes, once daily	CHM (You Gui pill), one pill, twice daily	4	Markedly improved on erectile function rate
Engelhardt et al (2003) [13]	T: 10, C: 11	T: 38.9, C: 38.9	Psychogenic	MA, 20 minutes, once or twice weekly	Sham acupuncture against headache acupoint, 20 minutes, once or twice weekly	6.2 (4–10)	Satisfaction of self-assessment rate, IIEF scores, adverse effects
Jiang et al (2014) [21]	T: 64, C: 64	T: 21–64, C: 22–65	Psychogenic	MA plus control, 30 minutes, once daily	CHM (self-prescribed herbal decoction), twice daily	3–5	Cure rate, IIEF scores
Jiang et al (2012) [22]	T: 51, C: 51	T: 28.73±3.27, C: 27.67±4.12	Psychogenic	MA plus control, 30 minutes, once daily	Physical training, 5–15 minutes each time, 12 times from 15 days	4	Satisfaction of self-assessment rate
Lin et al (2005) [23]	T: 64, C: 32	T: 38.3±8.1, C: 39.1±6.7	Psychogenic	MA plus control, 30 minutes, once daily	CHM (self-prescribed herbal decoction), twice daily	4–8	Markedly improved on erectile function rate, penile erection angle
Liu et al (2016) [24]	T: 32, C: 30	T: 32, C: 30	Psychogenic	AIHE plus control, injection 1 mL/time, once every 2 day	Tadalafil tablet, 5 mg/times, once daily	12	Cure rate, IIEF scores

Table 1. Continued

Study ID	Sample[a]	Age (y)[b]	Type of ED	Intervention	Control	Duration of treatment (wk)[c]	Outcome measure
Liu (2017) [25]	T: 31, C: 31	T: 42.68±2.35, C: 42.56±2.45	Psychogenic	MA with moxibustion plus control, MA: 30 minutes, once daily	Tadalafil tablet, 10 mg/times, 3 times daily	4	Cure rate, adverse effects
Liu and Ren (2015) [14]	T: 30, C: 30	T: 47.4±6.01, C: 47.8±6.51	ED with type-2 diabetes	MA plus control, 20 minutes, once daily	Psychotherapy and exercise	8	Cure rate, IIEF scores
Shan (2001) [26]	T: 60, C: 30	T: 43.6, C: 43.6	NR	MA plus control, 20 minutes, once daily	CHM (self-prescribed herbal decoction), twice daily	12	Markedly improved on erectile function rate
Xie (2016) [27]	T: 40, C: 40	T: 42.8±8.35, C: 43.19±8.07	Psychogenic	MA plus control, 30 minutes, once daily	CHM (Cong Rong Yi Shen granules), twice daily	16	Cure rate, IIEF scores, adverse effects
Yang and Tian (2008) [34]	T: 20, C: 20	T: 40, C: 40	NR	MA plus control, 30 minutes, once daily	CHM (self-prescribed Shen Qi Er Xian herbal decoction), twice daily	4–8	Satisfaction of self-assessment rate
Ye and Chen (2017) [28]	T: 20, C: 20	T: 34.15±6.43, C: 36.25±5.25	Psychogenic	MA plus control, 30 minutes, once daily	CHM (Huan Shao capsule), 2.1 g/times, 3 times daily	4	Cure rate, IIEF scores
Jia (2018) [29]	T: 20, C: 20	T: 40.15±1.68, C: 40.86±1.91	Psychogenic	MA with moxibustion plus control, 30 minutes, once daily	Tadalafil tablet, 5 mg/times, once daily	3	Cure rate, IIEF scores, adverse effects
Li et al (2018) [15]	T: 45, C: 45	T: 45.26±4.17, C: 46.14±4.51	ED with type-2 diabetes	EPAS plus control, 4 min/time for one acupoint, total 24 minutes, once daily	Tadalafil tablet, 5 mg/times, once daily	4	Cure rate, IIEF scores, adverse effects
Yu et al (2018) [30]	T: 20, C: 20	T: 34.15±6.43, C: 36.25±5.25	Psychogenic	MA plus control, 30 minutes, once daily	Sildenafil tablet, 12.5 mg/times, twice daily	6	Cure rate, IIEF scores

"Cured" refers to patients who reported that their clinical symptoms disappeared, they had no problem with sexual activity, and/or with International Index of Erectile Function (IIEF-5) score was ≥22 [31]. 'Markedly improved on erectile function' refers to that all the three below items were met: the self-report disappearance of clinical symptoms, the erection angle of penis is more than 90 degrees in sexual activity, and the success rate of sexual intercourse is over 75%.

ED: erectile dysfunction, T: treatment group, C: control group, NR: not reported, EA: electro acupuncture, MA: manual acupuncture, AIHE: acupoint injection of herbal extract, EPAS: moderate—frequency electrical pulse acupoint stimulation, CHM: Chinese herbal medicine.

[a]Values are presented as number only. [b]Values are presented as mean±standard deviation, range, or mean only. [c]Values are presented as mean only, range only, or median (range).

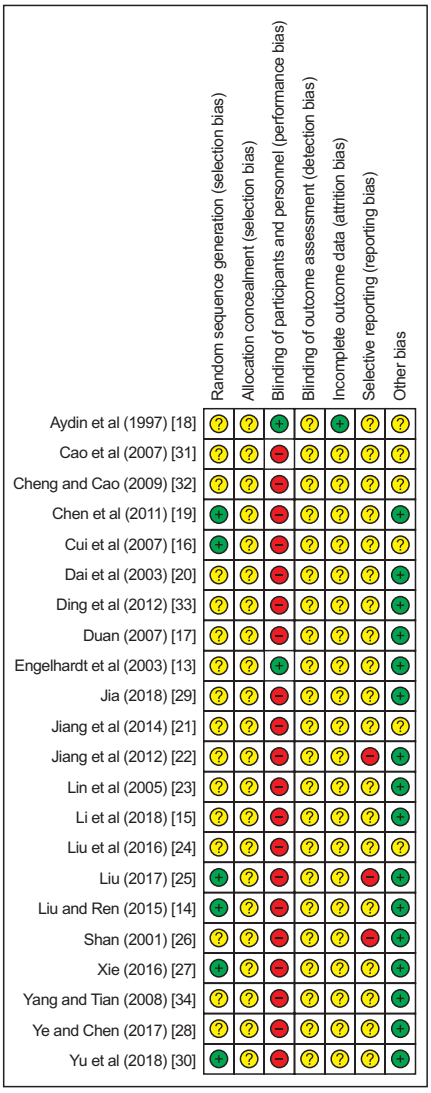

Fig. 2. Risk of bias summary.

60 participants). No other results were reported from these two trials.

2) Acupuncture plus western medicine *versus* western medicine

Two trials [15,24] compared acupuncture plus tadalafil compared with tadalafil alone. The combination therapy showed better effect on increasing cure rate (RR, 1.31; 95% CI, 1.00–1.71; I^2=0%; 2 trials; 152 participants) and IIEF-5 scores (MD, 5.38; 95% CI, 4.46–6.29; I^2=0%; 2 trials; 152 participants). Another trial [30] compared acupuncture plus sildenafil compared with sildenafil alone, and the combination therapy showed better effect on increasing IIEF-5 scores (MD, 3.23; 95% CI, 2.12–4.34; 1 trial; 70 participants). There was no significant between-group difference in terms of cure rate (RR, 3.0; 95% CI, 0.65–13.86; 1 trial; 70 participants).

3) Manual acupuncture plus moxibustion *versus* tadalafil tablet

Two trials [25,29] compared acupuncture plus moxibustion compared with tadalafil alone. There was no significant difference between groups in cure rate (RR, 1.40; 95% CI, 0.74–2.66; 2 trials; I^2=0%; 102 participants). No difference between groups was found from one trial [29] in IIEF-5 scores (MD, 1.15; 95% CI, 1.37–0.93; 40 participants).

4) Acupuncture *versus* herbal medicine

Two trials [17,33] compared acupuncture with herbal medicine and another trial [16] compared acupoint injection of herbal extracts with oral herbal medicine. There was no difference between acupuncture and herbal medicine in terms of markedly improved on erectile function rate (RR, 1.40; 95% CI, 0.42–4.69; I^2=46%; 2 trials; 148 participants) [17,33]. However, the acupoint injection of herbal extracts significantly increased the IIEF-5 scores compared to oral herbal medicine (MD, 4.0; 95% CI, 3.66–4.34; 1 trial; 100 participants) [16].

5) Acupuncture plus herbal medicine *versus* herbal medicine alone

Acupuncture plus herbal medicine was tested in seven trials [20,23,26,27,31-33], which showed significant better effect on markedly improved rate on erectile function (as measured by the erection angle and success rate of sexual intercourse) than herbal medicine alone (RR, 1.68; 95% CI, 1.31–2.15; I^2=0%; 7 trials; 601 participants).

By excluding three trials [26,31,32] for not reporting types information of ED, remaining four trials only involving ED patients with psychogenic also show that better effect on markedly improved rate on erectile function in combination therapy group (RR, 1.63; 95% CI, 1.21–2.19; I^2=0%; 4 trials; 393 participants). The pooled results also showed significantly better effects of the combination therapy on cure rate (RR, 1.36; 95% CI, 1.12–1.65, I^2=0%; 2 trials; 168 participants) [21,28] and rigidity (as measured by erectile angle) in sexual intercourse (MD, 6.73 degree; 95% CI, 4.10–9.36; I^2=0%; 2 trials; 228 participants) [23,33]. However, no difference was found between groups in the rate of satisfaction and self-assessment (RR, 1.67; 95% CI, 0.64–4.36; I^2=75%;

Table 2. Effect estimates of included 22 trials

Outcome and comparison	Study	Participant	Effect estimate (95% CI) REM	p-value	Study ID
Electronic acupuncture *versus* sham acupuncture with electrical stimulation					
Satisfaction of self-assessment rate	1	60	RR 1.50 (0.71–3.16)	-	Aydin et al (1997) [18]
Manual acupuncture *versus* sham acupuncture					
Satisfaction of self-assessment rate	1	60	RR 7.53 (1.13–50.00)	-	Engelhardt et al (2003) [13]
Acupuncture plus tadalafil tablet *versus* tadalafil tablet					
Cure rate	2	152	RR 1.31 (1.00–1.71), I^2=0%	0.48	Liu et al (2016) [24], Li et al (2018) [15]
IIEF-5 score	2	152	MD 5.38 (4.46–6.29), I^2=0%	0.04	Liu et al (2016) [24], Li et al (2018) [15]
Acupuncture plus sildenafil tablet *versus* sildenafil tablet					
Cure rate	1	70	RR 3.00 (0.65–13.86)	-	Yu et al (2018) [30]
IIEF-5 score	1	70	MD 3.23 (2.12–4.34)	-	Yu et al (2018) [30]
Manual acupuncture plus moxibustion *versus* tadalafil tablet					
Cure rate	2	102	RR 1.40 (0.74–2.66), I^2=0%	0.3	Liu (2017) [25], Jia (2018) [29]
IIEF-5 score	1	40	MD 1.15 (1.37–0.93)	-	Jia (2018) [29]
Acupuncture *versus* herb medicine					
Markedly improved on erectile function rate	2	148	RR 1.40 (0.42–4.69), I^2=46%,	0.18	Ding et al (2012) [33], Duan (2007) [17]
IIEF-5 score	1	100	MD 4.00 (3.66–4.34)	-	Cui et al (2007) [16]
Acupuncture point injection of herbal extracts *versus* oral herbal medicine					
IIEF-5 score	1	100	MD 4.0 (3.66–4.34)	-	Cui et al (2007) [16]
Markedly improved on erectile function rate	1	100	RR 1.94 (0.69–5.43)	-	Cui et al (2007) [16]
Acupuncture plus herbal medicine *versus* herbal medicine alone					
Cure rate	2	168	RR 1.36 (1.12–1.65), I^2=0%	0.77	Jiang et al (2014) [21], Ye and Chen (2017) [28]
Markedly improved on erectile function rate	7	601	RR 1.68 (1.31–2.15), I^2=0%	0.90	Cao et al (2007) [31], Cheng and Cao (2009) [32], Dai et al (2003) [20], Ding et al (2012) [33], Lin et al (2005) [23], Shan (2001) [26], Xie (2016) [27]
Satisfaction of self-assessment rate	2	163	RR 1.67 (0.64–4.36), I^2=75%	0.3	Chen et al (2011) [19], Yang and Tian (2008) [34]
IIEF-5 score	3	331	No pooled data of trials for I^2=95%	<0.05	Chen et al (2011) [19], Jiang et al (2014) [21], Xie (2016) [27]
Erectile angle	2	228	MD 6.73° (4.10–9.36), I^2=0%	0.94	Ding et al (2012) [33], Lin et al (2005) [23]
Manual acupuncture plus physical therapy *versus* physical therapy					
Cure rate	1	102	RR 1.56 (0.99–2.43)	-	Jiang et al (2012) [22]
IIEF-5 score	1	60	MD 2.90 (2.59–3.21)	-	Liu and Ren (2015) [14]

CI: confidence interval, REM: random effect model, IIEF: International Index of Erectile Function, RR: risk ratio, MD: mean difference.

2 trials; 163 participants) [19,34]. Moreover, three trials [19,21,27] favored the combination therapy of acupuncture and herbal medicine in higher IIEF-5 scores (MD, 3.53) to herbal medicine alone, but the results could not be pooled due to high statistical heterogeneity (I^2=97%).

6) Acupuncture plus psychological therapy *versus* psychological therapy

Two trials compared acupuncture plus psychological therapy with psychological therapy alone. One of them [22] found no difference between groups for cure rate (RR, 1.56; 95% CI, 0.99–2.43; 1 trial; 102 participants). Another trial [14] involving 60 ED participants with type-2 diabetes and found the combination therapy appeared to be better on higher IIEF-5 scores (MD, 2.90; 95% CI, 2.59–3.21; 1 trial; 60 participants).

6. Adverse events

Seven trials reported the outcome of adverse events and side effects [13,15,16,18,25,27,29]. One trial [16] reported five cases of dyspepsia, two cases of dizziness and one case of dry mouth from tadalafil in the control group; and one case having facial red and one case of dizziness in acupuncture group. Another one trial [29] reported three patients suffered from needle sticking and pruritus during treatment in acupuncture group; and there were two cases having dry mouth and headache from tadalafil in control group. No adverse effect or side effect was found in the remaining 5 trials.

7. Overall quality of evidence by GRADE

We graded the overall quality of available evidence using GRADE criteria. When combination of acupuncture compared to tadalafil, the quality of evidence for cure rate and IIEF-5 scores was low. In comparison of other interventions and outcome assessments, the quality of evidence was mainly low or very low due to high risk of bias, imprecision (small number of total events or small sample size), or indirectness (outcome measures). Detail of result is show in Table 3.

8. Additional analysis

We tried to do the subgroup analyses according to the types of ED participants, but failed, due to the insufficient number of trials and related information. We could not perform other meaningful sensitivity analysis either.

DISCUSSION

1. Summary of the main results

Twenty-three RCTs were included in this review. The majority of the included studies were having high or unclear risk of bias. Low quality evidence showed there was no difference between acupuncture alone and sham acupuncture, tadalafil, or herbal medicine on symptoms improvement for ED. Combination of acupuncture appeared to show beneficial effect of acupuncture as adjunctive treatment for ED participants with psychogenic or partly with type-2 diabetes, when compared with other conventional therapies (such as tadalafil, psychological therapy or herbal medicine). However, the level of evidence for all outcomes were assessed as "low" or "very low" due to high risk of bias, imprecision or indirectness among included trials. The findings need to be seen as inconclusive due to small sample size and poor methodological quality. Safety of acupuncture was insufficiently reported in the included trials.

2. Comparison with previous studies

There are two published reviews on this topic. One included 3 RCTs involving 183 participants with ED [9], which compared acupuncture with sham acupuncture and psychological therapy respectively. The included RCTs in this review failed to show a specific therapeutic effect of acupuncture, and had methodological flaws as concluded by the authors. And the other recent one only involved Chinese database and included 6 RCTs, control treatment were only involving Chinese herbal medicine and details of treatment information were not clearly specified [10]. In addition, the findings of both two reviews of included trials were not finally pooled due to statistical and clinical heterogeneity, which failed to show a specific therapeutic effect of acupuncture for ED. Compared to the previous two reviews, this update review covered a broader combination of studies, including acupuncture with moxibustion, the acupoint injection and different comparisons, and additional outcome assessments. We performed analyses based on different comparisons and found that although the strength of the evidence was weak, the findings showed there was a potential add-on effect of acupuncture for patients with ED. A total of 31.8% (7/22) of included trials had reported adverse information from acupuncture. This review provided latest evi-

Table 3. Summary of main findings of RCTs on acupuncture for erectile dysfunction

Outcome	No. of participant (No. of RCT)	Quality of the evidence	Relative effect (95% CI)	Anticipated absolute effect	
				Risk with control	Risk difference with intervention (95% CI)
Electronic acupuncture *versus* sham acupuncture					
Satisfaction of self-assessment rate	30 (1)	⊕○○○[acd]	RR 1.50 (0.71–3.16)	400 per 1,000	200 more per 1,000 (116 more to 864 more)
Manual acupuncture *versus* sham acupuncture					
Satisfaction of self-assessment rate	30 (1)	⊕○○○[acd]	RR 7.53 (1.13–50.00)	91 per 1,000	594 more per 1,000 (12 more to 1,000 more)
Acupuncture plus tadalafil tablet *versus* tadalafil tablet					
Cure rate	152 (2)	⊕⊕○○[ac]	RR 1.31 (1.00–1.71)	467 per 1,000	145 more per 1,000 (0 more to 331 more)
IIEF-5 score	152 (2)	⊕⊕○○[ac]	N/A		MD 5.38 higher (4.46 higher to 6.29 higher)
Acupuncture *versus* herb medicine					
Markedly improved on erectile function rate	204 (3)	⊕○○○[acd]	RR 1.51 (0.96–2.38)	194 per 1,000	99 more per 1,000 (8 fewer to 268 more)
IIEF-5 score	100 (1)	⊕⊕○○[ac]	N/A		MD 4 higher (3.66 higher to 4.34 higher)
Acupuncture plus herb medicine *versus* herb medicine					
Cure rate	168 (2)	⊕⊕○○[ac]	RR 1.36 (1.12–1.65)	607 per 1,000	219 more per 1,000 (73 more to 395 more)
Markedly improved on erectile function rate	601 (7)	⊕○○○[acd]	RR 1.68 (1.31–2.17)	241 per 1,000	164 more per 1,000 (75 more to 281 more)
Satisfaction of self-assessment rate	163 (2)	⊕○○○[abc]	RR 1.67 (0.64–4.36)	463 per 1,000	310 more per 1,000 (167 fewer to 1,557 more)
IIEF-5 score	331 (3)	⊕⊕○○[ab]	N/A		MD 3.53 higher (0.65 higher to 6.4 higher)
Erectile angle	228 (2)	⊕○○○[acd]	N/A		MD 6.73 higher (4.1 higher to 9.36 higher)

GRADE Working Group grades of evidence. High quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low quality: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low quality: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

RCT: randomized controlled trial, CI: confidence interval, IIEF: International Index of Erectile Function, RR: risk ratio, N/A: not applicable, MD: mean difference.

[a]Risk of bias: All the trials had high risk of performance bias for not blinding the participants. Methodological quality of these trials was graded as "high risk of bias," due to the design of comparison (acupuncture therapy *versus* conventional medications) is difficult to blind personnel and participants. The trials also had unclear risk of performance bias for not reporting blinding the outcome assessor. [b]Inconsistency; There is significantly statistical heterogeneity indicating by I^2 value. [c]Imprecision: For dichotomous outcomes, the total number of events is less than 300, for continuous outcomes, the total population size is less than 400 or pooled results included no effects. [d]Indirectness. For outcomes of satisfaction of self-assessment rate, markedly improved on erectile function rate, and erectile angle. This was not internationally applied outcome measures. ⊕: Very low quality of the evidence; ⊕⊕: Low quality of the evidence.

dence of acupuncture for ED.

There are also some limitations of this systematic review. Firstly, the findings are summarized from original included trials with the poor quality and small sample size, which contributed to reduced internal validity of the pooling result. Secondly, it should be point out that although some combination of acupuncture appeared to show beneficial effect of acupuncture as an adjunctive treatment for ED according to the symptom improvement assessed by IIEF-5 scores scale or self-assessment,our analysis was not able to reach a clear recommendation regarding the effect of acupuncture on ED because most studies showed no benefit of acupuncture alone and variable outcome measure-

ments used among studies. It is difficult to draw a conclusion addressing the usage of acupuncture in ED without well-designed trials with a definitive outcome measurement.

3. Implications for practice

According to this review, the main acupuncture points used in the treatment of ED were *Guan Yuan* (CV4), *San Yin Jiao* (SP6), *Shen Shu* (BL23), *Zu San Li* (ST36), *Ming Men* (DU4), *Tai Chong* (LR3), *Tai Xi* (KI3), and *Ci Liao* (BL32). The stimulation of these acupionts aimed to achieve the needle sensation (*de qi*) during treatment. In addition, selecting acupionts of abdominal and lumbosacral regions (such as *Guan Yuan* [CV4], *Ci Liao* [BL32]) were expected to spread the sensation to the front of the penis or the perineum during the treatment period as well. TCM theory states that ED is usually caused by kidney yang or qi deficiency, the treating acupionts of *Shen Shu* (BL23), *Zhao Hai* (KI6) and *San Yin Jiao* (SP6) were prescribed accordingly [21,23,27,33]. ED may also be caused by other TCM pathophysiological factors such as "the damp-heat pouring downward", the treating acupionts of *Qu Quan* (LR8), *Zhong Wan* (RN12), and *Yin Ling Quan* (SP9) were prescribed accordingly [23,29,33]. However, current clinical evidence is insufficient to support its clinical use. Considering potential therapeutic effects of acupuncture, practitioners may consider its use based clinical experience and preference of patients.

4. Implications for research

Considering the variety of acupuncture therapy for ED, future trials should develop optimal acupuncture regimens for ED through Delphi process and/or experts' consensus, validated measurements or tools, such as IIEF-5 scales, to support appropriate interpretation of the findings [11]. In addition, the rational of acupuncture regimen and control should be specified appropriately, and avoid using of comparisons with unclear evidence of effect. To analyze if acupuncture therapy was effective in what kind of ED, the type information of ED participants will be expected to specify clearly in future trials. Furthermore, long-term effect of acupuncture for ED remains unclear. We suggest a follow-up period should be considered in future trials for the assessment of quality of sexual intercourse or sexual life progression.

To improve the quality of trial design and transparent reporting, we strongly suggest future trials should be prospectively registered on international registry platforms, conducted according to "good clinical practice", and reported according to the Consolidated Standards of Reporting Trials (CONSORT) and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) statement [35].

CONCLUSIONS

Due to insufficient and weak evidence that was summarized, the potential effect of acupuncture as adjunctive treatment (such as compared with tadalafil, psychological therapy or herbal medicine) mainly on psychogenic ED participants is inconclusive and safety of acupuncture was insufficiently reported. Findings of this review should be confirmed in large, rigorously designed and well-reported trial with a definitive outcome measurement.

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Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contribution

Conceived of the study: Liu JP. Searched literature, identified studies: Yang XY, Li XL. Extracted data: Li XL, Jia LY, Lai BY. Assessed study quality, analyzed data: Jia LY, Lai BY. Conducted the design of the study and drafted the manuscript: Lai BY. Revised the manuscript: Cao HJ, Yang GY, Grant S, Wong E, Fei YT. Read and approved the final manuscript: all authors.

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Appendix. Components of intervention and control in 22 included trials

Study ID	Comparison	The description of acupuncture component of prescription	Control treatment and component of prescription
Aydin et al (1997) [18]	EA *vs*. C1 or C2 or C3	EA: Qichong (ST30), Zusanli (ST36), Zhaohai (KI6), Guanyuan (CV4), Qihai (CV6). Follow-up for 7.6 months.	C1: Hypnotic therapy (3 times a week, later once a month). C2: placebo oral placebo (vitamin pill). C3: placebo needle different points compared to classical acupuncture points, 3 Hz direct-current (dc). Follow-up for 7.6 months.
Cao et al (2007) [31]	MA plus CHM *vs*. CHM	MA: Guanyuan (CV4), Shenshu (BL23), Mingmeng (EX-B6), Zusanli (ST36), Sanyinjiao (SP6), Zhibian (BL54), Taixi (KI3), and for guanyuan (CV4) expecting the sense of needle to radiate into the glans penis.	CHM (self-prescribed herbal decoction): Dodder (tu si zi) 20 g, Epimedium (yin yang huo) 15 g, Curl (xian mao) 15 g, Gekko gecko (ge jie) 2 g, Lycium barbarum (gou qi zi) 15 g, Radix rehmanniae (shu di huang) 18 g, Yam (shan yao) 21 g, Plantago (che qian zi) 12 g, Ginseng (ren shen) 10 g, Chinses Angelica (dang gui) 12 g, Achyranthes bidentate (niu xi) 12 g, Licorice (gan cao) 6 g.
Cheng and Cao (2009) [32]	MA plus CHM *vs*. CHM	MA: Zhibian (BL54). The tip of the needle to the direction of the genitals, and the needle sensation radiate to the penis with twirling and lifing-thrusting slightly.	CHM (self-prescribed herbal decoction): Dodder (tu si zi) 20 g, xian ling braned (xian ling pi) 15 g, Curl (xian mao) 15 g, Gekko gecko (ge jie) 2 g, rhizoma cibotii (gou ji) 12 g, Radix rehmanniae (shu di huang) 18 g, Yam (shan yao) 21 g, Plantago (che qian zi) 12 g, Ginseng (ren shen) 10 g, Chinses Angelica (dang gui) 12 g, Cistanche Cistanche (rou cong rong) 12 g, Chinese chive seed (jiu cai zi) 10 g.
Chen et al (2011) [19]	MA plus CHM *vs*. CHM	EA: Huiyang (BL35), Ciliao (BL32), Qugu (RN2), Huiyin (RN1), all points achieving qi with electrical stimulation.	CHM (compound Xuan Ju): Black ants (hei ma yi), epimedium (yin yang huo), Lycium barbarum (gou qi zi), and Fructus Cnidium (she chuang zi) etc.
Cui et al (2007) [16]	AIHE *vs*. AIS or CHM	AIHE: Guanyuan (CV4), Zuwuli (LR36), Huiyin (RN1), acupoint injection of herbal extract (Salvia miltiorrhiza injection and bupleurum injection), injection 2 mL/times, all points achieving qi, and the needle sensation radiate to the penis site for guanyuan (CV4) and huiyin (RN1).	C1: Guanyuan (CV4), Zuwuli (LR36), Huiyin (RN1), 1 mL/times, acupoint injection with saline, injection 2 mL/times, injection 2 mL/times, all points achieving qi, and the needle sensation radiate to the penis site; C2: CHM (Chun Yi capsule): Velvet antler (lu rong), Radix Rehmanniae Preparata (shu di huang), locust Yang (suo yang), Dodder (tu si zi), Chinese yam (shan yao), Polygonum multiflorum (he shou wu), Flos Sophorae (huai hua), Morinda officinalis (ba ji tian) Lycium barbarum (gou qi zi), Cistanche Cistanche (rou cong rong), Yellowish essence (huang jing), astragalus (huang qi), rhizoma cibotii (gou ji), Psoralen (bu gu zhi) etc., 0.5 g/times.
Dai et al (2003) [20]	MA plus CHM *vs*. CHM	MA: Baihui (DU20), Sishencong (EX-HN5), Yintang (EX-HN3), Qihai (CV6), Guanyuan (CV4), Sanyinjiao (SP6), Taixi (KI3), Ganshu (BL18), Shensu (BL23), Yinlingquan (SP9), Yongquan (KI1), Mingmen (EX-B6), all points achieving qi, and the needle sensation radiate to the penis for acupionts in abdomen. Follow-up for 2 weeks.	CHM (Kang Wei Ling decoction): centipede (wu gong) 18 g, Chinses Angelica (dang gui) 60 g, Paeonia lactiflora (bai shao) 60 g, Licorice (gan cao) 60 g, 2.5–4.5 g/times. Follow-up for 2 weeks.

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Appendix. Continued 1

Study ID	Comparison	The description of acupuncture component of prescription	Control treatment and component of prescription
Ding et al (2012) [33]	MA plus CHM *vs*. CHM	MA: Taichong (LR3), Guanyuan (CV4), Zhongfeng (LR4), Ganshu (BL18), Zusanli (ST36), Xuehai (SP10); kidney deficiency plus Shenshu (BL23), Sanyinjiao (SP6); dampness and heat downlink plus Ququan (LR8), Zhongwan (BN12), Fenglong (ST40), all points achieving qi, stimulating with 5 minutes interval.	CHM (Si Ni decoction): Tribulus terrestris (ci ji li) 30 g, Amethyst (zi shi ying) 30 g, Astragalus (huang qi) 30 g, Paeonia lactiflora (bai shao) 20 g, Fructus aurantii (zhi qiao) 20 g, Bupleurum Bupleurum (chai hu) 15 g, Chinses Angelica (dang gui) 15 g, Achyranthes bidentate (niu xi) 15 g, Hive (feng fang) 10 g, Dodder (tu si zi) 10 g, xian ling braned (xian ling pi) 10 g, centipede (wu gong) 10 g, kidney yin deficiency plus Lycium barbarum (gou qi zi) 10 g, Rehmannia glutinosa (sheng di huang) 20 g; kidney yang deficiency plus Curl (xian mao) 15 g, downward flow of dampness-heat plus Coix seed (yi yi ren) 30 g.
	MA *vs*. CHM	MA: Taichong (LR3), Guanyuan (CV4), Zhongfeng (LR4), Ganshu (BL8), Zusanli (ST36), Xuehai (SP10), kidney deficiency plus Shenshu (BL23), Sanyinjiao (SP6), dampness and heat downlink plus Ququan (LR8), Zhongwan (BN12), Fenglong (ST40), all points achieving qi, stimulating every 5 minutes.	CHM (modified herbal decoction): Tribulus terrestris (ci ji li) 30 g, Amethyst (zi shi ying) 30 g, Astragalus (huang qi) 30 g, Paeonia lactiflora (bai shao) 20 g, Fructus aurantii (zhi qiao) 20 g, Bupleurum (chai hu)15 g, Chinses Angelica (dang gui) 15 g, Achyranthes bidentate (niu xi) 15 g, Hive (feng fang) 10 g, Dodder (tu si zi) 10 g, xian ling braned (xian ling pi) 10 g, centipede (wu gong) 10 g, kidney yin deficiency plus Lycium barbarum (gou qi zi) 10 g, Rehmannia glutinosa (sheng di huang) 20 g, kidney yang deficiency plus Curl (xian mao) 15 g, downward flow of dampness-heat plus Coix seed (yi yi ren) 30 g.
Duan (2007) [17]	MA *vs*. CHM	MA: Shenshu (BL23), Taixi (KI3); Mingmen fire failure plus Mingmen (EX-B6), all points achieving qi.	CHM (You Gui pill): Radix rehmanniae (shu di huang), Monkshood (fu zi), Cinnamon (rou gui), Yam (shan yao), Fructus Corni (shan zhu yu), Dodder (tu si zi), Antler gum (lu jiao jiao), Lycium barbarum (gou qi zi), Chinses Angelica (dang gui).
Engelhardt et al (2003) [13]	MA *vs*. sham acupuncture	MA: Zhaohai (KI6), Shufu (KI27), Guanyuan (CV4), Qihai (CV6), Wangu (SI4), Sanyinjiao (SP6), Shenshu (BL23), 6.2 (range, 4–10 weeks).	Sham acupuncture: Xuanzhong (GB39), Jiexi (ST41), Tianshu (ST25) acupoints for headache.
Jiang et al (2014) [21]	MA plus CHM *vs*. CHM	MA: Taichong (LR3), Guanyuan (CV4), Qihai (CV6), Sanyinjiao (SP6), Zusanli (ST36), Ciliao (BL32), Shenshu (BL23), kidney deficiency plus Zhaohai (KI6), Shenshu (BL23), liver depression Taixi (KI3), Ganshu (BL18), all points achieving qi, stimulating every 3–5 minutes.	CHM (self-prescribed herbal decoction): Astragalus (huang qi) 25 g, Cur (xian mao) 12 g, Morinda officinalis (ba ji tian)15 g, Salvia miltiorrhiza (dan shen) 25 g, Radix Paeoniae Rubra (chi shao) 15 g, Poria cocos (fu ling) 15 g, Plantago (che qian zi) 12 g, Fructus Corni (shan zhu yu) 15 g, Achyranthes bidentate (niu xi) 15 g, Tribulus terrestris (bai ji li) 20 g.
Jiang et al (2012) [22]	MA plus physical training *vs*. physical training	MA: abdominal acupoint: Qihai (CV6), Guanyuan (CV4), Zhongji (BN3), Sanyinjiao (SP6), Taichong (LR3), Xingjian (LR2), Taixi (KI3), Yongquan (KI1), Neiguan (PC6), Shenmen (HT7), Baihui (DU20); back acupionts: Xinshu (BL15), Shenmen (HT7), Shenshu (BL23), Qihaishu (BL24), Mingmen (DU4), making the needle sensation spreads to penis or the buttocks for acupionts in abdomen, all points achieving qi.	Physical training: caress training for non genitalia and genitals (penis), encouraging patients to have sexual fantasies and imagine successful sexual intercourse, to increase the strength of the disgraced caudal muscle with abdominal breathing.

Appendix. Continued 2

Study ID	Comparison	The description of acupuncture component of prescription	Control treatment and component of prescription
Lin et al (2005) [23]	MA plus CHM *vs*. CHM	MA: Taichong (LR3), Zhongfeng (LR4), Ganshu (BL18), Zusanli (ST36); kidney deficiency plus Shenshu (BL23), Sanyinjiao (SP6); dampness and heat downlink plus Ququan (LR8), Zhongwan (BN12), all points achieving qi, stimulating needle every 3–5 minutes.	CHM (self-prescribed herbal decoction), paeoniae alba (bai shao) 20 g, Bupleurum (chai hu) 15 g, Chinses Angelica (dang gui) 15 g, Achyranthes bidentate (niu xi) 15 g, Pericarp (qing pi) 15 g, rhizoma cyperi (xiang fu) 10 g, Peach kernel (tao ren) 10 g, Clematis (wei ling xian) 10 g, Centipede (wu gong) 3 g, kidney yin deficiency plus Lycium barbarum (gou qi zi) 10 g, Rehmannia glutinosa (sheng di huang) 20 g; kidney yang deficiency plus Curl (xian mao) 15 g, Epimedium (xian ling pi) 15 g, downward flow of dampness-heat plus Phellodendron (huang bai) 10 g, Plantago (che qian zi) 10 g.
Liu et al (2016) [24]	AIHE plus tadalafil *vs*. tadalafil	AIHE: Huiyin (BN1), once every two days, injection of miltiorrhiza for acupoint, making points achieving qi, 1 mL/times.	Tadalafil tablet, 5 mg/times.
Liu (2017) [25]	MA plus moxibustion *vs*. tadalafil tablet	MA plus moxibustion: Taichong (LR3), Zhongfeng (LR4), Ganshu (BL18), Zusanli (ST36); kidney deficiency plus Shenshu (BL23), Sanyinjiao (SP6) downward flow of dampness-heat plus Ququan (LR8), Zhongwan (BN12), making points obtain qi, 10 sessions as a course, for 4 weeks, a moxibustion stick was put on the handle of the needle, 30 minutes.	Tadalafil tablet, 10 mg/time.
Liu and Ren (2015) [14]	MA plus psychotherapy *vs*. psychotherapy	MA: Mingmen (DU4), Shenshu (BL23), Guanyuan (CV4), Zhongji (BN3), Neiguan (PC6), Taixi (KI3), Qihai (RN6), Baihui (DU20), Sanyinjiao (SP6), Zhibian (BL54), Shuidao (ST28), to conduct the sensation of needle spread towards the perineum for acupionts in abdomen, all points achieving qi.	Psychotherapy: no detail treatment information.
Shan (2001) [26]	MA plus CHM *vs*. CHM	MA: Zhongji (RN3), Huiyang (BL35), radiating the sense of needle into the glans penis, all points achieving qi.	CHM (self-prescribed herbal decoction): Dodder (tu si zi) 15 g, Radix rehmanniae (shu di huang)15 g, Lycium barbarum (gou qi zi) 15 g, paeoniae alba (bai shao), Chinses Angelica (dang gui), Safflower (hong hua) 10 g, Ligusticum wallichii (chuan xiong) 10 g, Yam(shan yao)10 g, Fructus Corni (shan zhu yu) 10 g, Mingmen Fire failure plus Epimedium (xian ling pi), Cistanche Cistanche (rou cong rong); deficiency of heart and spleen plus Codonopsis pilosula (dang shen), Astragalus membranaceus (huang qi); depression of liver-qi plus Bupleurum Bupleurum (chai hu), Fructus aurantii (zhiqiao); downward flow of dampness-heat plus Gentian (long dan cao), Scutellaria baicalensis (huang qin).
Xie (2016) [27]	MA plus CHM *vs*. CHM	MA: Taichong (LR3), Guanyuan (CV4), Shenshu (BL23), Zusanli (ST36), Sanyinjiao (SP6), Ciliao (BL32), liver depression plus Ganshu (BL18), Taixi (KI3); kidney deficiency plus Yaoshu (DU2), Zhaohai (KI6), all points achieving qi, stimulating needle every 3–5 minutes.	CHM (Cong Rong Yi Shen granules): Schisandra chinensis (wu wei zi), Cistanche Cistanche (rou cong rong), Poria cocos (fu ling), Dodder (tu si zi).

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Appendix. Continued 3

Study ID	Comparison	The description of acupuncture component of prescription	Control treatment and component of prescription
Yang and Tian (2008) [34]	MA plus CHM *vs*. CHM	MA: Shenshu (BL23), Mingmen (DU4), Zhishi (BL52), Ciliao (BL32), Sanyinjiao (SP6), Zusanli (ST36), Qihai (RN6), Guanyuan (CV4), Qugu (RN2), all points achieving qi, stimulating needle every 10 minutes.	CHM (self-prescribed Shen Qi Er Xian herbal decoction): Astragalus (huang qi) 25 g, Salvia miltiorrhiza (dan shen) 30 g, Morinda officinalis (ba ji tian) 12 g, Curl (xian mao) 12 g, Epimedium (xian ling pi) 12 g, fructus psoraleae (bu gu zhi) 12 g.
Ye and Chen (2017) [28]	MA plus CHM *vs*. CHM	MA: Guanyuan (CV4), Sanyinjiao (SP6), Qu quan (LR8), Mingmen (DU4), Shenshu (BL23), Zusanli (ST36), all points achieving qi, stimulating needle every 5 minutes.	CHM (Huan Shao capsule): Radix rehmanniae (shu di huang), Lycium barbarum (gou qi zi), Yam (shan yao), Fructus Corni (shan zhu yu), Eucommia ulmoides (du zhong), Morinda officinalis (ba ji tian), Cistanche Cistanche (rou cong rong), Schisandra chinensis (wu wei zi), Fennel (xiao hui xiang), fructus broussonetiae (chu shi zi), Achyranthes bidentate (niu xi), Poria cocos (fu ling) etc. 2.1 g/times.
Jia (2018) [29]	MA plus moxibustion *vs*. tadalafil tablet	Guanyuan (CV4), Sanyinjiao (SP6), Baihuanshu (BL30), Huiyang (BL35), Ciliao (BL32), Zusanli (ST36), all points obtaining qi, for baihuanshu (BL30), huiyang (BL35), conduct ing the sensation of needle spread towards the perineum.	Tadalafil tablet, 5 mg/times.
Li et al (2018) [15]	EPAS plus tadalafil *vs*. tadalafil	Taichong (LR3), Guanyuan (CV4), Shenshu (BL23), Zusanli (ST36), Ciliao (BL32), Sanyinjiao (SP6), all acupionts were treated with EPAS.	Tadalafil tablet, 5 mg/times.
Yu et al (2018) [30]	MA plus sildenafil *vs*. sildenafil	SHangliao (BL31), Ciliao (BL32), ZHongliao (BL33), Xialiao (BL34), the needle handle is left on the skin flat and fixed with adhesive tape, maintaining 24 hours.	Sildenafil tablet, 12.5 mg/times, plus 25 mg one hour before sexual intercourse.

EA: electro acupuncture, MA: Manual Acupuncture, CHM: Chinese herbal medicine, AIHE: acupoint injection of herbal extract, AIS: Acupoint injection with saline, EPAS: moderate—frequency electrical pulse acupoint stimulation.