Effectiveness of acupuncture in the management of restless leg syndrome: a systematic review and meta-analysis

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Background: Acupuncture is an important component of traditional Chinese medicine which is used to treat an array of health conditions. This study evaluates the effectiveness of acupuncture in the management of restless leg syndrome (RLS).

Methods: A comprehensive literature survey was conducted in electronic databases to identify studies evaluating the effectiveness of acupuncture in the treatment of RLS. Cure, marked effect, effective, ineffective, and total effective rates of individual studies were pooled to achieve their respective overall estimates and a meta-analysis of mean change from baseline in International Restless Legs Syndrome Rating Scale (IRLSRS) was performed.

Results: A total of 18 studies were included in this meta-analysis, among which 640 RLS patients were treated with acupuncture alone or combined with other therapies (acupuncture group) and 447 RLS patients were treated with non-acupuncture therapies (control group). Cure, marked effect, and effective rates were 47.8% [95% confidence interval (CI): 38.3% to 57.3%], 27.4% (95% CI: 20.3% to 34.8%), and 24.2% (95% CI: 16.9% to 31.5%) in patients treated with acupuncture either alone or combination with other treatments, and 21.7% (95% CI: 20.7% to 22.7%), 28.0% (95% CI: 20.0% to 32.9%), and 22.3% (95% CI: 17.0% to 27.6%) in patients treated with non-acupuncture therapies, respectively. The ineffective rate was 4.7% (95% CI: 4.3% to 5.0%) in the acupuncture group and 32.9% (95% CI: 22.2% to 43.7%) in non-acupuncture groups. IRLSRS scores improved significantly after acupuncture treatment [mean change from baseline –9.45 (95% CI: –18.42 to –0.49); P=0.04].

Discussion: Although the overall quality of the included studies was low, the results of this meta-analysis suggested that acupuncture is an effective treatment option for RLS. Well-designed randomized controlled trials especially those involving a sham-acupuncture arm are needed to confirm these outcomes.

Keywords: Restless leg syndrome (RLS); acupuncture; moxibustion; cure; effect

Introduction

Restless leg syndrome (RLS) is a "movement-responsive nocturnal focal akathisia with dysesthesia" (1) characterized by an urge to fold and unfold the legs rapidly accompanied by an unpleasant sensation that interferes with sleep. These symptoms, which most often arise at night, are worse at rest and are relieved upon moving legs or walking (2,3). There are 2 forms of RLS: primary RLS has a strong hereditary background and onsets early in life to peak at an age of 20 years. Up to 40–60% of individuals with RLS have a family history of RLS. Secondary RLS is an adult condition and appears later in life. It is characterized by sporadic symptoms with slower regression which may also be associated with peripheral neuropathy (3).

The condition of RLS is under-diagnosed. The prevalence of RLS is reported to be between less than 1% to 15% in various parts of the world (11.4% for Swedish women and 5.8% for Swedish men, 10.8% for French women and 5.8% for French men, 9.8% for German elderly 65–83 years old, 10% in Canada, and 1% in Singapore) (4). RLS has been found to be associated with risk of cardiovascular disease (CVD) even after controlling for age, gender, race, body mass index, systolic blood pressure, antihypertensive drug use, diabetes, cholesterol, smoking, and apnea-hypoapnea index (5,6). Insomnia and daytime distress have also been found to be significantly associated with RLS (7). Age, pregnancy, lower socioeconomic status, low iron levels, poor health, poor mental health, Parkinson's disease, and end-stage renal disease have been identified as the risk factors for RLS (3).

Dopaminergic drugs such as levodopa are the first-line treatment for RLS (8). The analogues of gamma-aminobutyric acid such as gabapentin have been shown to be safe and efficacious in treating RLS of hemodialysis patients (9,10). Opioids, benzodiazepines, 4-phenyl-piperidine analogues, and alpha-2 adrenergic receptor agonists are also used for RLS treatment (11). Repetitive transcranial magnetic stimulation, pneumatic compression devices, counter-strain manipulation, infrared therapy, vibration pads, yoga, cryotherapy, and acupuncture are among the notable non-pharmacological treatments of RLS.

Acupuncture is an important component of traditional Chinese medicine (TCM) which is used to treat an array of health conditions. Insertion of acupuncture needles in various acupoints targeting energy channels is postulated to restore a balance that maintains health (12). Several studies have reported the outcomes of acupuncture in the management of RLS either as sole treatment or in combination with other related therapies, but the designs and the outcomes vary across these studies which necessitates a systematic review of this topic. The aim of the present study was to evaluate the effectiveness of acupuncture for the treatment of RLS by reviewing the outcomes of relevant studies in literature. We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2309).

Methods

Eligibility criteria

The inclusion criteria of the present study were: a study (I) evaluated the effectiveness of acupuncture either alone or with other related therapies for the management of RLS; (II) reported quantitative outcomes depicting the efficacy; and (III) reported the outcome measure/s which could depict the effectiveness in alleviating the symptoms of RLS such as sleep quality, pain, activity, and so on. The exclusion criteria were: other TCM methods were utilized without acupuncture; reported the outcomes without differentiating acupuncture from other therapies; or did not report quantitative information.

Literature search

For literature search, electronic databases consulted were: China National Knowledge Infrastructure (CNKI), Google Scholar, PubMed, and Wangfang. The important medical subject headings and keywords used as different phrases were: restless leg syndrome, RLS, acupuncture, acupoints, electro-acupuncture, hydro-acupuncture, tuina, massage, moxibustion, acuinjection, warm needle, stone scraping, traction, plum-blossom, and cupping. The search was delimited to original research papers published in English or Chinese language before October 2020.

Data and analyses

Important data pertaining to the demographic and clinical characteristics of patients, treatments, outcome measures, and outcomes were extracted from research articles by 2 authors independently. Inter-rater reliability was high (Cohen kappa =0.94). The primary endpoint for the
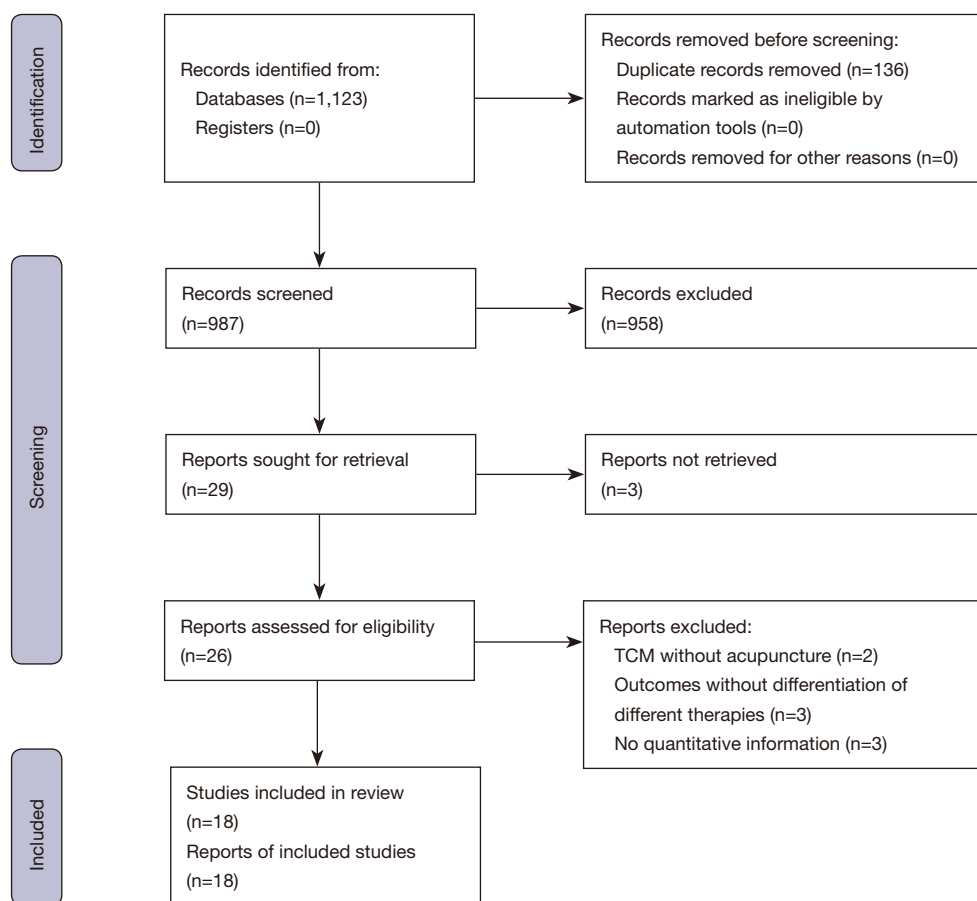
Figure 1 Flowchart of the study screening and selection process. TCM, traditional Chinese medicine.

present study was 'total effective rate' defined as the sum of 'cure rate', 'marked effect rate', and 'effective rate' of the treatment, where 'cure' was the disappearance of the symptoms of RLS with sufficient sleep (≥6 h); 'marked effect' was remission of the symptoms of RLS with almost normal sleep (5–6 h); 'effective rate' was relieving of the symptoms of RLS with alleviation of insomnia (4–5 h sleep); and 'ineffective rate' meant no remission of the symptoms (13). Additional endpoints were the changes in the International Restless Legs Syndrome Rating Scale score, Epworth Sleep Scale score, and the Pittsburgh Sleep Quality Index score.

For achieving the pooled effect size of the percent effectiveness rates, random effects meta-analyses were performed with Stata software (version 12; Stata Corp.; College Station, TX, USA) using DerSimonian-Liard method where the standard errors of the effectiveness rates were derived from sample sizes.

Statistical analysis

For the estimation of the change in the International Restless Legs Syndrome Rating Scale scores, a meta-analysis of mean differences was performed with Cochrane Review Manager software (version 5.3) using random-effects inverse-variance method.

Quality assessment of the included studies was performed with Newcastle-Ottawa Scale for the assessment of quality of observational cohort studies. Between-study inconsistency in outcomes (statistical heterogeneity) was estimated with I^2 index and sensitivity analyses were performed. Begg's test was performed to assess publication bias.

Results

A total of 18 studies (13-30) were included in this meta-analytical review (*Figure 1*). In these studies, 640 patients

with RLS were treated with acupuncture either alone or in combination with any other therapy and 447 patients were treated with non-acupuncture control therapies. A total of 10 studies performed acupuncture alone and rest of the studies performed acupuncture in combination with other therapies including moxibustion (n=3), cupping (n=1), injection (n=1), TCM herbal fumigation (n=1), gabapentin (n=1), and levodopa (n=1). Control treatments included levodopa with or without benserazide (n=5), non-acupuncture TCM (n=1), alprazolam/oryzanol (n=1), gabapentin (n=1), and vitamin $B_{1/12}$-Danshen (n=1). Quality of the included study was low to moderate in general (*Table 1*).

The total effective rate was 90.5% [95% confidence interval (CI): 86.2% to 94.9%] in patients treated with acupuncture either alone or in combination with other related treatments and 65.8% (95% CI: 52.1% to 79.5%) in patients treated with non-acupuncture therapies (*Figure 2*). Cure, marked effect, and effective rates were 47.8% (95% CI: 38.3% to 57.3%), 27.4% (95% CI: 20.3% to 34.8%), and 24.2% (95% CI: 16.9% to 31.5%) in patients treated with acupuncture either alone or in combination with other treatments and 21.7% (95% CI: 20.7% to 22.7%), 28.0% (95% CI: 20.0% to 32.9%), and 22.3% (95% CI: 17.0% to 27.6%) in patients treated with non-acupuncture therapies, respectively. The ineffective rate was 4.7% (95% CI: 4.3% to 5.0%) in the acupuncture group and 32.9% (95% CI: 22.2% to 43.7%) in non-acupuncture groups.

There was no difference in the total effective rate between acupuncture alone [91.6% (95% CI: 90.6% to 92.6%)] and acupuncture in combination with other therapies [92.2% (95% CI: 90.9% to 93.5%)]. Cure rate was higher in patients treated with acupuncture alone [51.1% (95% CI: 44.4% to 57.8%)] than in those treated with acupuncture in combination with other related therapies [44.1% (95% CI: 25.9% to 62.2%); *Figure 3*], but marked effect rate was lower in patients treated with acupuncture alone [16.1% (95% CI: 11.0% to 21.2%)] than in those treated with acupuncture in combination with other related therapies [38.7% (95% CI: 24.0% to 53.4%); *Figure 4*]. There was not much difference in the effective rate [24.8% (95% CI: 16.5 to 33.1) of acupuncture alone *vs.* 23.5% (95% CI: 12.5% to 34.6%) combination] but ineffective rate was slightly higher in the acupuncture group [9.22% (95% CI: 5.36% to 13.1%)] than in acupuncture in combination with other therapies [2.48% (95% CI: 2.12% to 2.84%)].

A meta-analysis of 2 studies showed significant improvement in International Restless Legs Syndrome Rating Scale scores after acupuncture treatment [mean change from baseline –9.45 (95% CI: –18.42 to –0.49); P=0.04; *Figure 5*].

Discussion

In this meta-analysis, we have found that acupuncture, especially in combination with other related therapies, was more effective than non-acupuncture therapies for RLS. However, some methodological issues kept this evidence at a low level. Only a few studies reported information about the number of acupuncture sessions performed; follow-up ranged from 1 month to 2 years; and majority of the included studies reported effectiveness rates without symptomatic improvement indices. Thus, well-designed randomized controlled trials are needed to confirm the findings of the present study.

Acupuncture is one of the important components of TCM that is recognized as an efficacious and safe treatment option for many health conditions including neurological and psychiatric diseases. Acupoints such as Shenshu (BL23), Xuehai (SP10), Chenshan (BL57), Zusanli (ST36), Sanyinjiao (SP6), and Taixi (KD3) are commonly involved in the treatment of RLS (31). As far as the mechanism of action is concerned, it is suggested that acupuncture may target the autonomic nervous system to manifest its effects. Acupuncture at Jianshi-Neiguan acupoints (PC5 to PC6 below median nerve) inhibits the sympathetic nerve and slows down excitatory cardiovascular reflexes via the opiate pathways which may trigger the inflammatory reflex and immune system (21). Moreover, acupuncture is reported to reduce oxidative stress in brain parts and promotes neuroprotection by increasing levels of BDNF, GDNF, and cyclophilin (32). Besides reducing oxidative stress, acupuncture treatment is also found to exhibit antiapoptotic and anti-inflammatory effects (33).

Acupuncturists emphasize that Yang deficiency in the legs causes symptoms like sensation of cold or fatigue in lower extremity whereas Yang stagnation which may represent disturbance of Shao Yang affects muscle tension. It is suggested that for improving Yang deficiency in the legs, needling in Tianshu (ST25) and Juxu Shanglian (ST37) acupoints can be useful whereas for the improvement in Yang stagnation, the acupoints Zhongdu (GB32) and Xiaoluo (TB12) are needed to be activated. Qi stagnation may also cause restlessness in the legs which can be treated by needling Dadun (LR1) and Yanglingquan (GB34). Ying deficiency and Yang stagnation leads to symptoms

Table 1 Newcastle–Ottawa scale for the assessment of quality of observational cohort studies

Study	Representativeness of exposed cohort?	Selection of non-exposed cohort?	Ascertainment of exposure	Comparability of cohorts on basis of design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohort
Lu & Yi, 2006 (13)	★		★		*		
Dai et al., 2006 (14)	★	★	★	★	*		
Di Stanislao et al., 2009 (15)	★		★		*	★	★
Jiang, 2013 (16)	★	★	★		*		
Li et al., 2007 (17)	★	★	★		*		
Li & Chen, 2011 (18)	★	★	★		*		
Liu, 2006 (19)	★		★		*	★	★
Liu et al., 2011 (20)	★	★	★		*	★	★
Pan et al., 2015 (21)	★		★		★		
Raissi et al., 2017 (22)	★	★	★		★		★
Shi & Wang, 2003 (23)	★		★	★	*	★	★
Tang & Tang, 2009 (24)	★	★	★		*		
Tian, 1994 (25)	★		★		*		
Wang & Zhang, 2011 (26)	★	★	★		*		
Wu et al., 2008 (27)	★	★	★		*		
Yu et al., 2016 (28)	★	★	★		*		
Zhang et al., 2014 (29)	★	★	★		*	★	★
Zhao et al., 2005 (30)	★	★	★		*	★	★

★, represents fulfillment of criterion using objective outcome measure; *, represents fulfillment of criterion using subjective outcome measure.

Study	Treatment	Cured	Marked effect	Effective	Ineffective	ES (95% CI)	% Weight
Treated							
Dai 2006	ACU-MOX	24		52		76.00 (72.58, 79.42)	5.51
Distanislao 2009	ACU G1	39	23	31	8	92.30 (87.08, 97.52)	5.27
Distanislao 2009	ACU G2					58.80 (55.15, 62.45)	5.48
Jiang 2013	ACU	48	16	16	19	80.65 (77.49, 83.81)	5.54
Liu 2006	ACU-INJ	84	14	2	0	100.00 (97.20, 100.00)	5.67
Liu 2011	ACU-TCM	35	50	15	0	100.00 (95.62, 100.00)	5.62
Lu 2006	ACU-MOX	43	33	24	0	100.00 (95.72, 100.00)	5.63
Li L 2007	ACU	51	24	21	0	100.00 (96.64, 100.00)	5.66
Li N 2011	ACU-MOX	38	24	29	10	90.50 (86.43, 94.57)	5.43
Shi 2003	ACU-St-ws	67.5	20	10	3	97.50 (94.44, 100.00)	5.57
Shi 2003	ACU-	47.5	15	12.5	25	75.00 (72.32, 77.68)	5.58
Tang 2009	ACU-DOPA		60	33	7	93.30 (90.48, 96.12)	5.57
Tian 1994	ACU					100.00 (97.75, 100.00)	5.68
Wang 2011	ACU-CUP	17	70		13	86.70 (83.37, 90.03)	5.52
Wu 2008	ACU	53		38		91.10 (89.00, 93.20)	5.63
Yu J 2016	ACU	57	21	14	7	92.90 (89.33, 96.47)	5.49
Zhao 2005	Mod ACU	73	7	17	2	97.60 (94.54, 100.00)	5.58
Zhang 2014	ACU	40	7	49	4	95.60 (92.74, 98.46)	5.57
Subtotal (I-squared = 98.4%, p = 0.000)						90.51 (86.18, 94.85)	100.00
.							
Control							
Dai 2006	L-Dopa	0		28	72	28.00 (25.93, 30.07)	8.35
Jiang 2013	Medoca	35	14	7	45	55.17 (52.47, 57.87)	8.34
Liu 2011	TCM	30	35	15	4	80.00 (76.08, 83.92)	8.31
Li L 2007	BENZ	40	15	20	26	75.00 (71.20, 78.80)	8.31
Li N 2011	L-Dopa	20	35	25	25	75.00 (71.20, 78.80)	8.31
Yu J 2016	L-Dopa	31	19	23	27	73.10 (69.81, 76.39)	8.33
Shi 2003	BENZ	45	15	17.5	22.5	77.50 (74.77, 80.23)	8.34
Tang 2009	L-Dopa		53	24	22	77.80 (75.22, 80.38)	8.34
Wang 2011	Vit B1/12	6.6	57		37	63.30 (60.45, 66.15)	8.34
Wu 2008	L-Dopa	0		30	70	30.40 (29.18, 31.62)	8.36
Zhao 2005	L-Dopa	35	15	25	25	75.00 (72.35, 77.65)	8.34
Zhang 2014	Trad ACU	27	22	31	20	80.00 (77.39, 82.61)	8.34
Subtotal (I-squared = 99.7%, p = 0.000)						65.83 (52.15, 79.51)	100.00

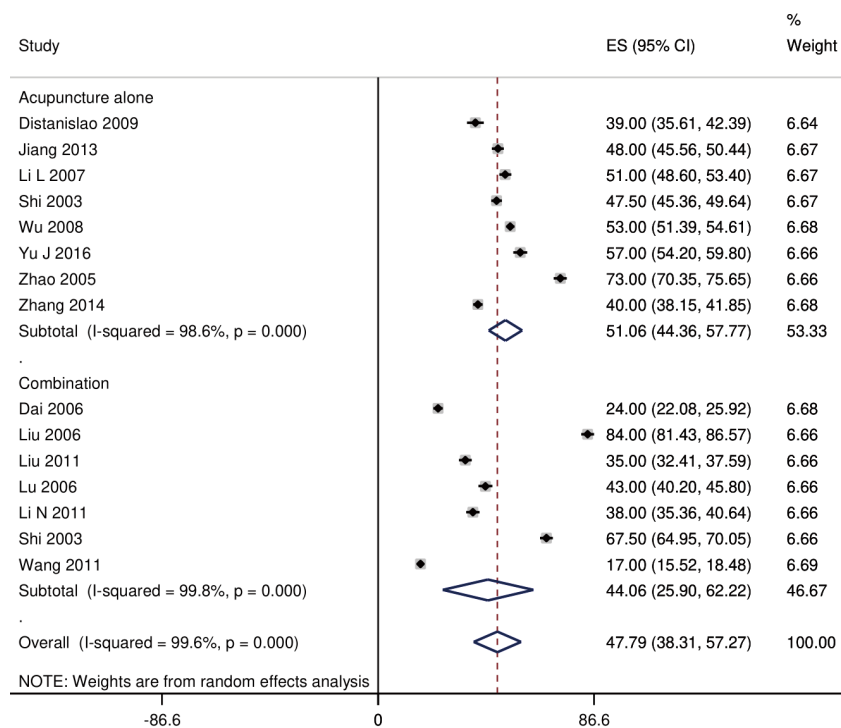NOTE: Weights are from random effects analysis

-100   0   100

Figure 2 Forest graph showing the total effective rates of treated and control groups. Columns after treatment are the percent values of cure, marked effect, effective, and ineffective rates. ACU, acupuncture; BENZ, bezodiazepine; DOPA-based therapy, dopamine, INJ, injection; L-DOPA, levodopamine, Mod, modern; MOX, moxibustion; St-ws, streaming and washing; TCM, traditional Chinese medicine; Trad, traditional; Vit, Vitamin.
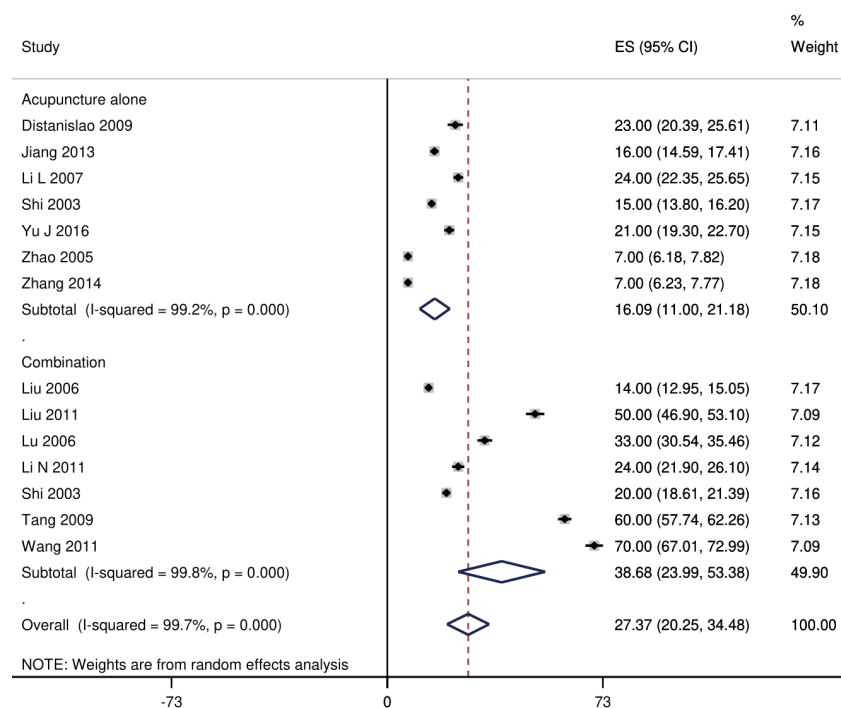
like cramps, cold feet, insomnia, urinary inconsistency, muscle tension, and urge for motion. Acupoints useful to address such symptoms are Zhongdu GB32 and LR6 (15). According to Pan *et al.*, liver yin and xue control lower limb activity at night and are also responsible for body and brain relaxation. When yin and xue become deficient, which may also be associated with qi imbalances, the conditions like RLS develop (21).

Among the included studies, Dai *et al.* (14) used Biguan (ST31) acupoint located on the line joining anterior superior iliac spine and the external edge of patella to dilate blood vessels and to activate qi which was substantiated

by the moxibustion heat conducting down the leg. Liu (19) who treated 49 RLS patients found a total eradication of symptoms in 41 patients and relief was persistent by 6-months follow-up. Liu (19) used Yanglingquan (GB34), Jinggu (BL64), Chengshan (BL57), Chengjin (BL57), Shangju (SP5), Ganshu (BL18), Shenshu (BL23), Taixi (KI3), Xuehai (SP10) and Sanyinjiao (SP6) acupoints. Pan *et al.* (21) used Shenshu (BL23), Mingmen (DU4), Xuehai (SP10), Chenshan (BL57), Taichun (LR3), Zusanli (ST36), Sanyinjiao (SP6), and Taixi (ST36) acupoints to apply standard acupuncture and found it effective in improving symptoms and sleep quality. Raisi

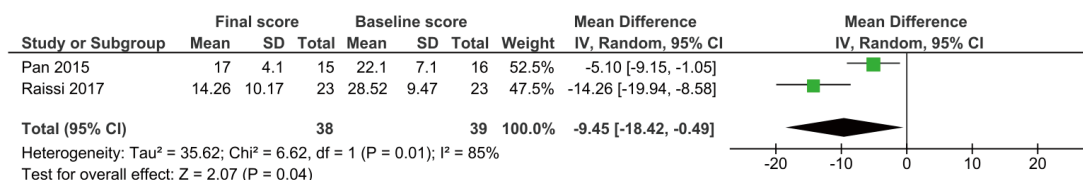| Study	ES (95% CI)	% Weight
Acupuncture alone		
Distanislao 2009	39.00 (35.61, 42.39)	6.64
Jiang 2013	48.00 (45.56, 50.44)	6.67
Li L 2007	51.00 (48.60, 53.40)	6.67
Shi 2003	47.50 (45.36, 49.64)	6.67
Wu 2008	53.00 (51.39, 54.61)	6.68
Yu J 2016	57.00 (54.20, 59.80)	6.66
Zhao 2005	73.00 (70.35, 75.65)	6.66
Zhang 2014	40.00 (38.15, 41.85)	6.68
Subtotal (I-squared = 98.6%, p = 0.000)	51.06 (44.36, 57.77)	53.33
.		
Combination		
Dai 2006	24.00 (22.08, 25.92)	6.68
Liu 2006	84.00 (81.43, 86.57)	6.66
Liu 2011	35.00 (32.41, 37.59)	6.66
Lu 2006	43.00 (40.20, 45.80)	6.66
Li N 2011	38.00 (35.36, 40.64)	6.66
Shi 2003	67.50 (64.95, 70.05)	6.66
Wang 2011	17.00 (15.52, 18.48)	6.69
Subtotal (I-squared = 99.8%, p = 0.000)	44.06 (25.90, 62.22)	46.67
.		
Overall (I-squared = 99.6%, p = 0.000)	47.79 (38.31, 57.27)	100.00
NOTE: Weights are from random effects analysis		

-86.6   0   86.6

Figure 3 Forest graph showing the cure rates of patients treated with acupuncture alone and acupuncture in combination with other related therapies.

Study	ES (95% CI)	% Weight
Acupuncture alone		
Distanislao 2009	23.00 (20.39, 25.61)	7.11
Jiang 2013	16.00 (14.59, 17.41)	7.16
Li L 2007	24.00 (22.35, 25.65)	7.15
Shi 2003	15.00 (13.80, 16.20)	7.17
Yu J 2016	21.00 (19.30, 22.70)	7.15
Zhao 2005	7.00 (6.18, 7.82)	7.18
Zhang 2014	7.00 (6.23, 7.77)	7.18
Subtotal (I-squared = 99.2%, p = 0.000)	16.09 (11.00, 21.18)	50.10
.		
Combination		
Liu 2006	14.00 (12.95, 15.05)	7.17
Liu 2011	50.00 (46.90, 53.10)	7.09
Lu 2006	33.00 (30.54, 35.46)	7.12
Li N 2011	24.00 (21.90, 26.10)	7.14
Shi 2003	20.00 (18.61, 21.39)	7.16
Tang 2009	60.00 (57.74, 62.26)	7.13
Wang 2011	70.00 (67.01, 72.99)	7.09
Subtotal (I-squared = 99.8%, p = 0.000)	38.68 (23.99, 53.38)	49.90
.		
Overall (I-squared = 99.7%, p = 0.000)	27.37 (20.25, 34.48)	100.00
NOTE: Weights are from random effects analysis		

-73   0   73

Figure 4 Forest graph showing the marked effect rates of patients treated with acupuncture alone and acupuncture in combination with other related therapies.

Study or Subgroup	Final score			Baseline score			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Pan 2015	17	4.1	15	22.1	7.1	16	52.5%	-5.10 [-9.15, -1.05]
Raissi 2017	14.26	10.17	23	28.52	9.47	23	47.5%	-14.26 [-19.94, -8.58]
Total (95% CI)			38			39	100.0%	-9.45 [-18.42, -0.49]

Heterogeneity: Tau² = 35.62; Chi² = 6.62, df = 1 (P = 0.01); I² = 85%
Test for overall effect: Z = 2.07 (P = 0.04)

Figure 5 Forest graph showing the meta-analysis of mean change from baseline in International Restless Legs Syndrome Rating Scale score after acupuncture treatment.

et al. (22) who treated RLS patients with acupuncture in combination with gabapentin, used Shenshu (BL23), Ganshu (BL18), Chenshan (BL57), Jinggu (BL64), Zusanli (ST36), Liangqiu (ST34), Shangqiu (SP5), Xuehai (SP10), Shanyijiao (SP6), Taixi (KI3), Yanglingquan (GB34), Xuanzhong (GB39) acupoints and found that the combinational therapy had some additive effect in comparison with gabapentin monotherapy.

In the present study, a meta-analysis of 2 studies found a statistically significant improvement in International Restless Legs Syndrome Rating Scale scores 6–8 weeks after acupuncture treatment. Pan *et al.* (21) also found changes in the Epworth Sleep Scale score, and sleep mean activity to be significantly better in acupuncture group than in control group 6 weeks after treatment. Raissi *et al.* (22) found a significant difference in the Pittsburgh Sleep Quality Index score between acupuncture and control groups 8 weeks after treatment.

Some other studies have also reported that acupuncture is an effective treatment option for RLS. In a retrospective analysis of 19 patients, Cripps (34) found acupuncture efficacious in alleviating the symptoms of RLS. He used BL57 and LR3 acupoints bilaterally and stimulated these with electroacupuncture for 20–30 minutes. Greater improvement was noticed in patients who had not received previous dopaminergic therapy. In a single-blind, randomized controlled trial, 60 hemodialysis patients with RLS received 12 sessions of near infrared (940 nm) treatment to acupoints in the lower limb 3 times a week. In this study, clinically significant improvement was observed, but upon discontinuation the effect was diminished (35). Describing 2 cases with RLS who were treated with acupuncture, Fukutome (36) reported that 4W-acuinjection in Zulinqi (GB41), Kunlun (BL60), Zusanli (ST36), and Sanyinjiao (SP6) acupoints led to immediate relief in the form of a calm sensation and cessation of involuntary movements in legs.

A recent review found that besides acupuncture, other non-pharmacological treatments including repetitive transcranial stimulation, precise physical exercises, sequential pneumatic compression devices, use of counterstain techniques, and infrared exposure also remain effective in relieving RLS symptoms (37). Regardless of the treatment strategy, several factors can have impacts on the incidence, prevalence, and treatment of RLS. Among the socioeconomic factors, female gender, unemployment, retirement, less education, and low income are found to be associated with RLS (38). Depression is frequently associated with RLS. In a study of community-dwelling elderly, 1 in 8 individuals with RLS had depression whereas 1 in 25 individuals without RLS had depression. Men with RLS were more likely to take antidepressant medication (39). There is evidence to suggest that the use of antidepressant medication can aggravate RLS (40).

Acupuncture effects observed in trials are often suspected for the presence of placebo effect or expectation bias (41,42). However, a recent randomized controlled trial found that raising expectations of the participants before acupuncture treatment had no effect on the outcomes, but the incidence of side effects was significantly more in the group that was intensely briefed about side effects possibilities (43). It is suggested that addition of a sham-acupuncture arm in acupuncture trials can yield a better clarity of the outcomes (44).

Among the notable limitations of the present study, less availability of non-Chinese literature is an important consideration. We observed high statistical heterogeneity in the pooled analysis which could be attributed to the use of many types of controls and many therapeutic combinations with acupuncture. To test sources of heterogeneity, we performed meta-regression analyses but neither study sample size nor follow-up duration, or year of study publication were significantly associated with total effective rate. Definitions of effectiveness rates were not given by

most of the included studies and there may have been some between-studies deviation in measuring the actual effect of therapy.

Conclusions

According to this meta-analysis, acupuncture either alone or in combination with other related therapies is an effective treatment option for RLS. Cure rate significantly differed between acupuncture and non-acupuncture therapies (48% *vs.* 22%). Several limitations, including the variations in combinational and control treatments, methodological inconsistencies, variation in follow-up durations, and the lack of effect measurement standards kept the level of this evidence low. Therefore, randomized trials with better designs and suitable controls especially with a sham-acupuncture arm are required to seek refined evidence.

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Footnote

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