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Review

Acupuncture for essential hypertension

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ABSTRACT

Background: To systematically assess the current clinical evidence of acupuncture for hypertension.
Search strategy: The PubMed, EMBASE, Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), and Wan-fang Data in the Cochrane Library were searched until January, 2013. All the randomized controlled trials (RCTs) based on acupuncture compared with western medicine, sham acupuncture or lifestyle intervention in patients with hypertension were included. RCTs were included as well as combined acupuncture with western medicine compared with western medicine. In addition, RCTs based on acupuncture compared with sham acupuncture combined with western medicine in patients with essential hypertension were included. No language restriction was used. Review Manager 5.1 software was used for data analysis. Study selection, data extraction, quality assessment, and data analyses were conducted according to the Cochrane standards.
Results: 35 randomized trials (involving 2539 patients) were included. The methodological quality of the included trials was evaluated as generally low. Two trials reported the effect of acupuncture compared with sham acupuncture in combinations of western medicine. Acupuncture significantly reduced SBP (−7.47 mm Hg, 95% CI −10.43 to −4.5, $P < 0.00001$) and DBP (−4.22 mm Hg, 95% CI −6.26 to −2.18, $P < 0.0001$) and no heterogeneity between studies was detected. However, other studies had substantial heterogeneity due to the quality of them was poor, and their sample sizes were not satisfactory as an equivalence study. Five trials described the adverse effects.
Conclusions: While there are some evidences that suggest potential effectiveness of acupuncture for hypertension, the results were limited by the methodological flaws of the studies. Therefore, further thorough investigation, large-scale, proper study designed, randomized trials of acupuncture for hypertension will be required to justify the effects reported here.

1. Introduction

Hypertension is a well-recognized risk factor for cardiovascular disease and stroke, which are the most frequent cause of deaths all over the world [1,2]. It has been estimated that 29% of the world's adult population, or ≈1.56 billion people, will have hypertension by the year of 2025 [3]. Essential hypertension (EH), a complex disease, which accounts for 95% of hypertensive cases, is an increasingly serious worldwide public-health challenge and is generally considered as a paradigmatic multi-factorial disease that is determined by a combination of genetic factors, environmental stimuli and their interaction [4,5]. The prevention and management of hypertension are major public health challenges. Evidence from randomized control trials (RCTs) has showed that a small reduction in blood pressure (BP) may result in a large reduction in the risk of stroke and myocardial infarction [6,7]. The antihypertensive treatment has made great progress in modern medicine. The therapeutic drugs include six classes of antihypertensive agents and fixed compound preparation [8–10]. However, there is concern that the benefits demonstrated in RCTs of antihypertensive medication are not implemented in everyday clinical practice and that the long-term use of western medicine will produce some side effects, even produce resistance and affect therapeutic efficacy, only 53% of patients treated for hypertension had blood pressure actually controlled to ≤140/90 mm Hg [11,12]. Therefore, seeking for a new effective decompression method is an important subject of hypertension treatment.

Complementary and alternative medicine (CAM) is recognized and accepted in Europe and America that have developed a high degree of modern medicine, as an important complement to the western mainstream medicine system [13,14]. Recent researches showed that CAM could be regularly recommended for lowering elevated blood pressure (BP) [15–17]. Traditional Chinese Medicine (TCM) is a main component of CAM, including herbal medicine, acupuncture, moxibustion, and cupping, Taichi and Qigong. Acupuncture has been a component of the

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Chinese health-care system for at least 2500 years and is widely practiced in the United States [18]. Acupuncture is based on the TCM concept that there are channels (or "meridians") of energy flow ("qi") within the body that help maintain the health of the individual and that disease and pain result from imbalances of qi [19]. Acupuncture as a nonpharmacological intervention has been used to treat a wide variety of condition to regulate cardiovascular diseases, and acupuncture therapy is used on patients with mild or borderline hypertension who want to avoid treatment cost, adverse effects, and complications [20]. Possible mechanisms by which acupuncture reduces blood pressure in hypertensive patients include decreases in plasma renin, aldosterone and angiotensin II activity [21,22], increased excretion of sodium and changes in plasma norepinephrine, serotonin and endorphin levels [23,24]. Meanwhile, there have been a large number of clinical trials of acupuncture on hypertension and RCTs [25,26]. In addition, several reviews claimed that acupuncture has therapeutic effects on blood pressure in patients with hypertension [27,28]. These reviews are, however, non-systematic and are therefore open to bias. The aim of this systematic review is to assess randomized clinical trials (RCTs) rigorously testing the effectiveness of acupuncture in human patients with hypertension.

2. Materials and methods

The supporting PRISMA checklist is available as supporting information; see Checklist S1.

2.1. Database and search strategies

Literature searches were conducted in the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (January, 2013), the PubMed, EMBASE, Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), Wan-fang Data. Databases in Chinese were searched to retrieve the maximum possible number of trials of acupuncture for essential hypertension because acupuncture is mainly used and researched in China. All of those searches ended on January, 2013. Ongoing registered clinical trials were searched in the website of international clinical trial registry by U.S. National Institutes of Health (http://clinicaltrials.gov/). The following search terms were used individually or combined: 'hypertension', 'blood pressure', 'essential hypertension', 'acupuncture', 'electroacupuncture' (EA), 'clinical trial', and 'randomized controlled trial'. The bibliographies of included studies were searched for additional references.

2.2. Inclusion criteria

All the parallel randomized controlled trials (RCTs) of all the prescriptions based on "acupuncture" compared with western medicine, sham acupuncture or lifestyle intervention in patients with hypertension were included. RCTs were included as well, combined "acupuncture" with western medicine compared with western medicine. In addition, RCTs based on acupuncture compared with sham acupuncture combined with western medicine in patients with essential hypertension were included. Studies were excluded if they were nonrandomized studies and/or involving other forms of acupuncture such as transcutaneous electrical nerve stimulation, laser acupuncture. There were no restrictions on population characteristics, language and publication type. The main outcome measure was blood pressure. Duplicated publications reporting the same groups of participants were excluded.

2.3. Data extraction and quality assessment

Two reviewers (W. Liu, X. J. Xiong) extracted data and evaluated data's quality and content independently. We conducted data extraction using a standardized procedure. Initially, abstracts were screened to exclude obviously ineligible reports, and then all remaining articles were reviewed. We classified trials and abstracts according to patient characteristics, study design, and therapy duration. Reviewing study design included the following criteria: methods of sequence generation, allocation concealment, complete description of those who were blinded, and use of intention-to-treat analysis and whether the trial was stopped prior to the planned duration, all methodological features in addition capable of impacting effect sizes. The outcome measures included BP and adverse events. The data was entered into an electronic database by the two reviewers separately, avoiding duplicate entries; in the case where the two entries did not match, an inspection will be conducted, and a third person may be involved for verification. In order to obtain full information regarding conference abstracts, we had contacted the study authors by email and/or telephone communication. Disagreement was resolved by discussion and reached consensus through a third party (J. Wang).

The methodological quality of trials was assessed independently using criteria from the Cochrane Handbook for Systematic Review of Interventions, Version 5.1.0 (W. Liu, X. J. Xiong) [29]. The items included random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases. The quality of all the included trials was categorized to low/unclear/high risk of bias ("Yes" for a low of bias, "No" for a high risk of bias, "Unclear" otherwise). Then trials were categorized into three levels: low risk of bias (all the items were in low risk of bias), high risk of bias (at least one item was in high risk of bias), unclear risk of bias (at least one item was in unclear).

2.4. Risk of bias across studies

Funnel plots were generated to visualize the possible publication bias.

2.5. Data synthesis

We used Revman 5.1 software provided by the Cochrane Collaboration for data analyses. Studies were stratified by the type of comparison. Continuous outcome will be presented as mean difference (MD) and its 95% CI. Heterogeneity was recognized significant when $I^2 \geq 50\%$. Fixed effects model was used if there is no significant heterogeneity of the data; random effects model was used if significant heterogeneity existed ($50\% < I^2 < 85\%$). Publication bias was explored using a funnel plot.

3. Results

3.1. Description of included trials

A flow chart depicted the search process and study selection (as shown in Fig. 1). After primary searches from the databases, 1081 articles were screened. After reading the titles and abstracts, 976 articles of them were excluded. Full texts of 35 articles [30–64] were retrieved, and 70 articles were excluded with reasons listed as the following: participants did not meet the inclusive criteria (n = 34), duplication (n = 5), no control group (n = 10), Patients complicated with other diseases (n = 10) and no data for extraction (n = 11). In the end, 35 RCTs were included, and all trials had been conducted in four different countries, most of the RCTs were conducted in China and published in Chinese (31 trials), a German journal [61], and English journals [60,62,63]. The characteristics of included trials were listed in Table 1.

2539 patients with essential hypertension were included, with the average number of 72 per trial, ranging from 14 to 192. There was a wide variation in the age of subjects (18–78 years). 24 trials specified 10 diagnostic criteria of hypertension, 11 trials [34,35,38,41,46–48,50,52,55,64] used 1999 WHO–ISH guidelines for the management of hypertension (1999 WHO–ISH GMH), 3 trials [30,40,56] used 1998 WHO–ISH guidelines for the management of hypertension (1998 WHO–ISH GMH), 3 trials [39,42,49] used Chinese Guidelines for the Management of Hypertension—2005 (CGMH—2005), one trials [37] used China Guidelines on Prevention and Management of High Blood Pressure—2006 (CGPMHBP—2006), 3 trials [43,44,51] used 2000 WHO–ISH guidelines for the management of hypertension (2000 WHO–ISH GMH), one trial [58] used the National Forum on Epidemiology of Cardiovascular Diseases in 1979, 2 trials [31,54] used 1978 WHO–ISH guidelines for the management of hypertension (1978 WHO–ISH GMH), 2 trials [53,60] used the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), one trial used the prevention and control of hypertension guidelines of China 2004, one trial [63] used European Society of Hypertension–European Society of Cardiology Guidelines 2003, and 7 trials [32,33,36,45,57,61,62] only demonstrated patients with essential hypertension.

Interventions included acupuncture or electro-acupuncture alone, or combined with western medicine. Acupuncture was the sole treatment in 25 trials, whereas in 10 trials, acupuncture was used as an adjunct treatment for medication. The controls included western medicine compared alone, sham acupuncture or combined with western medicine, and lifestyle intervention. As for control, sham acupuncture was adopted for control in 3 trials [61,62], 2 trials [57,63] used sham acupuncture plus western medicine, whereas 29 [30–56,58,59] and one trial [64] used lifestyle intervention. Participants received 10 to 30 min per session acupuncture treatments for mean 32 days (ranged

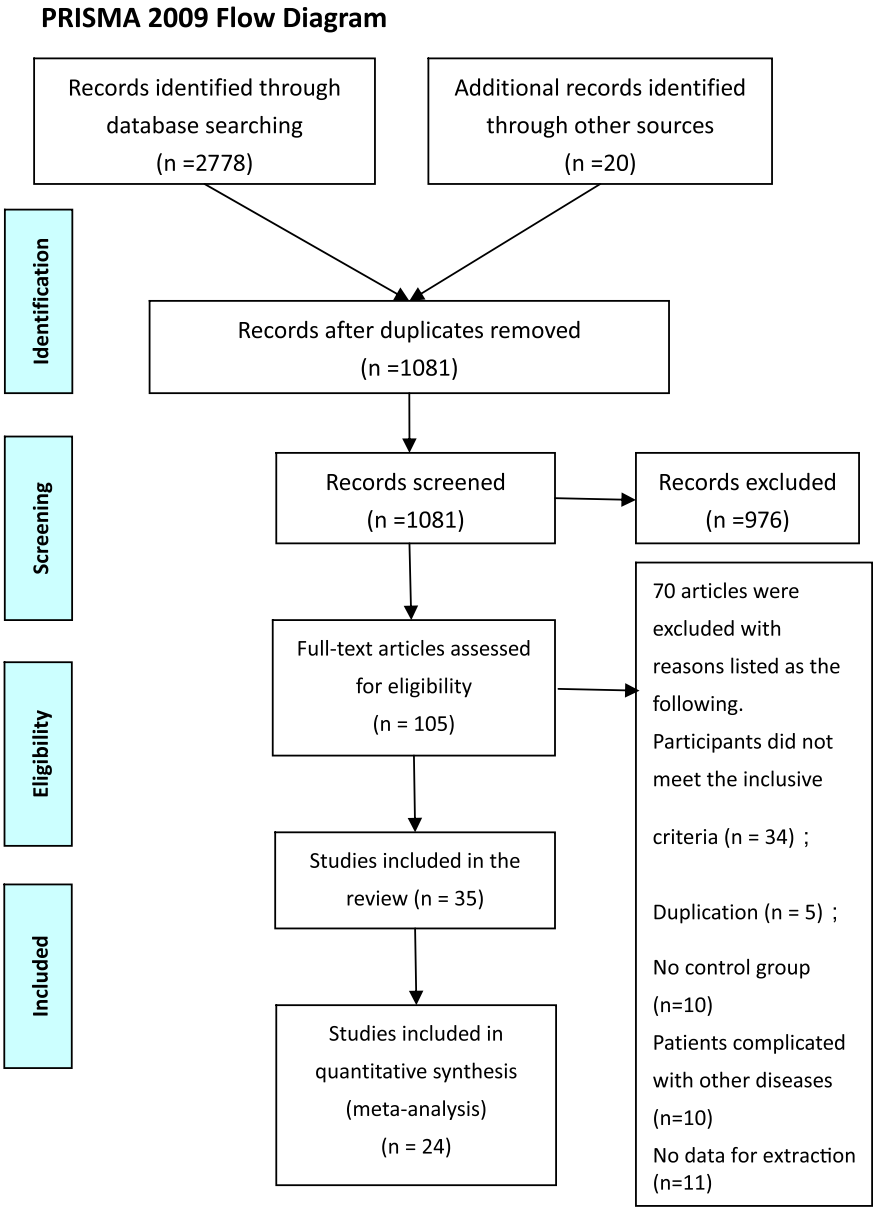

Fig. 1. PRISMA 2009 Flow diagram.

from 10 to 90 days). The most frequently used acupoints were HeGu (LI4), Tai Chong (LR3), Feng Chi (GB20), Qu Chi (LI11), and Bai Hui (GV20), followed by, Feng Long (ST40) and Nei Guan (PC6). All of the 24 trials used the BP as the outcome measure, and 5 trials described the adverse effect [54,57,60–62].

3.2. Methodological quality of included trials

The methodological quality of most included trials was generally "poor" according to the predefined quality assessment criteria (Table 2). The randomized allocation of participants was mentioned in all trials; however, only 8 trials stated the methods for sequence generation including random number table [30,36,37,50,57,59,62] and drawing [34]. However, insufficient information was provided to judge whether or not it was conducted properly. Allocation concealment was only mentioned in 4 RCTs [57,60,62,63]. Double-blind was not mentioned in all trials. However, as the testing acupuncture and controlled drug were in different forms, neither the participants nor the investigators were likely to be blinded. Only one trial reported drop-out or withdraw [59]. However, the trial did not intend to analyze the cause, and no trials used intention-to-treat analysis. None of the trials had a pre-trial estimation of sample size. Five trails reported information on follow-up [32,53,59,61,62]. Selective reporting was generally unclear in the RCTs due to the inaccessibility of the trail protocol.

3.3. Effect of the interventions

35 RCTs were included in the group of studies of patients with essential hypertension ([30–64]). The effect estimates of acupuncture were shown in the Figs. 2–3.

3.3.1. Acupuncture versus western medicine

A total of 19 trials [30,31,33,34,37,41,42,44–52,54,55,59] reported the effect of acupuncture compared with western medicine on hypertension. A change in blood pressure was reported in 11 trials [37,41,42,44,45,47,48,50,52,54,59] of the included RCTs.

Only 4 independent trials did show better effect: Yang [37] demonstrated that electro-acupuncture on Qu Chi (LI11) and Tai Chong (LR3)

Table 1
Characteristics and methodological quality of included studies.

Study ID	Sample (M/F)	Age (yrs)	Diagnosis standard	Intervention	Control	Course (day)	Outcome measure
Feng and Wu [30]	60 T:18/12; C:14/16	T:47.35 ± 11.59 C:48.35 ± 10.64	1998 WHO–ISH GMH	Acupuncture	Captopril tablets (25 mg tid)	30 (7 days/week; 20 min per day)	BP
Li and Niu [31]	59 T:15/13; C:17/14	T:61.4 ± 9.2 C:61.7 ± 9.6	1978 WHO–ISH GMH	Acupuncture	Nimodipine (40 mg tid)	10 (30 min per day, 5 days/course)	BP
Luo [32]	68 T:25/13; C:21/9	T:61.2 C:63.2	Hypertension diagnostic criteria (unclear)	Acupuncture plus western medicine	Western medicine	90 (15 days/course)	BP
Liu [33]	50 M/F:18:32; T:24; C:26	18 to 70 (T/C not reported)	Hypertension diagnostic criteria (unclear)	Acupuncture	Captopril tablets	30 (once a day, 10 days/course)	BP
Yang and Zhou [34]	60 M/F:35:25; T1:20 T2:20 C:20	35 to 75 (T/C not reported)	1999 WHO–ISH GMH	Acupuncture	Hydrochlorothiazide (12.5–25 mg bid)	21 (once a day, 7 days/course)	BP
Liu [35]	86 T:25/23; C:22/16	T:63.2 C:61.5	1999 WHO–ISH GMH	Acupuncture plus western medicine	Captopril tablets (12.5 mg bid or tid)	90 (once a day, 15 days/course)	BP
Zhang [36]	80 T:29/16; C:24/11	T:53.62 ± 9. 83 C:52.16 ± 10.04	Hypertension diagnostic criteria (unclear)	Acupuncture plus western medicine	Benzene sulfonic acid amlodipine piece (2.5 mg qd)	28 (20 min per day, 28 days/course)	BP
Yang [37]	98 T:17/13; C:20/10	T:40.4 ± 5.2 C:41.7 ± 4.2	China Guidelines on Prevention and Management of High Blood Pressure—2006 (CGPMHBP—2006)	Electroacupuncture	Captopril tablets (12.5 mg tid)	14 (30 min once a day)	BP
Wang and Cheng [38]	59 34/25	25 to 60 (T/C not reported)	1999 WHO–ISH GMH	Electroacupuncture plus western medicine	Benazepril hydrochloride tablets (10 mg qd)	56 (30 min once a day, 56 days/course)	BP
Jia et al. [39]	92 T:32/14; C:30/16	T:46.4 ± 5.7 C:44.7 ± 6.8	Chinese Guidelines for the Management of Hypertension—2005 (CGMH—2005)	Acupuncture plus western medicine	Left-hand amlodipine (5 mg qd)	30 (30 min per day, 28 days/course)	BP
Liu et al. [40]	106 T:30/23; C:28/25	T:46.4 ± 5.2 C:45.2 ± 6.3	1998 WHO–ISH GMH	Acupuncture plus western medicine	Captopril tablets (12.5 mg tid)	30 (20 min per day)	BP
Liao et al. [41]	90 T:31/28; C:17/14	T:56.5 ± 7.9 C:55.6 ± 8.6	1999 WHO–ISH GMH	Acupuncture	Captopril tablets (12.5 mg tid) and Aspirin enteric-coated tablets (75 mg qd)	14 (30 min every time; twice a day, 7 days/course)	BP
Ma et al. [42]	80 T:25/15; C:22/18	T:66.39 ± 5.4 C:64.58 ± 7.1	Chinese Guidelines for the Management of Hypertension—2005 (CGMH—2005)	Electroacupuncture	Nicardipine piece (20 mg tid)	15 (10 min once a day, 15 days/course)	BP
Hu et al. [43]	60 T:20/10; C:22/8	T:77.8 ± 4.2 C:77.1 ± 3.4	2000 WHO–ISH guidelines for the management of hypertension (2000 WHO–ISH GMH)	Acupuncture plus western medicine	Amlodipine (5 mg qd)	20 (30 min once a day, 10 days/course)	BP
Chen et al. [44]	70 T:19/16; C:19/16	T:63.57 ± 8.08 C:65.20 ± 8.86	2000 WHO–ISH GMH	Acupuncture	Nifedipine (10–20 mg tid)	14(15–30 min once a day, 14 days/course)	BP
Guo et al. [45]	60 T:16/14; C:17/13	T:32 to 64 C:32 to 65	Hypertension diagnostic criteria (unclear)	Acupuncture	Enalapril maleate (10 mg qd)	30 (30 min once a day, 28 days/course)	BP
Huang et al. [46]	60 T:18/12; C:20/10	T:54.75 ± 7.12 C:51.72 ± 10.38	1999 WHO–ISH GMH	Acupuncture	Metoprolol (100 mg qd)	14 (30 min once a day)	BP
Wang et al. [47]	60 T:20/10; C:21/9	T:54.75 ± 7.1 C:67.8 ± 12.0	1999 WHO–ISH GMH	Acupuncture	Metoprolol (100 mg qd)	28 (30 min once a day, 14 days/course)	BP
Guo [48]	80 T:22/18; C:23/17	T:43.84 ± 8.3 C:44.20 ± 8.4	1999 WHO–ISH GMH	Acupuncture	Enalapril maleate (10 mg qd)	30 (30 min once a day, 30 days/course)	BP
Cheng [49]	84 T:27/15; C:24/18	30 to 65 (T/C not reported)	Chinese Guidelines for the Management of Hypertension—2005 (CGMH—2005)	Acupuncture	Levamlodipine besylate tablets (2.5 mg qd)	20 (30 min every time, the next day at a time, 10 times/course)	BP
Huang et al. [50]	60 T:14/16; C:13/17	T:56.51 ± 6.28 C:58.12 ± 6.15	1999 WHO–ISH GMH	Acupuncture	Captopril tablets (25 mg tid)	28 (30 min every time)	BP
Zhang et al. [51]	60 T:22/8; C:20/10	T:56.5 C:55.5	2000 WHO–ISH GMH	Acupuncture	Compound reserpine tablets (1 tablet tid)	15 (30 min once a day)	BP
Ye et al. [52]	100 T:28/22; C:26/24	T:42 to 64 C:41 to 64	1999 WHO–ISH GMH	Acupuncture	Metoprolol sustained release tablet (12.5 mg bid)	14 (30 min once a day)	BP
Shen et al. [53]	50 T:15/10; C:16/9	T:57.32 ± 8.2 C:58.21 ± 7.3	Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)	Acupuncture plus western medicine	Extended release Nifedipine tablets (20 mg bid)	25 (30 min once a day, 10 days/course)	BP
Dan [54]	52 T:19/7; C:18/8	T:57.8 ± 10.9 C:58.4 ± 11.6	1978 WHO–ISH GMH	Acupuncture	Nifedipine (10 mg tid)	21 (20–30 min once a day, 5 days/week)	BP; adverse effect
Wu et al. [55]	60 T1:7/13; T2;6/14 C:11/9	T1:55.9 ± 8.1 T2:55.6 ± 6.0 C:55.00 ± 6.4	1999 WHO–ISH GMH	Acupuncture	Captopril tablets (25 mg tid)	5 (30 min once a day, 5 days/course)	BP
Zhang et al. [56]	75 T:28/17; C:19/11	T:63.60 ± 8.20 C:65.20 ± 8.00	1998 WHO–ISH GMH	Acupuncture plus western medicine	Nifedipine (10 mg tid)	20 (30 min once a day, 20 days/course)	BP

Table 1 (*continued*)

Study ID	Sample (M/F)	Age (yrs)	Diagnosis standard	Intervention	Control	Course (day)	Outcome measure
Yin et al. [57]	41 T:4/11; C:5/10	T:49 to 56 C:51 to 57	Hypertension diagnostic criteria (unclear)	Acupuncture	Sham acupuncture plus antihypertensive medication	56 (30 min a day at an easy pace during the 8 week period)	BP; adverse effect
Jiang et al. [58]	60 T:24/6; C:22/8	T:56.7 ± 10.3 C:57.5 ± 9.9	The National Forum on Epidemiology of Cardiovascular Diseases in 1979	Acupuncture plus western medicine	Captopril (12.5–25 mg tid)	21 (30 min a day, once a day, for 6 days as one therapeutic course)	BP
Wan et al. [59]	60 T:19/1; C:17/13	T:63.72 ± 8.23 C:65.24 ± 6.41	2004 The prevention and control of hypertension guidelines of China	Electroacupuncture	Nicardipine tablets (20 mg tid)	15 (10 min once a day, 5 days/course)	BP
Kim et al. [60]	33 T:8/4; C:8/8	T:52.08 ± 8.69 C:52.38 ± 10.3	Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)	Acupuncture	Sham acupuncture	56 (20 min/time, twice a week)	BP; adverse effect
Kraft K. et al. [61]	14 (T/C not reported)	50.0 ± 4.6 (T/C not reported)	Hypertension diagnostic criteria (unclear)	Acupuncture	Sham acupuncture	84 (20 min/day)	BP; adverse effect
Macklin [62]	192 T1:64 T2:64 C:64	T1:56.8 ± 8.4 T2:55.9 ± 10.6 C:53.2 ± 9.5	Hypertension diagnostic criteria (unclear)	Acupuncture	Sham acupuncture	70 (twice-weekly 30 min)	BP; adverse events
Flachskampf [63]	160 T:54/46; C:40/60	T:58.8 ± 8.2 C:58.0 ± 7.9	European Society of Hypertension–European Society of Cardiology Guidelines 2003	Acupuncture	Sham acupuncture plus antihypertensive medication	42 (each session lasted 30 min. during the first 2 weeks, 5 sessions were administered weekly, and in the following 4 weeks, 3 sessions were administered weekly)	BP; adverse events
Zhao and Fan. [64]	60 T:19/11; C:18/12	T:40.3 ± 11.4 C:46.1 ± 14.2	1999 WHO–ISH GMH	Acupuncture	Lifestyle intervention	30 (20 min/day, 10 days/course)	BP

Abbreviations: T, intervention group; C, control group.

Table 2
Quality assessment of included randomized controlled trials.

Included trials	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Risk of bias
Feng [30]	Table of random number	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear
Li [31]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Luo [32]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Liu [33]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Yang [34]	Drawing	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear
Liu [35]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Zhang [36]	Table of random number	Unclear	Unclear	Unclear	Yes	No	Unclear	Unclear
Yang [37]	Table of random number	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Wang [38]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Jia et al. [39]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Liu et al. [40]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Liao et al. [41]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Ma et al. [42]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Hu et al. [43]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Chen et al. [44]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Guo et al. [45]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Huang et al. [46]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Wang et al. [47]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Guo [48]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Cheng [49]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Huang et al. [50]	Table of random number	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Zhang et al. [51]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Ye et al. [52]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Shen et al. [53]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Dan [54]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Wu et al. [55]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Zhang et al. [56]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Yin et al. [57]	Table of random number	opaque envelopes	Unclear	Unclear	Yes	No	Unclear	Unclear
Jiang et al. [58]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	High
Wan et al. [59]	Table of random number	Unclear	Unclear	Unclear	No	No	Unclear	Unclear
Kim et al. [60]	Unclear	opaque envelopes	Unclear	Unclear	Yes	No	Unclear	Unclear
Kraft K. et al. [61]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High
Macklin [62]	Table of random number	opaque envelopes	Unclear	Unclear	Yes	No	Unclear	Unclear
Flachskampf [63]	Unclear	opaque envelopes	Unclear	Unclear	Yes	No	Unclear	Unclear
Zhao and Fan. [64]	Unclear	Unclear	Unclear	Unclear	Yes	No	Unclear	High

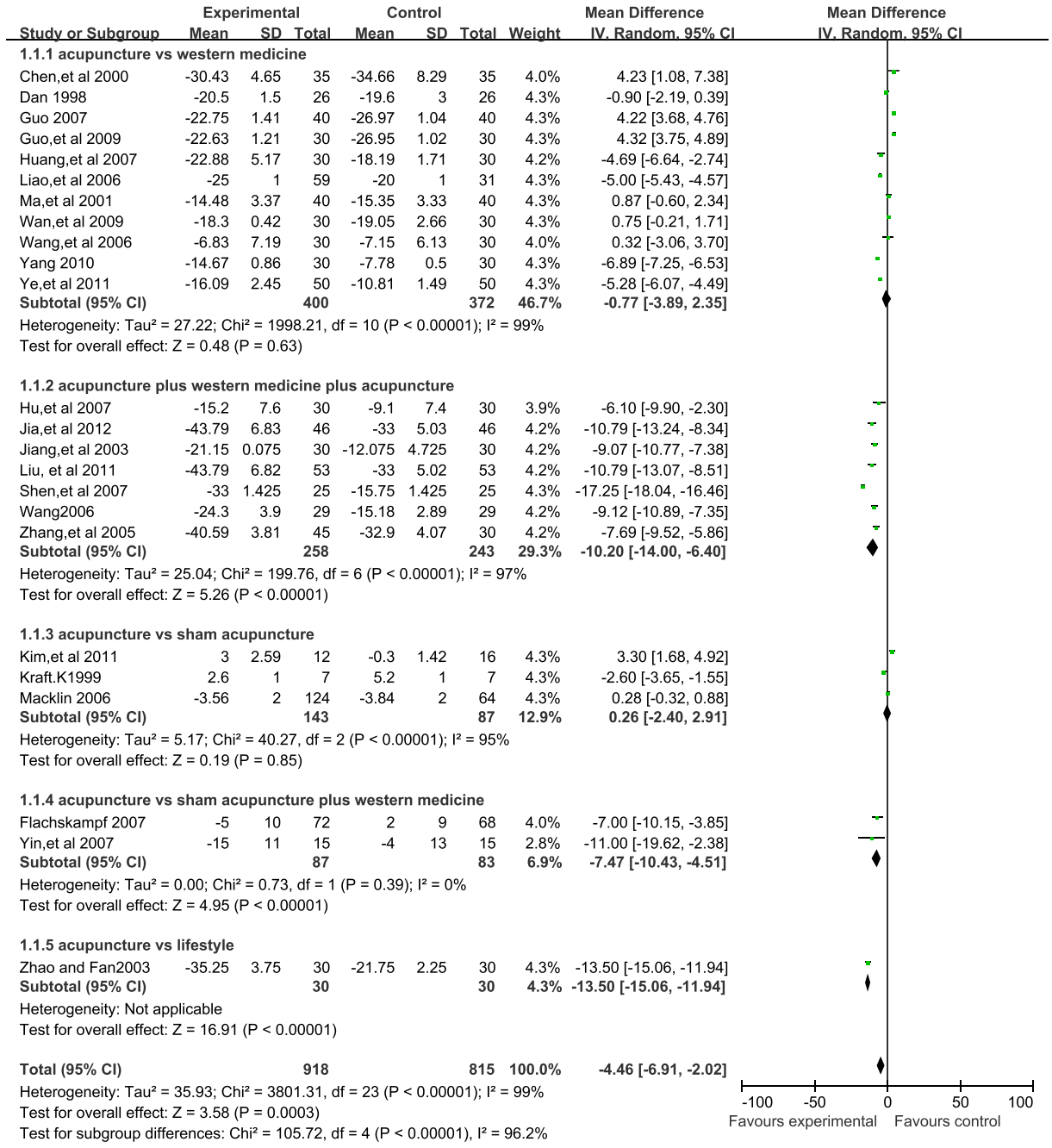

Fig. 2. The forest plot of outcome measure SBP.

has long-term antihypertensive effect and improves effectively day–night rhythm variation in young patients with hypertension (systolic blood pressure [SBP]: mean difference = −6.89 mm Hg, 95% confidence intervals = −7.25 to −6.53; diastolic blood pressure [DBP]: −1.12, −1.94 to −0.30); Liao et al. [41] have shown that "reducing south and reinforcing north" needling method have better effect than oral administration captopril tablets and Aspirin in reducing blood pressure (SBP: −6.89, −5.43 to −4.57; DBP: −3.00, −4.31 to −1.69); Huang et al. [50] considered that acupuncture treatment has obvious effect of decreasing blood pressure with very significant differences as compared with those before treatment and the control group (SBP: −4.69, −6.64 to −2.74; DBP: −3.31, −4.58 to −2.04); Ye et al. [52] discovered that acupuncture has obvious antihypertensive effect, and the buck than metoprolol sustained release tablet groups (SBP: −5.28, −6.07 to −4.49; DBP: −1.68, −2.30 to −1.06).

3.3.2. Acupuncture plus western medicine versus western medicine

Ten trials [32,35,36,38–40,43,53,56,58] compared the combination of acupuncture plus medicine compared with medicine compared. A change in blood pressure was reported in 7 trials [38–40,43,53,56,58] of the included RCTs. Among them, all trials demonstrated acupuncture combined western medicine is better than western medicine alone on SBP, and 5 trials [38,43,53,56,58] showed there are no statistically significant differences on DBP. Acupuncture plus benazepril hydrochloride tablets [38] showed better effect compared to benazepril hydrochloride tablets. The combinations of acupuncture and left-hand amlodipine [39] had better effect compared to left-hand amlodipine. Acupuncture combined with captopril tablets [40,58] is superior to captopril tablets. Acupuncture plus amlodipine [43] is better than amlodipine used alone. The combination of acupuncture and extended release nifedipine tablets [53,56] surpassed extended release nifedipine tablets.

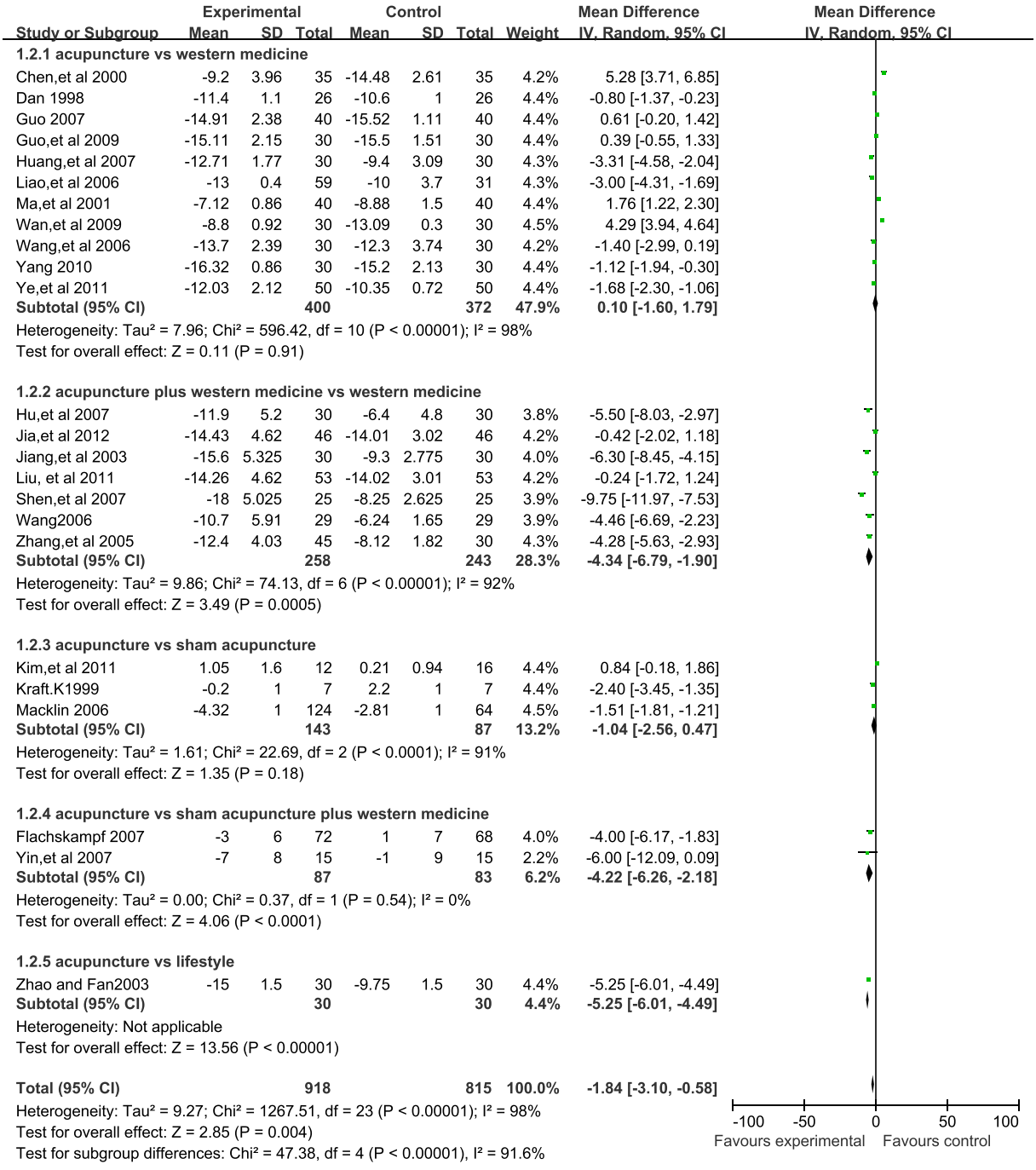

Fig. 3. The forest plot of outcome measure DBP.

3.3.3. Acupuncture versus sham acupuncture

A total of three trials [60–62] reported the effect of acupuncture individually compared with sham acupuncture. Among them, only one trial [61] discovered the better effect on both SBP and DBP (SBP: −2.60, −3.65 to −1.55; DBP: −2.40, −3.45 to −1.35). One trial [62] described acupuncture is superior to sham acupuncture to reduce DBP (−1.51, −1.81 to −1.21).

3.3.4. Acupuncture versus sham acupuncture plus western medicine

Two trials reported the effect of acupuncture compared with sham acupuncture in combinations of western medicine. One trial [57] discovered the better effect on both SBP and DBP (SBP: −7.00, −10.15 to −3.85; DBP: −4.00, −6.17 to −1.83). The other trial [63] described that acupuncture is superior to the combination group to reduce SBP (−11.00, −19.62 to −2.38).

3.3.5. Acupuncture versus lifestyle intervention

Only one trial showed acupuncture individually versus lifestyle intervention. There are statistically significant differences on the acupuncture group to lifestyle intervention using alone (SBP: −13.50, −15.06 to −11.94; DBP: −5.25, −6.01 to −4.49).

3.4. Adverse effect

Only six trials [54,57,60–63] described the adverse even. Among them, two trials recorded two specific symptoms including transient

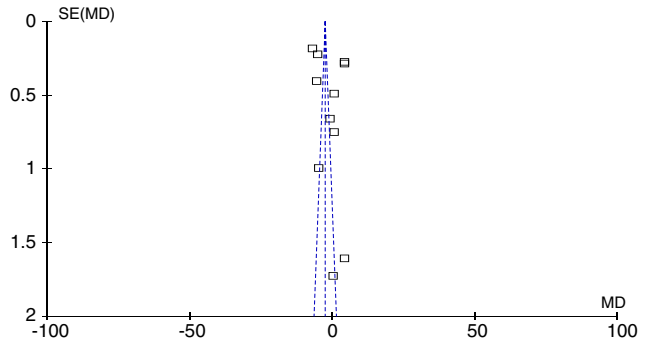

Fig. 4. Comparison of SBP in acupuncture versus western medicine.

slight injection-site pain [63] and small bleeding or spot-bleeding [57] in the acupuncture group. One trial reported three cases of serious adverse events, in which patients stopped antihypertensive drugs during study period [62], two participants experienced hypertensive urgencies in the acupuncture group and one congestive heart failure in the control group during follow-up. In addition, no adverse events were found in three trials [54,60,61].

3.5. Publication bias

The forest plot of comparison of acupuncture versus western medicine for the outcome blood pressure was shown in the Figs. 4–5.

4. Discussion

Hypertension is a major public health problem with serious medical and financial consequences. Medical interventions for those with severe hypertension generally have to use antihypertensive drugs such as diuretics, α- and β-blockers, angiotensin-converting enzyme inhibitors, and long-acting calcium-channel blockers [65]. However, barriers to successful conventional pharmacological treatment include side effects, out-of-pocket expenses, patient noncompliance and insufficient dosages of prescribed medications [66–69]. An advantage of acupuncture is its relatively low incidence of serious or debilitating side effects [70]. Two SRs [71,72] of acupuncture on hypertension have been reported, however, most of languages the selected databases of them are English except 4 [60–63], much of the acupuncture literature in hypertension is in non-English language publications. Furthermore, electronic literature searches for RCTs to June 2007 and September 2008, they might have left out some important studies, and new high-quality RCTs have been recently published. Therefore, we decided to assess the current clinical evidence of acupuncture for hypertension.

Based on the paper and meta-analyses of the outcome on either SBP or DBP, acupuncture may have positive effects for lowing BP. Five subgroups were analyzed based on methodological variables of acupuncture arms and control arms. The BP-lowering effect of acupuncture plus western medicine was significantly higher than that of western medicine (SBP: −10.20, −14.00 to −6.40, P < 0.0001; DBP: −4.34, −6.79 to −1.90, P = 0.0005). The BP also decreased significantly from baseline with acupuncture than sham acupuncture plus western medicine (SBP: −7.47, −10.43 to −4.5, P < 0.00001; DBP: −4.22, −6.26 to −2.18, P < 0.0001). Acupuncture achieved significant effect modification on BP change magnitude compared with lifestyle (SBP: −13.50, −15.06 to −11.94, P < 0.00001; DBP: −5.25, −6.01 to −4.49, P < 0.00001), whereas, compared with western medicine, acupuncture showed no significant effect modification (SBP: −0.77, −3.89 to −2.35, P = 0.63; DBP: 0.10, −1.60 to 1.79, P = 0.91). Compared with sham acupuncture, acupuncture statistically showed no significant effect modification with statistically significant heterogeneity (SBP: 0.26, −2.40 to 2.91, P = 0.25; DBP: −1.04, −2.56 to 0.47, P = 0.18). However, according to potential publication bias and low-quality trials, available data are not adequate to draw a definite conclusion of acupuncture for essential hypertension. And the positive findings should be interpreted conservatively.

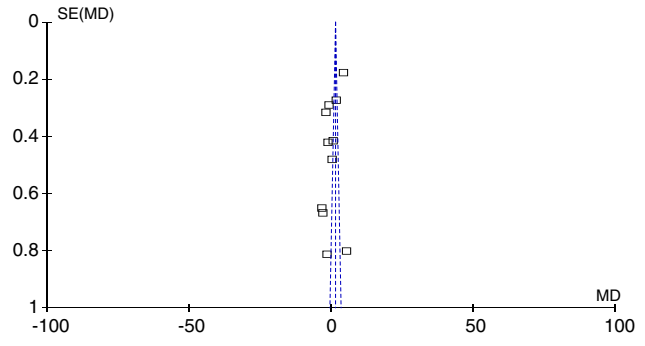

Fig. 5. Comparison of DBP in acupuncture versus western medicine.

Before recommending the conclusion of this review to clinical practice, we have to consider the following weaknesses in this review. Firstly, in accordance with previous studies [73], the quality of the included RCTs was generally low. The 35 trials included in this paper had risk of bias in terms of design, reporting, methodology. Only 8 RCTs stated randomization procedure, for the rest 27 trials, they just mentioned that 'the patients were randomized into two groups' with no further information. Allocation concealment was only mentioned in 4 RCTs [57,60,62,63]. A number of trials [32,33,35–37,48,49,54] only have one author, which is impossible for an RCT to be done properly in terms of randomization procedure and the allocation concealment. Therefore, we could suspect the truth of some of these claimed RCTs. In addition, all the trials did not describe the blinding in details. It directly led to performance bias and detection bias due to patients and researchers being aware of the therapeutic interventions for the subjective outcome measures. If poorly designed, all the trials would show larger differences compared with well designed trials [74,75].

Secondly, heterogeneity is worthy of being paid attention to. Many factors affect the effects of heterogeneity, such as acupuncture modalities, acupoint selection, frequency and duration of the treatment sessions. One of the major limitations was the application of various kinds of acupuncture point treatments used in different trials. More than 30 different acupoints were investigated in the 35 trials. The acupoints differed in meridians, syndromes, and the clinical efficacy. It is difficult to assess the effect of a particular acupuncture point by means of the evidence synthesis of studies. As a result, it is impossible to conduct meaningful meta-analysis for a specific acupoints, or difficult to undertake subgroup analyses to explore specific factors that may have an impact on the effects of the treatment regimen. In addition, two acupuncture modalities were reported, i.e. manual acupuncture and electroacupuncture. Most of them used manual acupuncture and electroacupuncture was selected in 4 RCTs [37,38,42,59]. In addition, the differences of frequency and duration of the treatment sessions (10 to 30 min per session acupuncture treatments, ranged from 10 to 90 days) affected the effects of acupuncture, thus made contributions to the great heterogeneity. Not only that, all trials specified 10 diagnostic criteria of hypertension without 7, selective reporting bias might exist in this conclusion, and reduce the homogeneity of the research objects. All the 24 RCTs prohibited us to perform meaningful sensitivity analysis.

Thirdly, only 6 trials of 24 trials did mention adverse effect. Even for the trials that reported adverse events, their report was very brief, providing limited information. Therefore, a conclusion about the safety of acupuncture cannot be made clearly. Five trails reported information on follow-up, but not mentioned the details. In order to properly assess

the safety of acupuncture, large-scale clinical trials with long-term follow-up are required.

In addition, of the 35 included trials, most of them were in Chinese language and only 3 in English language, and one in German language. China generates virtually no 'negative' studies at all. In other word, publication and other biases may play an important role. We tried to take all measures to contact authors to get further information either by telephone, letter, or e-mail. Unfortunately, we got no replies, and we are not sure, the trials were conducted as true RCT.

In summary, our study showed that acupuncture could lower SBP and DBP, however, because of the unclear methodological quality of these identified trials, a definite conclusion on efficacy and adverse events associated with acupuncture cannot be drawn from this review. Therefore, further thorough investigation, large-scale, rational study design, randomized trials of acupuncture for hypertension will be required to justify the effects reported here. Future trials should overcome the limitations of the trials presented in this review; particularly, they should assure adequate concealment of allocation and blinding of outcome assessors and use functional outcome as the primary outcome measured at long-term follow-up. Reports of the trials should conform to the recommendations of the CONSORT statement [76]. If reliable RCT results confirmed acupuncture positive effects for treatment of hypertension, it would be blessing news to use complementary and alternative medicine for hypertension.

Authors' contribution

Jie Wang and Xingjiang Xiong contributed equally to this paper.

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