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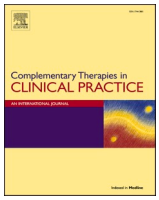

Association between acupuncture and grade 1 hypertension: A systematic review and meta-analysis

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ABSTRACT

Background: Acupuncture is a traditional therapy that can be potentially effective for treating high blood pressure. Grade 1 hypertension is a relatively mild form of hypertension. This meta-analysis aims to assess the efficacy and safety of acupuncture in patients with grade 1 hypertension.
Methods: We systematically searched the EMBASE, PubMed, Cochrane, China National Knowledge Infrastructure, and Wan Fang databases for randomised controlled trials investigating acupuncture therapy for grade 1 hypertension through March 2021. The primary outcomes were changes in blood pressure after acupuncture and efficacy of acupuncture. The secondary result was an adverse reaction to the treatment. Data were pooled and analysed using Review Manager 5.3 and Statistical Package for the Social Sciences software version 19.0.
Results: Ten randomised controlled trials involving 1196 patients were included. Our meta-analysis demonstrated that in terms of changes in systolic blood pressure (MD 3.62 mmHg; 95% CI, 1.34 to 5.90; $I^2 = 56\%$), diastolic blood pressure (MD 3.12 mmHg; 95% CI, 1.03 to 5.20; $I^2 = 77\%$), and treatment efficacy (RR 2.12; 95% CI, 1.38 to 3.26; $I^2 = 93\%$), acupuncture is more effective in treating grade 1 hypertension than a placebo, no treatment at all, or interventions that improve lifestyle alone, with a low incidence of adverse effects. However, we did not find a suitable subgroup to reduce heterogeneity. Interventions, acupuncture methods, and treatment courses were not the only sources of heterogeneity among the studies.
Conclusion: Existing evidence shows that acupuncture could be used for treating hypertension; however, higher-quality randomised controlled trials are needed to better evaluate the safety and efficacy of acupuncture.

1. Introduction

Hypertension, also known as high blood pressure, is a condition in which there is sustained elevated blood vessel pressure. Hypertension increases the incidence of secondary diseases, such as heart, brain, and kidney damage, which are additional health burdens. According to the World Health Organization (WHO) [1], hypertension is the leading cause of premature death worldwide, and approximately 1.13 billion people suffer from hypertension. However, for various reasons, fewer than one in five hypertensive patients on an average receive adequate treatment.

According to the Eighth Joint National Committee (JNC-8) [2] and 2018 Chinese guidelines for the management of hypertension [3], grade 1 hypertension refers to systolic blood pressure (SBP) of 140–159 mmHg and/or diastolic blood pressure (DBP) of 90–99 mmHg. However, most patients with grade 1 hypertension do not present with obvious cardiovascular symptoms; thus, they receive lesser attention from doctors than those with grades 2 and 3 hypertension [4,5]. Few patients and clinicians believe that for patients with mild hypertension, antihypertensive treatment has little benefit [6]. In contrast, an increasing number of studies have shown that antihypertensive treatment is helpful and can provide positive cardiovascular effects by reducing the probability of stroke, myocardial infarction, acute decompensated heart failure, and death from cardiovascular causes [7,8]. Therefore, it is necessary to actively control grade 1 hypertension and prevent further deterioration, which agrees with the preference of Chinese medicine for prompt disease treatment to avoid complications.

Currently, the most commonly used treatment for hypertension in

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clinical practice is drug therapy, which mainly includes angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, beta blockers, or thiazide diuretics [2]. However, it is worth noting that due to their inability to persist in taking the drugs, 50% of patients stop treatment after 1 year [9]. Drug side effects are common reasons for treatment discontinuation. For example, beta-blockers can cause bradycardia [10]. Approximately 9% of patients discontinue medication because of unpleasant side effects, and they may prefer other treatment options. Consequently, it is essential to introduce an alternative or complementary therapy to reduce or eliminate the number of medicinal pills taken daily, thereby increasing the treatment compliance by 20% [11,12].

Acupuncture is a safe and effective choice; Acupuncture therapy originated in China more than 3000 years ago and spread to Europe and the United States from the 16th to the 19th century [13]. Previous studies have confirmed that acupuncture, in addition to antihypertensive treatment, has a better blood pressure-lowering effect and can assist antihypertensive drugs to enhance their blood pressure-lowering potency [14–16]. However, in the existing literature, there is no systematic review on acupuncture interventions for grade 1 hypertension. Therefore, we conducted a systematic review and meta-analysis to evaluate the safety and effectiveness of acupuncture for the treatment of grade 1 hypertension.

2. Materials and methods

This systematic review was registered (Invoice Number: CRD42021246343) in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/) and has been reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Assessing the Methodological Quality of Systematic Reviews (AMSTAR) Guidelines [17,18].

2.1. Search strategy

We searched the EMBASE, PubMed, Cochrane, China National Knowledge Infrastructure (CNKI), and Wan Fang databases. The following keywords combined with Medical Subject Headings (MeSH) terms were used for searching: “acupuncture”, “acupuncture therapy”, “needle therapy”, “needle warming therapy”, “moxibustion”, “electro-acupuncture”, “needle”, “pinprick”, “acupoint”, “hypertension”, “essential hypertension”, “high blood pressure”, “grade 1 hypertension”, “grade I hypertension”, “mild hypertension”, “blood pressure”, “clinical study”, “clinical trial”, “clinical research”, “randomised controlled trial”, “randomised”, “RCT”. The detailed search strategy is presented in Supplementary Table S1. In addition, we carefully scanned the references of randomised controlled trial articles and related reviews that met the search criteria to ensure that the literature search for meta-analyses was complete. No language restrictions were applied. Data collection was completed in March 2021 and we searched documents in the databases up to that point.

2.2. Eligibility criteria

Two researchers independently evaluated the literature according to the inclusion criteria listed below. If there was any dispute, a third reviewer made the final decision.

Inclusion criteria:

(1) Randomised controlled trials (RCTs) of acupuncture for the treatment of hypertension.
(2) Patients were diagnosed with grade 1 hypertension with SBP ranging from 140 to 159 mmHg and/or DBP ranging from 90 to 99 mmHg.
(3) The treatment group received acupuncture therapy (including acupuncture, electroacupuncture, moxibustion, and needle warming therapy), with or without non-acupuncture hypertension treatment measures.
(4) Outcome indicators included at least one of the following: changes in blood pressure after treatment (BP change = prior treatment BP value−post-treatment BP value), efficacy of treatment, and side effects.
(5) Patients’ age ≥18 years.

Exclusion criteria:

(1) Duplicate literature in the test population.
(2) Case studies, animal experiments, and ethical exploration.
(3) Comparison of different acupuncture methods and acupoints.
(4) Literature on participants suffering from mental illnesses or other diseases.
(5) Inability to convert the blood pressure data unit to mmHg.
(6) Simple randomised controlled trials, semi-randomised controlled trials, and self-controlled trials.
(7) Controversial reported results in the literature.

2.3. Data extraction

Two reviewers independently screened and evaluated all the included studies and used the Excel software to extract data. The data included the following: first author, publication date, number of patients, average age of patients, acupuncture treatment method, acupuncture points and frequency, control type, course of treatment, average blood pressure before treatment, average blood pressure after treatment, average blood pressure change, effective rate of treatment, and adverse events. Missing data or information was sought from the main author via email or phone if necessary. In case of disagreement between the two reviewers, a third reviewer made the final decision.

2.4. Assessment for risk of bias

Two reviewers used the Cochrane collaborative tool to assess the risk of bias in RCTs and divided the literature into “high risk of bias”, “low risk of bias”, and “unclear risk of bias” groups according to the following seven aspects: (1) random sequence generation (selection bias); (2) allocation concealment (selection bias); (3) blinding of participants and personnel (performance bias); (4) blinding of outcome assessment (detection bias); (5) incomplete outcome data (attrition bias); (6) selective reporting (reporting bias); and (7) any other bias [17]. A third evaluator was consulted to resolve disagreements, if any.

2.5. Statistical analysis

Data were assembled and analysed using Review Manager (RevMan) version 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark) and the Statistical Package for the Social Sciences (SPSS) V.19.0 (SPSS Inc., Chicago, Illinois, USA). Continuous data were presented as mean differences (MDs) with 95% confidence intervals (CI), and dichotomous data were presented as relative risks (RR) with 95% CI. We used the I^2 statistic to check for heterogeneity and defined $I^2 > 50\%$ as significant heterogeneity. The fixed effects model was used in case of no significant heterogeneity and random effects model was used in case of significant heterogeneity; the possible causes were investigated from a clinical perspective through subgroup analysis. Funnel plots were used to detect publication biases.

3. Results

3.1. Literature retrieval

In the initial search stage, we included a total of 4641 articles, 998 of which were excluded due to duplication. After examining the titles and

abstracts, we further excluded 3494 articles. Finally, among the remaining 149 articles, 10 were included in this study. The flow diagram is presented in Fig. 1.

3.2. Research characteristics

The 10 eligible studies were published between 2009 and 2020, and a total of 1196 participants (minimum 60, maximum 313) were recruited. The participants in these studies were recruited in outpatient clinics in six studies, and in outpatient clinics and wards in two studies. No recruitment methods were described in two studies. The mean age of the participants in six studies was 45–50 years, in three studies was 55–60 years, and one study did not report the mean age. The mean disease duration in five studies was less than 5 years, while the other five studies did not report this information. Seven studies excluded patients with target organ damage and secondary hypertension, and three studies did not report this information. Seven studies had a male-to-female ratio close to 1:1, one study had more men, one study had more women, and one study did not report the number of male and female participants.

For acupuncture methods, five articles used ordinary acupuncture, two used intradermal needles, two used electric acupuncture, and one used scalp acupuncture. Among the six articles detailing acupuncture points, LT11 (quchi) was the most common acupoint (used three times), followed by GV20 (baihui), LI4 (hegu), and LR3 (taichong), each of which was selected twice. Among the randomised controlled experiments, nine were controlled by lifestyle adjustment, placebo, or no treatment measures, and one was controlled by acupuncture and massage at the same acupoint. Four trials used blood pressure change as the outcome indicator and eight used the effective rate as the outcome indicator. One article reported adverse reactions, and nine did not specify any adverse reactions. In addition, all studies described the methods of acupuncture, while none described the background of acupuncturists.

Six studies clearly pointed out “Deqi” which refers to two things: a feeling of soreness, numbness, bloating, and heaviness in the patient and that of heaviness and tightness while handling the needle in the acupuncturist’s hands. The presence of “Deqi” indicates that acupuncture was effective.

The median duration of treatment included in the statistics was 36 days (range, 28–90 days). The results of the included studies were the BP value after treatment, pre-post BP change value, response rate of treatment, and adverse effects. The detailed characteristics of the studies are summarised in Tables 1 and 2.

Regarding the risk of bias, two trials had a low risk of bias, two had an unclear risk of bias, and six had a high risk of bias. Three trials were

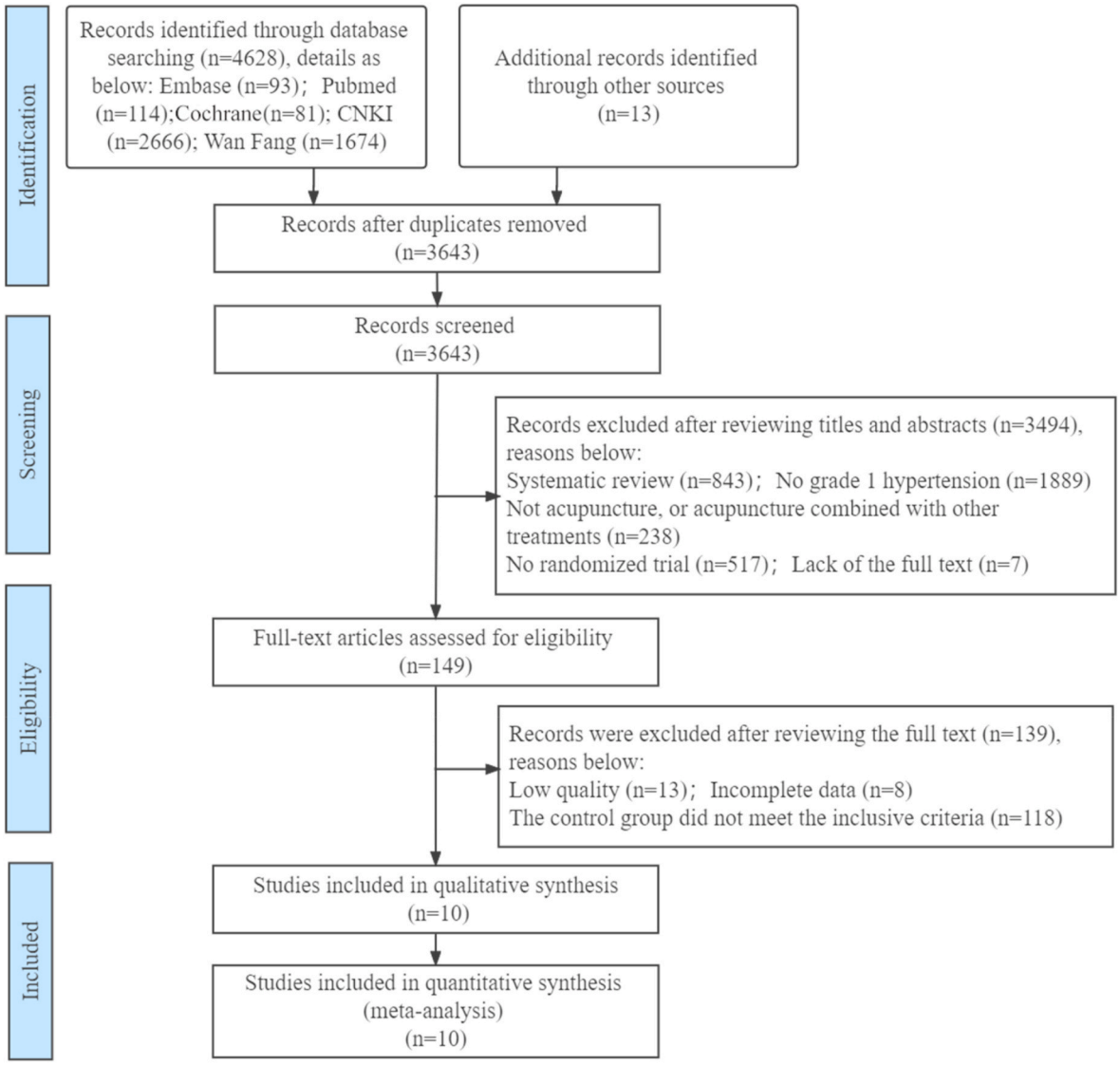

Fig. 1. Flow chart of literature search process.

Table 1
Characteristics and main outcomes of included studies.

Study (year)	Participants (Male/ Female)	Mean age		Intervention		No. of patients evaluated		Course	Acupuncture methods	Background of acupuncturists	Deqi	#Outcome
		Treatment	Control	Treatment	Control	Treatment	Control					
Zheng Z (2020) [19]	78(35/43)	49.42	49.63	IN + AL	MA + AL	38	40	4 weeks	YES	NA	NA	1/2/3
Tang M (2020) [20]	100(61/39)	60.2	58.8	IN + AL	PL + AL	50	50	36 days	YES	NA	NA	3
Feng WQ (2020) [21]	100(NA)	NA	NA	IN	PL	50	50	36 days	YES	NA	YES	3
Hui Z (2019) [22]	313(154/159)	58.2	60.4	EL	NT	209	104	6 weeks	YES	NA	YES	2
Hong XJ (2017) [23]	194(94/100)	56.69	57.59	EL	NT	97	97	6 weeks	YES	NA	YES	1/2/4
Liu H (2016) [24]	60(25/35)	42.13	45.6	AC + AL	AL	30	30	90 days	YES	NA	YES	1/3
Hong HY (2014) [25]	84(37/47)	50	50	AC	PL	42	42	30 days	YES	NA	YES	1/2/3
Yang ZB (2012) [26]	60(27/33)	49.67	49.33	AC	PL	30	30	30 days	YES	NA	NA	3
Sun J (2009) [27]	87(48/39)	47.23	48.42	AC + AL	AL	44	43	NA	YES	NA	NA	1/3
Chen ZB (2009) [28]	120(64/56)	48.13	49.34	AC + AL	AL	60	60	2 months	YES	NA	YES	1/3

*Outcomes: 1, BP value after treatment; 2, Pre-post BP change value; 3, response rate of treatment; 4, adverse effects. AC, acupuncture; AL, adjust lifestyle; EL, electro acupuncture; IN, intradermal needle; MA, massage; NT, no treatment; PL, placebo; NA, not applicable.

Table 2
Acupuncture points and frequency.

Study (year)	Acupoints	Frequency
Zheng Z (2020) [19]	LT11, ST36, ST40, SP6, EP	Two days at a time, one day off every three times
Tang M (2020) [20]	LT11	Once a day
Feng WQ (2020) [21]	LT11	Once a day
Hui Z (2019) [22]	NA	Three times a week, 30 min each time
Hong XJ (2017) [23]	NA	Once every two days, three times a week
Liu H (2016) [24]	GV20, GV16, GV14, GV9, GV11, GV24, GV4	Once every two days, every 30 min
Hong HY (2014) [25]	NA	Once a day
Yang ZB (2012) [26]	NA	Once a day
Sun J (2009) [27]	LI4, LR3, GV20, GV29	Twice a week, 30 min each time
Chen ZB (2009) [28]	LI4, LR3	Three times a week

Note: LT11, quchi; ST36, zusanli; ST40, fenglong; SP6, sanyinjiao; EP, ear point; GV20, baihui; GV16, fengfu; GV14, dazhui; GV9, zhiyang; GV11, shendao; GV24, shenting; GV4, mingmen; LI4, hegu; LR3, taichong; GV29, yintang.

grouped using the random number table method, one using the central random method, and one using the stratified random method. These five studies were evaluated as having a low selection risk, whereas one trial used random voluntary grouping and was evaluated as having a high selection risk. The selection risk of the remaining four studies was not clear. More than half of the trials did not specify whether the allocation plan was hidden or if blinding was used. Two of the trials were blinded to the patients. Additionally, two trials were blinded to the evaluators and statisticians. In three trials, participants were lost to follow-up or dropped out of the study. Other risks of bias were judged by whether the trials described Deqi; six trials did so, and four did not (Figs. 2 and 3).

3.3. The effect of acupuncture on the treatment of grade 1 hypertension

3.3.1. Pre-post treatment BP change value

Four articles [19,22,23,25] with 1176 participants reported reductions in SBP and DBP. As shown in Figs. 4 and 5, acupuncture reduced the SBP and DBP in patients with grade 1 hypertension to a certain extent (SBP: MD 3.62 mmHg, 95% CI 1.34 to 5.90, $I^2 = 56\%$; DBP: MD 3.12 mmHg, 95% CI 1.03 to 5.20, $I^2 = 77\%$). However, we did not find a suitable subgroup to reduce heterogeneity. Interventions, acupuncture methods, and treatment courses were not the only sources of heterogeneity among the studies.

3.3.2. Response rate

Eight studies [19–21,24–28] with a total of 1278 participants reported response rates. As shown in Fig. 6, acupuncture combined with lifestyle adjustment had a better effect on improving grade 1 hypertension than simple lifestyle adjustment (RR 2.12, 95% CI 1.38 to 3.26, $I^2 = 93\%$). Unfortunately, we did not find a source of heterogeneity to conduct the subgroup analysis.

3.4. Adverse effects

Only one study [23] reported adverse reactions, mainly subcutaneous haemorrhage and fainting due to use of needles. These reactions did not require medical treatment and the symptoms resolved spontaneously. As most of the studies failed to report adverse effects in a standard manner [29], it was impossible to conduct a quantitative analysis of the

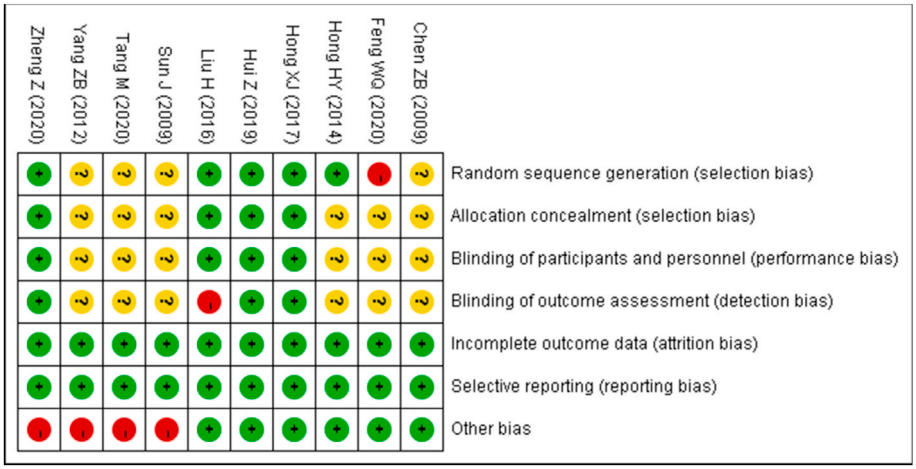

Fig. 2. The risk of bias assessment for each included study.

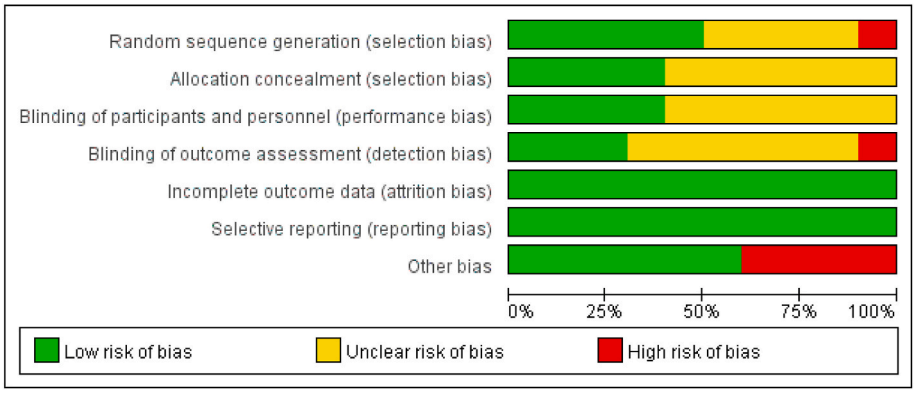

Fig. 3. Risk of bias summary of included randomised controlled trials (RCTs).

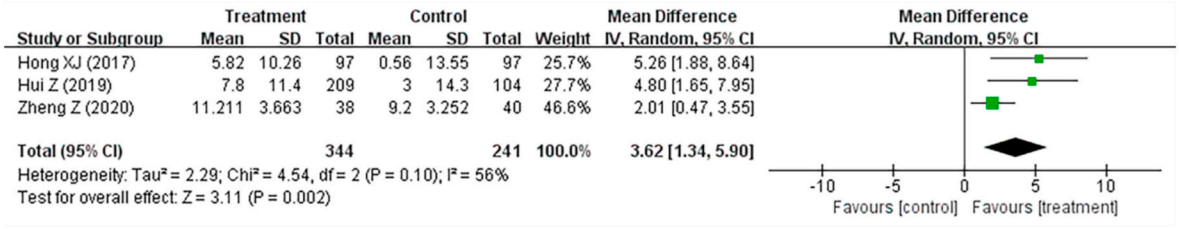

Fig. 4. Forest plot of systolic blood pressure (SBP) change.

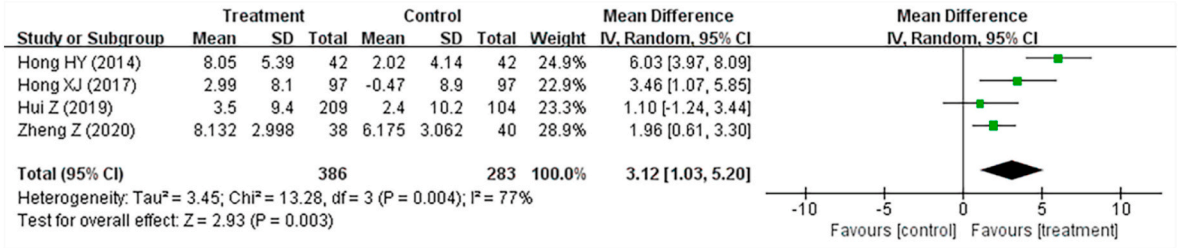

Fig. 5. Forest plot of diastolic blood pressure (DBP) change.

adverse effects in this review.

3.5. Publication bias assessment

Funnel plot analysis revealed strong asymmetry (Fig. 7), suggesting potential publication bias, probably due to the small sample sizes of the

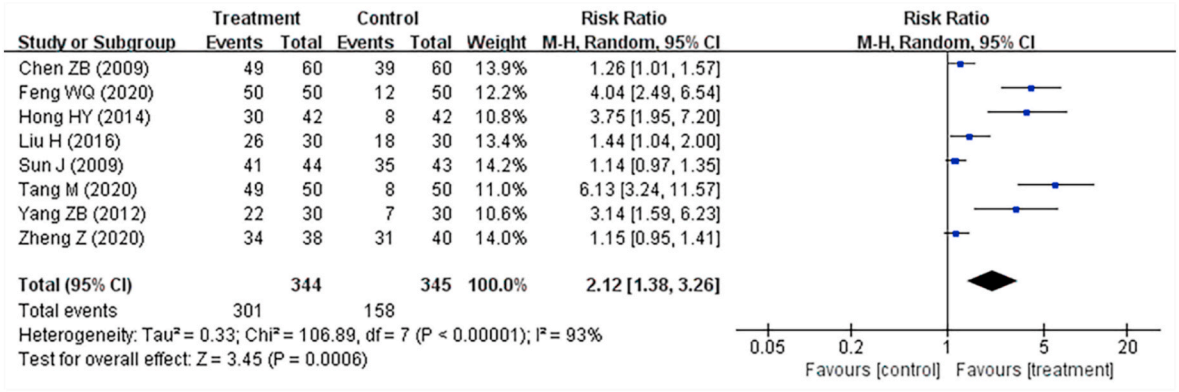

Fig. 6. Forest plot of response rate of treatment.

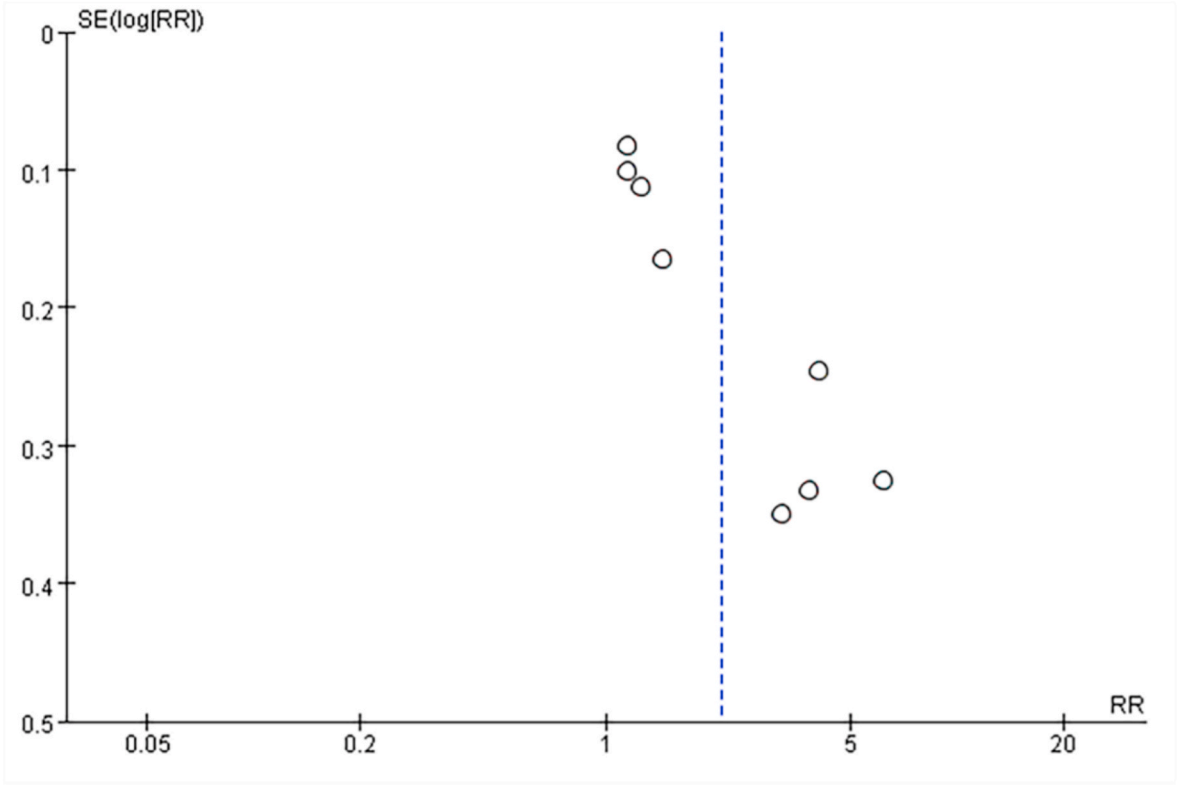

Fig. 7. Funnel plot of response rate of treatment.

included studies.

4. Discussion

Studies have confirmed that acupuncture is one of the most effective complementary and alternative therapies for hypertension; its mechanism is multifaceted. First, acupuncture can reduce the activity of renin, lower the levels of angiotensin-converting enzyme and angiotensin II receptor, reduce the concentrations of angiotensin II and aldosterone in plasma, and antagonise the renin-angiotensin-aldosterone system [30,31]. Second, acupuncture regulates oxidative stress, inhibits nicotinamide adenine dinucleotide phosphate oxidase, and increases superoxide dismutase levels to reduce reactive oxygen species [32]. Third, in terms of protecting the function of vascular endothelial cells, acupuncture activates the expression of endothelial nitric oxide synthase, reduces the production of endothelin, and maintains the balance between endothelial-dependent relaxing factors and endothelial-dependent contractile factors [33,34]. Fourth, acupuncture can reduce the levels of tumour necrosis factor-α, interleukin-6, C-reactive protein, and other inflammatory factors in the blood, thus attenuating the interaction between inflammation and hypertension [35]. In addition, the neuroendocrine mechanism by which acupuncture lowers blood pressure is equally important. Acupuncture can activate neurones in the arcuate nucleus, ventrolateral grey matter, and raphe nucleus to inhibit angiotensin type 1 (AT1) receptors in the rostral ventrolateral medulla, reduce sympathetic nerve activity, and lower blood pressure [36].

This article reviews 10 original articles on the treatment of grade 1 hypertension using acupuncture and is the first and only meta-analysis to focus on this topic. In this study, acupuncture for grade 1 hypertension was found to be more effective than lifestyle modification alone, placebo treatment, or no treatment at all. Acupuncture offers an exciting opportunity to lower SBP and DBP with higher response rates. In addition, the adverse effects of acupuncture are milder and less frequent. Therefore, acupuncture is expected to be a complementary alternative

therapy for grade 1 hypertension.

However, few studies have focused on the health economic indicators and patient preference for acupuncture treatment for grade 1 hypertension. Since most of the included studies were published in Chinese journals, the cultural background of different regions and countries may have led to the potential publication bias. Accumulating evidence suggests that the Asia-Pacific region is more inclined towards acupuncture treatment and publishes positive results [37]. At the same time, clinical RCTs lack standardisation. A small sample size poses a problem, and sample size estimates are less clearly stated. In few studies, the duration of grade 1 hypertension was not limited and the method of acupoint selection was not clearly described. A significant number of studies lack observation and documentation of Deqi, and it should be noted that substandard acupuncture practice also increases the risk of bias. Therefore, failure to report in accordance with the Reporting Standards for Acupuncture Control Therapy Interventions (STRATIA) [38] guidelines resulted in these articles being of low quality. Furthermore, the standards for randomised control grouping and blood pressure measurement were not sufficiently accurate, which increased the risk of bias in the research results. For these reasons, the response to acupuncture for hypertension in patients in other countries around the world cannot be reasonably predicted, and a large number of high-quality RCTs are needed.

Based on this systematic review, we make the following recommendations for future clinical trials of acupuncture treatment for grade 1 hypertension: the control and treatment of grade 1 hypertension deserves more attention, and the sample size of the study should be appropriately expanded. The patient's age, disease course, sex, region, primary or secondary hypertension, and target organ damage should be clearly specified in the inclusion or exclusion criteria. The grouping of included patients should be generated by random methods, such as random number tables and central randomisation, rather than by patient's preferences. Rational application of blinding is also important as blinding of the outcome assessment can make the conclusions more credible. However, due to the particularity of acupuncture, blinding of participants and personnel was rarely used in the above clinical trials. Therefore, the use of sham acupuncture or alternative sham surgery as a control is a promising strategy. Blood pressure is the most important outcome indicator; therefore, the accurate collection of blood pressure data is crucial. A 24-h ambulatory blood pressure monitoring is much better than regular non-automated blood pressure recording using cuffs and sphygmomanometers [39]; however, only two [22,23] articles in the included literature used this method. In addition, the specific factors of acupuncture treatment, such as the course of treatment, frequency of intervention, and acupoint selection, should be fully considered in the future as the dose and location of acupuncture are also related to the efficacy of acupuncture. Moreover, a detailed description of Deqi and the background of the acupuncturists can ensure the accuracy of the experimental results.

5. Conclusions

In summary, this review suggests an effect of acupuncture treatment on grade 1 hypertension, showing that acupuncture can help lower blood pressure and cause fewer adverse reactions than other treatments. Owing to few limitations, higher quality of randomised controlled trials with larger sample sizes are needed to better evaluate the results of acupuncture in the treatment of grade 1 hypertension.

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Data availability

All data is public.

Author contribution

Muxin Zhang and Yushuo zhu collected, extracted and analysed the data, and drafted the manuscript. Muxin Zhang and Zhen Hua performed statistical analyses. Jinghan Wang contributed to the risk of bias assessment. Yunlun Li contributed to manuscript revision. All the authors read the manuscript and approved the final submission.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctcp.2022.101649.

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