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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