

**Commentary****Acupuncture to treat hypertension: a recent systematic review and implications for subsequent research****Jungtae Leem**^{a,b,*}^a Korean Medicine Clinical Trial Center, Kyung Hee University Korean Medicine Hospital, Seoul, Korea^b Department of Clinical Research of Korean Medicine, College of Korean Medicine, Kyung Hee University, Seoul, Korea

ARTICLE INFO

Article history:

Received 10 November 2015

Received in revised form

1 December 2015

Accepted 3 December 2015

Available online 29 December 2015

1. Focal article

Zhao XF, Hu HT, Li JS, Shang HC, Zheng HZ, Niu JF, Shi XM, Wang S. Is acupuncture effective for hypertension? A systematic review and meta-analysis. *PLoS One*. 2015 Jul 24;10(7):e0127019. doi:10.1371/journal.pone.0127019. eCollection 2015.

2. Aim

To review a meta-analysis of the effectiveness of acupuncture in treating hypertension patients.

3. Data sources

The authors searched for relevant articles in the following databases: PUBMED, EMBASE, Cochrane Central Register of

controlled trials, International Clinical Trials Register Platform of the World Health Organization (WHO), Chinese Scientific Journal Database, China National Knowledge Infrastructure (CNKI), and the Chinese Evidence-Based Medicine Database.¹ Articles had publication dates between the inception of the databases and April 2014.

4. Study selection

The authors only included randomized controlled trials (RCTs). The criteria for hypertension in the focal review were: systolic blood pressure (SBP) \geq 140 mmHg and/or diastolic BP (DBP) \geq 90 mmHg. Furthermore, the authors selected trials according to the following criteria: (1) active and/or sham control procedure used; and (2) primary outcome measurement of absolute BP before and after intervention, difference between BP values before and after treatment, or efficacy rate.

* Corresponding author. Korean Medicine Clinical Trial Center, Kyung Hee University Korean Medicine Hospital, 23 Kyungheedaero, Dongdaemun-gu, Seoul 02447, Korea.

E-mail address: julcho@naver.com

<http://dx.doi.org/10.1016/j.imr.2015.12.001>

2213-4220/© 2016 Korea Institute of Oriental Medicine. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Clinical trials that used acupressure, laser acupuncture, transcutaneous electrical nerve stimulation, or herbal medicine as a control intervention were excluded. Ultimately, 23 studies were included in the review.

5. Data extraction

Data were collected regarding the participants themselves, acupuncture treatment, control groups, course of treatment, treatment sessions, and primary and secondary outcomes (i.e., SBP or DBP after intervention, SBP or DBP differences after treatment, efficacy rate, and adverse events).¹

6. Intervention

The *acupuncture* group included patients who had been treated using (electro-) acupuncture, both as monotherapy or in combination with Western medicine. The control group consisted of patients treated using sham acupuncture, Western medicine, or lifestyle modification and Western medicine combined with sham acupuncture.

7. Main outcome measurements

The main outcome measurements were: SBP after intervention, DBP after intervention, SBP change, DBP change, and efficacy rate.

8. Main results

- 1) Absolute BP after intervention: neither SBP nor DBP were significantly different after treatment (11 trials).
- 2) Change in BP after intervention:
 - A. Acupuncture versus sham acupuncture: acupuncture did not differ from sham acupuncture in terms of SBP change after intervention; but the change in DBP was significant [2 trials, 216 patients; DBP mean difference (MD) = -1.40, 95% confidence interval (CI) = -2.37 to -0.44, $I^2 = 8\%$].
 - B. Acupuncture combined with Western medication versus Sham acupuncture combined with Western medication: acupuncture combined with Western medication was more beneficial than sham acupuncture combined with Western medication (2 trials, 170 patients; SBP MD = -7.47, 95% CI = -10.43 to -4.51, $I^2 = 0\%$; DBP MD = -4.22, 95% CI = -6.26 to -2.18, $I^2 = 0\%$).
- 3) Efficacy rate: acupuncture did not differ from Western medicine in terms of efficacy rate (10 trials). However, acupuncture combined with Western medication had a greater efficacy rate than Western medication alone [4 trials, 230 patients; odds ratio (OR) = 4.19, 95% CI = 1.65 to 10.67, $I^2 = 0\%$].
- 4) Safety: only four trials reported adverse events. Spot bleeding, hypertensive urgency, and congestive heart failure were reported. Pain was reported as a minor adverse event.

9. Authors' conclusions

Both SBP change and DBP change were greater when acupuncture was combined with Western medication than when sham acupuncture was combined with Western medication. Furthermore, acupuncture combined with Western medication had a greater efficacy rate. This implies that acupuncture has an additive effect when combined with medication to treat hypertension. However, there is not enough evidence to confirm that acupuncture alone has an effect.

10. Comment/critique

Several systematic reviews (SRs) have addressed the use of acupuncture to treat hypertension; each had its own limitations. Some reviews did not include all relevant trials conducted in China only included trials published before 2010.^{2,3} Li et al⁴ published an SR in 2014 that contained only four RCTs. Another SR, written in 2013 by Wang et al⁵, included trials that were not rigorous RCTs. To overcome such limitations, the authors of the focal review broadened the search by removing language restrictions, adding recently published trials, and including only methodologically rigorous RCTs in their review. Nonetheless, several limitations remained; for instance, most trials included had been conducted in China—trials which usually report positive results, perhaps as a result of bias.¹

Substantial heterogeneity among studies, as well as a high risk of bias due to poor description of methods calls into question the results of this meta-analysis.¹ In addition, several studies used an efficacy rate that, although common in Chinese clinical trials, is not an internationally accepted standard in the field of hypertension. Efficacy rate is defined as the proportion of patients who reach a target blood pressure, set in advance. Interestingly, acupuncture combined with Western medicine had a greater efficacy rate than Western medicine alone, while the two did not differ in terms of either SBP or DBP. This controversial result implies that efficacy rate is not a rational and powerful outcome, and that we should therefore be cautious when interpreting the results of this review.¹

In the focal review, there were several implications for future studies. Firstly, blood pressure should be evaluated using a 24-hour ambulatory blood pressure monitoring (ABPM) device. It is known that a decrease in SBP of 10 mmHg, or in DBP of 5 mmHg, reduces the risk of strokes by 41%, and of coronary heart disease by 22%.⁶ Furthermore, even a small change in SBP (2–4 mmHg) is clinically relevant; for this reason, the authors recommend precise BP measurement.¹ In the focal review, only three trials used an ABPM device. A recently published trial by Li et al⁷, which was not included in this SR, did use an ABPM device; the trial showed a significant BP reduction in the acupuncture group. Li et al⁸ reported a protocol for acupuncture to treat mild hypertension; they also used an ABPM device, because ABPM is better than clinical BP measurement in predicting cardiovascular events. Specifically, in a 5-year follow-up study, ABPM predicted cardiovascular risk even after adjustment for the clinical BP measurement.

Therefore, the adoption of 24-hour ABPM in cases of hypertension is desirable.

Another implication for the future was that the duration, dose, and frequency of acupuncture treatment are important. In the focal review, treatment duration ranged from 7 days to 56 days, and the number of treatment sessions from five to 45. In a previous investigation, 5 days of acupuncture treatment did not reduce BP.⁹ Conversely, a pilot trial by Liu et al¹⁰ that addressed acupuncture for mild hypertension showed a reduction in DBP of 5.7 mmHg after 4 weeks of treatment which was not included in the focal review. On the basis of previous research,¹¹ as well as the pilot trial result, Liu et al¹⁰ suggested a treatment duration of more than 4 weeks, with a frequency of more than twice/wk.

The focal review also made it clear that the location of the acupoints is important. The most frequently selected acupoints among the hypertension clinical trials were LR3 (taichong, 12 trials), LI11 (quchi, 11 trials), GB20 (fengchi, 10 trials), and ST36 (zusanli, 8 trials); these were followed in frequency by LI4 (hegu, 5 trials), SP6 (sanyinjiao, 5 trials), CV4 (guanyuan, 5 trials), and PC6 (neiguan, 4 trials).¹ It is known that increased activity in the renin-angiotensin-aldosterone system (RAAS), as well as in the sympathetic nervous system (SNS), causes hypertension.¹² In a preliminary study, acupuncture reduced elevated renin, aldosterone, and norepinephrine levels, implying lowered activity in both the RAAS and the SNS.⁷ In some clinical trials, the results of treatment using acupoint combinations such as PC5-6 or ST36-37 have been better than those of treatment using LI6-7 or GB37-39; this implies that acupoint specificity is important.^{7,12} According to a review by Longhurst¹³, the use of acupoints located on deep somatic nerves (such as PC5-6, ST36-37, LI4-7, and LI10-11) evoked greater activity in the rostral ventrolateral medulla, and reduced BP more, than the use of acupoints located on superficial nerves. The authors of the focal review stated that sham acupuncture may not be a proper placebo control¹; for this reason, selecting appropriate acupoint combinations on the basis of several previous mechanistic and clinical studies is essential in both the treatment and control groups.

Other controversies, such as those of manual acupuncture versus electroacupuncture and low frequency versus high frequency electroacupuncture stimulation, are under investigation.¹³ Small sample size of included RCTs is also a challenge of acupuncture research. By referring to issues raised in this SR and commentary, future researchers may improve the methodological quality of acupuncture research in the field of hypertension; this should lead to more reliable results.

Conflicts of interest

None declared.

REFERENCES

1. Zhao XF, Hu HT, Li JS, Shang HC, Zheng HZ, Niu JF, et al. Is acupuncture effective for hypertension? A systematic review and meta-analysis. *PloS One* 2015;10:e0127019.
2. Lee H, Kim S-Y, Park J, Kim Y-J, Lee H, Park H-J. Acupuncture for lowering blood pressure: systematic review and meta-analysis. *Am J Hypertens* 2009;22:122-8.
3. Kim L-W, Zhu J. Acupuncture for essential hypertension. *Altern Ther Health Med* 2010;16:18-29.
4. Li DZ, Zhou Y, Yang YN, Ma YT, Li XM, Yu J, et al. Acupuncture for essential hypertension: a meta-analysis of randomized sham-controlled clinical trials. *Evid Based Complement Alternat Med* 2014;2014:279478, <http://dx.doi.org/10.1155/2014/279478>. Epub 2014 Mar 4.
5. Wang J, Xiong X, Liu W. Acupuncture for essential hypertension. *Int J Cardiol* 2013;169:317-26.
6. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009;338:b1665, <http://dx.doi.org/10.1136/bmj.b1665>.
7. Li P, Tjen-A-Looi SC, Cheng L, Liu D, Painovich J, Vinjamury S, et al. Long-lasting reduction of blood pressure by electroacupuncture in patients with hypertension: randomized controlled trial. *Med Acupunct* 2015;27:253-66.
8. Li J, Zheng H, Zhao L, Li Y, Zhang Y, Chang XR, et al. Acupuncture for patients with mild hypertension: study protocol of an open-label multicenter randomized controlled trial. *Trials* 2013;14:380, <http://dx.doi.org/10.1186/1745-6215-14-380>.
9. Chen H, Dai J, Zhang X, Wang K, Huang S, Cao Q, et al. Hypothalamus-related resting brain network underlying short-term acupuncture treatment in primary hypertension. *Evid Based Complement Alternat Med* 2013;2013:808971, <http://dx.doi.org/10.1155/2013/808971>. Epub 2013 May 27.
10. Liu Y, Park JE, Shin KM, Lee M, Jung HJ, Kim AR, et al. Acupuncture lowers blood pressure in mild hypertension patients: A randomized, controlled, assessor-blinded pilot trial. *Complement Ther Med* 2015;23:658-65.
11. Flachskampf FA, Gallasch J, Gefeller O, Gan J, Mao J, Pfahlberg AB, et al. Randomized trial of acupuncture to lower blood pressure. *Circulation* 2007;115:3121-9.
12. Painovich J, Longhurst J. Integrating acupuncture into the cardiology clinic: can it play a role? *Sheng Li Xue Bao* 2015;67:19-31.
13. Longhurst J. Acupuncture's cardiovascular actions: a mechanistic perspective. *Med Acupunct* 2013;25:101-13.