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Acupuncture lowers blood pressure in mild hypertension patients: A randomized, controlled, assessor-blinded pilot trial

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ABSTRACT

Objectives: To preliminarily assess the effects of acupuncture on prehypertension and stage I hypertension, and to provide data for further research.
Design: A randomized, controlled, assessor-blinded study with an 8-week intervention period and a 4-week follow-up.
Interventions: Participants were patients with systolic blood pressure (SBP) of 120–159 mmHg or diastolic blood pressure (DBP) of 80–99 mmHg.Thirty participants were allocated to acupuncture group or untreated control group at a 1:1 ratio. The acupuncture group received standard acupuncture twice weekly for 8 weeks, and was followed-up for 4 weeks after treatment; the control group did not receive any type of anti-hypertensive treatment for 12 weeks.
Main outcome measures: Primary outcome measure was SBP and DBP at post-treatment. The secondary outcomes were SBP and DBP at follow-up; Euro Quality of life (EQ-5D), heart rate variability (HRV), body mass index (BMI), and blood lipid profile.
Results: DBP (−5.7 mmHg; $P=0.025$), but not SBP (−6.0 mmHg; $P=0.123$), was significantly different between groups at post-treatment. Both DBP (−7.8 mmHg; $P=0.004$) and SBP (−8.6 mmHg; $P=0.031$) were significantly different at follow-up. Among the HRV indices, only high frequency power was significantly different between groups at weeks 4 and 8 ($P=0.047$ and $P=0.030$, respectively). There were no differences between groups in EQ-5D, BMI or lipid profile.
Conclusion: The results of this study show that acupuncture might lower blood pressure in prehypertension and stage I hypertension, and further RCT need 97 participants in each group. The effect of acupuncture on prehypertension and mild hypertension should be confirmed in larger studies.
Trial registration: KCT0000496.

1. Introduction

With more than a quarter of the world's adult population being affected, hypertension is an increasingly important medical and public health issue.[1] In South Korea, the prevalence of hypertension is 29.0%.[2] Globally, 51% deaths from cerebrovascular disease and 45% deaths from ischemic heart disease are attributable to high blood pressure (BP). [3] Hypertension, alongside heart disease, is one of the top ten causes of direct health expenditures.[4] In South Korea, hypertension ranks first in healthcare costs, and fourth among all chronic diseases in quality of life.[2,5]

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure has defined prehypertension as a systolic BP (SBP) of 120–139 mmHg or a diastolic BP (DBP) of 80–89 mmHg.[6] Research indicates that prehypertension is an independent risk factor for cardiovascular events that recommends anti-hypertensive management for patients with prehypertension.[7] Prehypertension alongside mild hypertension are recommended intensive lifestyle

Abbreviations: BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HRV, heart rate variability; EQ-5D, EuroQoL-5 dimension questionnaire; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CI, confidence interval; SD, standard deviation.

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management rather than anti-hypertensive drugs for their initial BP lowering.[8] Furthermore, the benefits of anti-hypertensive drugs for mild hypertension is not clear,[9] and medication is accompanied by unwanted side effects. Such situation and the difficulty to adopt and maintain lifestyle changes, have highlighted the limitations of drugs in treating prehypertension and stage I hypertension.

Acupuncture is a form of traditional Chinese medicine that has been used in Eastern countries to treat a number of diseases, including those related to the cardiovascular system,[10] such as hypertension.[11] Although several well-designed large scale studies have investigated the effects of acupuncture on hypertension,[12–14] yet there are few studies to determine the effects of acupuncture on prehypertension and mild hypertension. In addition, recent systematic review studies pointed out that due to low-quality clinical methodology and heterogeneity, it is hard to draw a conclusion on acupuncture and hypertension.[15]

Therefore, we designed a randomized control study to preliminarily assess the effects of acupuncture in the patients with prehypertension and stage I hypertension. If the study feasibility was acceptable, we would calculate the appropriate sample size for a further larger-scale trial. Our findings will provide scientific evidence to acupuncture studies on early stage hypertension, and could be useful for studies whose participants are un-medicated.

2. Materials and methods

2.1. Design

This was an assessor-blinded, parallel 2-armed, randomized preliminary study. The two arms were acupuncture group versus untreated control group. Participants had been recruited and were allocated one of the groups at a 1:1 ratio. Participants in the acupuncture group had received standardized acupuncture treatment 20 min a session, twice weekly for 8 weeks, and followed up 4 weeks after treatment completion; and participants in control group did not receive any antihypertensive related treatment during the study.

The study protocol was approved by the Institutional Review Board at Dunsan Oriental Hospital, Deajeon University, South Korea. All participants received information about the study, signed an informed consent sheet, and kept a duplicate of the signed informed consent sheet. If a participant initiated anti-hypertensive treatment due to hypertension or hypertension-related symptoms, the participant was immediately withdrawn from the study. After study completion, the control group was offered acupuncture treatment.

2.2. Patients

Participants were eligible if they were aged 20–65 years, and had hypertension with SBP 120–159 mmHg or DBP 80–99 mmHg. We excluded participants with SBP > 160 mmHg or DBP > 100 mmHg; and those who had had acupuncture or any antihypertensive-related treatment in the previous six months. Other exclusion criteria were secondary hypertension; diabetes; a history of cerebrovascular or cardiovascular disease; kidney, liver, thyroid gland or hemorrhagic diseases; a history of active tuberculosis or other infectious diseases; vicious tumors; and pregnancy, lactation or pregnancy planning.

2.3. Randomization ***and*** blinding

A blinded statistician generated the random allocation sequence using SAS® 9.3 (SAS Institute Inc., Cary, NC, USA). Group allocation was sealed in opaque envelopes and the envelopes were given to one of the researchers. To minimize selection bias, the researcher opened the envelopes sequentially in front of the participants only after they were included in the study, and informed them of the allocation immediately. It was impossible to blind the participants to group allocation, because participants in the control group did not receive any treatment, but the assessors and the statistician were blinded.

2.4. Intervention

Participants in the acupuncture group were treated with standardized acupuncture. We used disposable stainless steel needles (diameter: 0.20 mm, length: 30 mm; DongBang Acupuncture, Inc., Seoul, South Korea). In each session, participants were given de qi sensation via manipulation right after inserting needle into the skin, plus 20 min of needle-retaining time. Four experts made consensus on acupuncture points as bilateral ST36, PC6, LR3, SP4, LI11, based on literatures,[16,17] and theory of Oriental Medicine (Fig. 1).

Participants in the control group maintained their previous lifestyle, and were not provided any anti-hypertensive treatment during the study period. They were asked to visit once every two weeks for BP monitoring.

Moreover, standard operation procedure was provided for consistency of procedure, and routine monitoring was undertaken to check out data management and the quality of study.

2.5. Outcome measures

The primary outcomes were mean differences of SBP and DBP changes from baseline to post-treatment between acupuncture group and control group. The secondary outcomes were (1) mean differences of SBP and DBP changes between groups from baseline to follow-up; (2) the differences of EuroQoL-5 dimension questionnaire (EQ-5D), heart rate variability (HRV) and body mass index (BMI) between acupuncture group and control group at 4 and 8 weeks and at follow-up; and (3) fasting blood lipid profile between groups at 8 weeks and follow-up. We also noted the mean differences of SBP and DBP within each of the two groups.

BP measurements were conducted at every visit for both groups; the data were obtained before acupuncture treatment for the treatment group. We used automatic BP monitor (FT-500, Jawon Medical Co., South Korea). At screening, BP levels were measured 3 times at both left and right arms in 5-min intervals in sitting position, the mean BPs of the higher BP's arm was chosen for consistent BP measurements. At all visits, BP levels took the mean BPs of 3 times measurement.

EQ-5D is a preference-based tool to assess general health status across five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). [18] We used a Korean version of the EQ-5D that has been validated in the Korean population.[19,20] The questionnaire scores referred to the South Korean population-based preference weights for EQ-5D, each answer ranging from 0 to 1. The higher the total score, the better the quality of life.[21]

HRV was analyzed using Canopy® (CANPY9, IEMBIO Co., Ltd., South Korea). Canopy converts parameters of frequency domain of HRV to natural logarithms from the decimal value. Four frequency domain variables were studied: total power (TP: 0.01–0.40 Hz), high frequency power (HF: 0.15–0.40 Hz), low frequency power (LF: 0.04–0.15 Hz), and very low frequency power (VLF: 0.01–0.04 Hz). HF reflects the parasympathetic activity, VLF reflects the sympathetic activity, LF represents both the sympathetic and parasympathetic tone of the heart, and TP represents the total power that generally represents overall autonomic activity. An increase of each index represents an increase of autonomic activity.[22] We also tested the fasting blood lipid profile and BMI. Based on recent standards, the following cutoff values were used to

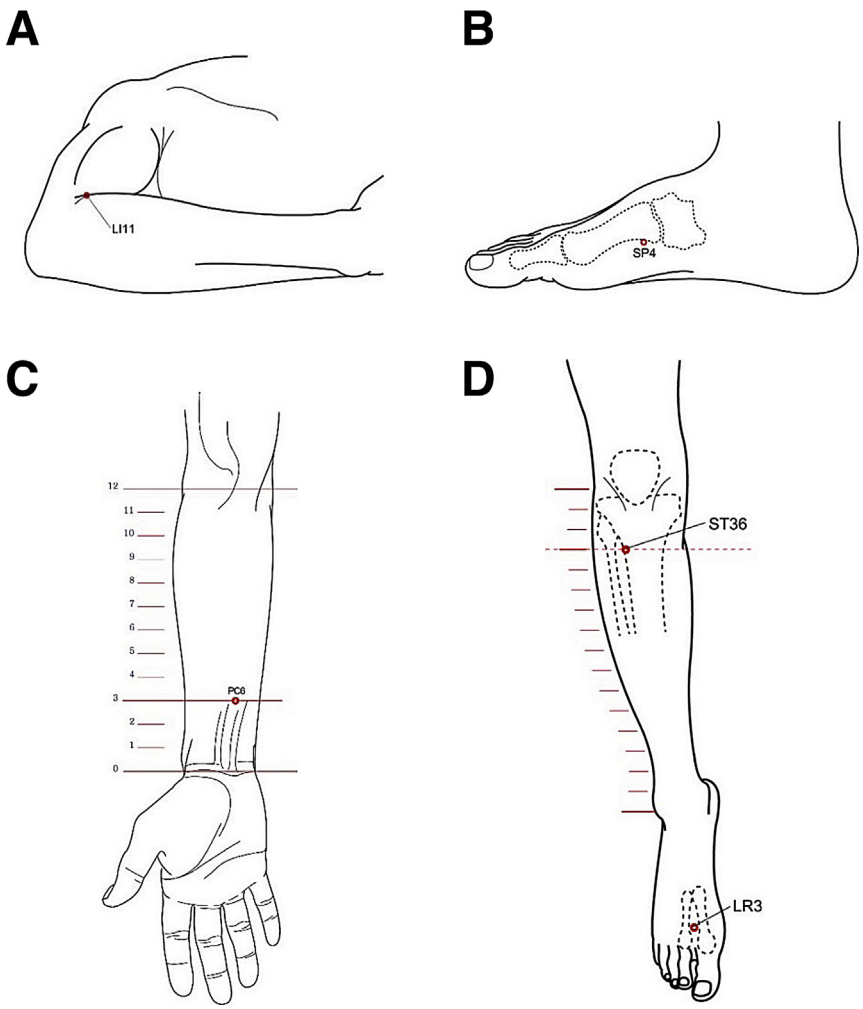


Fig. 1. Acupuncture points selected for the hypertension treatment. (A) LI11; (B) SP4; (C) PC6; (D) ST36 and LR3.

determine the desirable levels of serum lipids: serum total cholesterol below 200 mg/dL, high-density lipoprotein (HDL) cholesterol above 40 mg/dL, low-density lipoprotein (LDL) cholesterol below 100 mg/dL, and the normal BMI ranges from 18.5 to 24.9.[23]

2.6. Data analysis

SAS® 9.3 was used to analyze data based on the intent-to-treat principle. Two-tailed test was used with a significance level of 5%. Because there was no previous study on the effect of acupuncture on prehypertension and stage I hypertension, we used a sample size of 12 per group, based on previous studies,[24,25] and considered a 20% dropout rate. Thus, we aimed to recruit 15 participants per group.

Differences between patients' characteristics at baseline were expressed as descriptive statistics. Analysis of covariance was conducted with baseline scores as covariates and groups as factors for between-group comparisons. To evaluate within-group differences, we used paired *t*-test or Wilcoxon signed-rank test. To cope with missing data, we used last observation carried forward method, with consideration that hypertension is a chronic disease and BP is relatively constant over time. The effect size was calculated by using the mean difference and standard deviation (SD) of BP between groups after acupuncture treatment, in order to calculate the appropriate sample size for further research.

3. Results

The study was carried out from June 2012 to June 2013 at Dunsan Oriental Hospital, Daejeon University, South Korea. Of the 69 potential participants contacted, 39 were excluded because they did not meet the inclusion criteria ($n = 33$) or refused to participate ($n = 6$). Fifteen participants were allocated to the acupuncture group, but two dropped out during the treatment period; another 15 participants were allocated to the control group, but two dropped out during the study period. During follow-up, there were two dropouts from the acupuncture group and one from the control group. 86.7% of both group participants finished the study period (Fig. 2).

3.1. Demographic data

The characteristics of the participants are summarized in Table 1. There was no difference between the two groups in terms of age, sex, BP, HRV, BMI, EQ-5D and the number of participation in each stage. HDL and total cholesterol were similar, but LDL was significantly higher in the acupuncture group than in the control group. However, since we used randomized allocation, this difference might be caused by chance (Table 1).

3.2. Primary outcome

There was a significant difference in DBP (−5.7 mmHg; 95% CI: −10.7, −0.8; $P = 0.025$) but a negligible difference in SBP

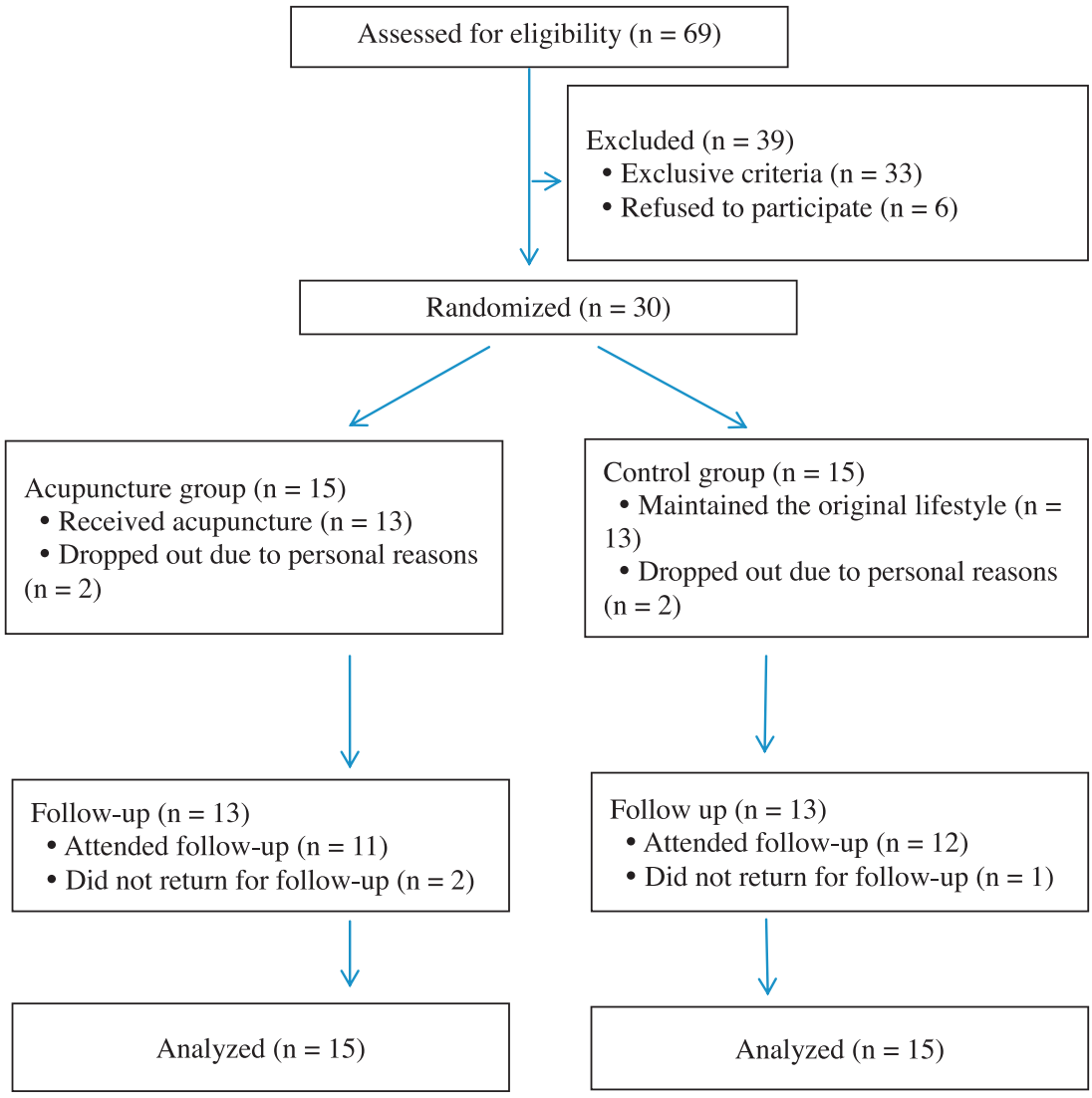


Fig. 2. Flow diagram of the study.

Table 1
Baseline demographic data for participants of each group.

	Acupuncture (n = 15)	Control (n = 15)	P[b]
Age, years	49.4 ± 8.4	53.4 ± 8.2	0.198
Males, N (%)	3 (20.0)[a]	4 (26.7)[a]	1.000
BP, mmHg			
SBP	137.1 ± 10.0	138.5 ± 10.9	0.708
DBP	86.4 ± 6.5	85.19 ± 8.1	0.662
HRV			
TP	5.9 ± 0.7	6.0 ± 0.7	0.637
VLF	5.1 ± 0.9	5.1 ± 0.7	0.764
LF	4.4 ± 0.8	4.5 ± 1.2	0.786
HF	4.6 ± 0.8	4.5 ± 1.1	0.721
Blood lipid profile, mg/dl			
HDL	50.5 ± 10.8	50.2 ± 12.8	0.939
LDL	125.6 ± 16.9	105.9 ± 19.1	0.006
Total cholesterol	198.5 ± 20.9	183.7 ± 27.7	0.109
BMI, kg/m^2	23.5 ± 3.1	24.5 ± 3.4	0.435
EQ-5D	0.93 ± 0.09	0.97 ± 0.06	0.172
Prehypertension/Stage I hypertension, N/N	10/5	11/5	–

[a] For "males" value, it is numbers (percentage), other values are the mean ± SD.
[b] P-value of comparison between groups.

(−6.0 mmHg; 95% CI: −13.7, 1.7; P = 0.123) change from baseline to post-treatment between acupuncture group and control group.

In the acupuncture group, there was a significant decrease in SBP (−6.5 mmHg; P = 0.042) and DBP (-4.9 mmHg; P = 0.006) from baseline to post-treatment. In the control group, the changes in SBP (−1.3 mmHg; P = 0.208) and DBP (1.2 mmHg; P = 0.934) were not statistically significant (Table 2).

Secondary outcome

4. Blood pressure

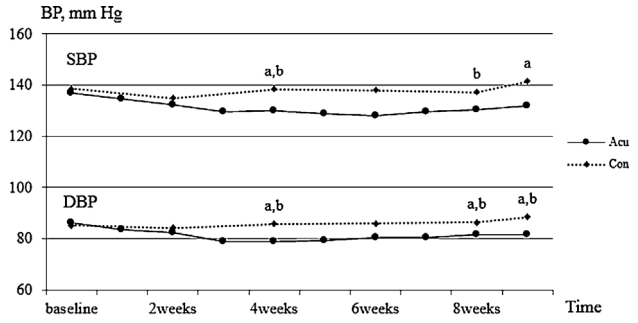
There were significant differences in SBP (−8.6 mmHg; 95% CI: −16.3, −0.8; P = 0.031) and DBP (−7.8 mmHg; 95% CI: −12.8, −2.8; P = 0.004) at follow-up between acupuncture group and control group. In the acupuncture group, there was a significant decrease in DBP (−4.6 mmHg; P = 0.002) but not in SBP (−5.0 mmHg; P = 0.135). In the control group, neither DBP nor SBP were significantly changed (Table 2, Fig. 3).

To better understand the duration of the treatment intervention, we analyzed the differences at week 4. There was a significant difference in SBP (−7.8 mmHg; 95% CI: −14.6, −0.9; P = 0.027) and DBP (−7.5 mmHg; 95% CI: −12.8, −2.2; P = 0.007) between the two groups. In the acupuncture group, there was a significant

Table 2
Changes in BP from baseline to week 4, week 8 and follow-up.

		Acupuncture ($n=15$)		Control ($n=15$)		Acupuncture vs. control	
		BP[a]	P[c]	BP[a]	P[c]	ΔBP[b]	P[d]
Baseline	SBP	137.1 ± 10.0	–	138.5 ± 10.9	–	–	–
	DBP	86.4 ± 6.5	–	85.19 ± 8.1	–	–	–
Changes in week 4	SBP	−7.1 ± 11.1	0.027*	−0.1 ± 9.7	0.963	−7.8	0.027*
	DBP	−7.5 ± 6.6	0.001***	0.6 ± 8.7	0.796	−7.5	0.007**
Changes in week 8	SBP	−6.5 ± 11.4	0.042**	−1.3 ± 11.5	0.208	−6.0	0.123
	DBP	−4.9 ± 5.2	0.006**	1.2 ± 8.0	0.934	−5.7	0.025*
Changes at follow-up	SBP	−5.0 ± 11.7	0.135	2.3 ± 10.8	0.525	−8.6	0.031*
	DBP	−4.6 ± 4.6	0.002**	3.3 ± 8.0	0.139	−7.8	0.004**

[a] Values are the mean ± SD (mmHg).
[b] Differences between groups; values are the difference (mmHg) by least squares method.
[c] *P*-value within group by paired *t*-test or Wilcoxon signed-rank test.
[d] *P*-value between groups by analysis of covariance adjustment.
* $P<0.05$.
** $P<0.01$.
*** $P<0.001$.



[a] $P < 0.05$ between group
[b] $P < 0.05$ within group

Fig. 3. Blood pressure during the study period.

decrease in SBP (−7.1 mmHg; $P=0.027$) and in DBP (−7.5 mmHg; $P=0.001$). In the control group, neither DBP nor SBP were significantly changed (Table 2).

5. Heart rate variability

Among the HRV indices (TP, VLF, LF and HF), only HF showed significant differences between groups at week 4 (0.7; 95% CI: 0.0, 1.4; $P=0.047$) and week 8 (0.7; 95% CI: 0.7, 1.3; $P=0.030$).

In the acupuncture group, all the HRV indices changed significantly at week 8: the change in TP was 0.6 ($P=0.001$), in VLF, 0.6 ($P=0.024$), in LF, 0.4 ($P=0.028$), and in HF, 0.5 ($P=0.024$). The HRV indices were not significantly changed in the control group (Table 3).

6. EQ-5D

There were no significant differences in EQ-5D scores between groups at week 4, week 8 or follow-up ($P=0.499$, $P=0.246$ and $P=0.839$, respectively). There were also no changes within groups (Table 4).

7. Lipid profile and BMI

There were no significant differences in BMI between groups at week 4, week 8 or follow-up ($P=0.988$, $P=0.917$ and $P=0.466$, respectively). Similarly, there were no significant differences in blood lipid profile indices, namely HDL ($P=0.641$), LDL ($P=0.356$) and total cholesterol ($P=0.172$) at week 8 (Table 5).

8. Sample size

We calculated the appropriate sample size for a further study based on the difference of SBP and DBP changes between groups, with consideration of a 5% significant level, two-tailed test, 80% power, and a *t*-test for comparison between groups.

Given a minimum effect size of 0.46 in SBP, the sample size would be 20 participants per group. Considering a 20% dropout rate, 25 participants per group would need to be recruited. Given a minimum effect size of 0.90 in DBP, the sample size would be 77 per group. Considering a 20% dropout rate, 97 participants per group would need to be recruited.

8.1. Safety

Previous studies of acupuncture on hypertension have reported that adverse events would be spot bleeding, feeling of pain in the skin-puncture site, and giddiness, hypertensive urgencies and congestive heart failure.[13,17] In this trial, it has not reported any adverse events.

9. Discussion

Recent meta-analyses have suggested that acupuncture is associated with reductions of 7.5 mmHg and 4.2 mmHg in SBP and DBP, respectively. [15] In this study, acupuncture decreased SBP and DBP by approximately 6.0 and 5.7 mmHg, respectively, suggesting its potential benefits for patients with prehypertension and stage I hypertension. There are three important differences between the present study and studies included in the meta-analyses mentioned above. First, studies in the meta-analyses used noninvasive sham acupuncture, and this study used no-treatment as the control. Second, the range of blood pressure of included participants was different. Although previous studies included participants with hypertension [15] or high stage BP, [16] this study included only pre and mild hypertension. Third, the frequency and duration of acupuncture treatment were different. These differences might contribute to a different effect on BP between studies. There was a 22% reduction in Coronary Heart Disease events and a 41% reduction in stroke for a BP reduction of 10 mm Hg SBP or 5 mm Hg DBP.[26] So, the reduction of DBP might clinically meaningful based on this study even though the change of SBP was not significant. However, due to small sample size of this pilot study, clinical impact of this results should be confirmed in larger trials. Further studies involving rigorously designed large-scale trials will be required to investigate the effect of acupuncture on hypertension, particularly on early-stage hypertension. The findings of such studies could help prevent or delay

Table 3
Changes in HRV from baseline to week 4, week 8, and follow-up.

		Acupuncture ($n=15$)[a]		Control ($n=15$)[a]		Acupuncture vs. Control[b]	
		Index[a]	P[c]	Index[a]	P[d]	ΔIndex[b]	P[c]
Baseline	TP	5.9 ± 0.7	–	6.0 ± 0.7	–	–	–
	VLF	5.1 ± 0.9	–	5.1 ± 0.7	–	–	–
	LF	4.4 ± 0.8	–	4.5 ± 1.2	–	–	–
	HF	4.6 ± 0.8	–	4.5 ± 1.1	–	–	–
Changes in week 4	TP	0.3 ± 0.7	0.096	−0.0 ± 0.7	0.927	0.3	0.214
	VLF	0.2 ± 0.5	0.305	0.0 ± 1.0	0.850	0.1	0.732
	LF	0.4 ± 1.0	0.127	0.0 ± 0.8	0.776	0.3	0.312
	HF	0.5 ± 1.0	0.097	−0.2 ± 0.8	0.324	0.7	0.047*
Changes in week 8	TP	0.6 ± 0.6[d]	0.001***	0.1 ± 0.9	1.000	0.5	0.072
	VLF	0.6 ± 1.0[d]	0.024*	0.2 ± 1.0	0.522	0.4	0.185
	LF	0.4 ± 0.6[d]	0.028*	0.2 ± 1.2	0.893	0.2	0.623
	HF	0.5 ± 0.8[d]	0.024*	−0.1 ± 0.9	0.542	0.7	0.030*
Changes at follow-up	TP	0.6 ± 1.2	0.111	0.2 ± 1.0	0.400	0.2	0.523
	VLF	0.6 ± 1.3	0.093	0.2 ± 1.1	0.456	0.3	0.417
	LF	0.4 ± 1.0	0.163	0.3 ± 0.9	0.215	0.0	0.897
	HF	0.4 ± 1.4	0.519	0.2 ± 0.9	0.839	0.2	0.642

** $P<0.01$.
[a] Values are the mean ± SD.
[b] Differences between groups; values are the differences by least squares method.
[c] P-value between groups was analyzed by analysis of covariance adjustment.
[d] Changes within group; $P<0.05$.
* $P<0.05$.
*** $P<0.001$.

Table 4
Changes in EQ-5D at week 4, week 8, and follow-up.

	Acupuncture ($n=15$)[a]	Control ($n=15$)[a]	Acupuncture vs. control[b]	P[c]
Baseline	0.93 ± 0.09	0.97 ± 0.06	–	–
Changes in week 4	0.91 ± 0.12	0.96 ± 0.06	−0.02	0.499
Changes in week 8	0.95 ± 0.08	0.94 ± 0.13	0.04	0.246
Changes at follow-up	0.90 ± 0.13	0.95 ± 0.07	−0.01	0.839

[a] Values are the mean ± SD.
[b] Values are the differences between groups with by least squares method.
[c] P-value between groups was analyzed by analysis of covariance adjustment.

Table 5
Changes in BMI and blood lipid profile at week 4, week 8, and follow-up.

		Acupuncture($n=15$)[a]	Control($n=15$)[a]	Acupuncture vs. control[b]	P[c]
Baseline	BMI, kg/m^2	23.5 ± 3.1	24.5 ± 3.4	–	–
Change in week 4		23.5 ± 3.1	24.5 ± 3.4	0.00	0.988
Change in week 8	BMI	23.5 ± 3.0	24.4 ± 3.4	−0.11	
Change at follow-up	BMI	23.6 ± 3.0	24.6 ± 3.4	−0.08	
Baseline	Blood lipid profile, mg/dl				
	HDL	50.5 ± 10.8	50.2 ± 12.8	–	–
	LDL	125.6 ± 16.9	105.9 ± 19.1	–	–
	Total cholesterol	198.5 ± 20.9	183.7 ± 27.7	–	–
Change in week 8	HDL	51.7 ± 9.9	52.3 ± 12.4	−0.90	0.641
	LDL	124.3 ± 21.8	114.9 ± 27.8	−7.78	0.356
	Total cholesterol	202.9 ± 25.5	197.5 ± 41.0	−11.15	0.172

[a] Values are the mean ± SD.
[b] Values are the difference CI by least squares method.
[c] P-value between groups was analyzed by analysis of covariance adjustment.

progression to hypertension, and ultimately reduce cardiovascular risk and cardiac mortality.

Choosing an appropriate duration and frequency for acupuncture treatment is an issue.[27] A study claimed that short-term (5 days) acupuncture does not significantly decrease BP.[28] Indeed, the duration and frequency of effective acupuncture for hypertension ranges from 6 to 8 weeks, 2 or 5 times a week.[13] In the present study, we found a significant reduction of DBP after 8 weeks of acupuncture treatment compared to control ($P=0.025$), and a significant reduction of SBP and DBP after only 4 weeks ($P=0.027$ and $P=0.007$, respectively). Based on this and previous studies, the duration and frequency of acupuncture for hypertension should be four weeks at least, two times or more per week.

Deregulation of the autonomic nervous system plays an important role in BP regulation.[29,30] The autonomic function can be measured by means of the HRV.[31] It has been reported that hypertensive patients have low HRV.[29,32] Therefore, HRV indices have been used to investigate the effects of anti-hypertensive therapies.[33,34] In this study, HF was significantly increased in the acupuncture group compared to control at week 8, which indicates an increase in parasympathetic activity in the acupuncture group. Additionally, all HRV indices showed significant improvement in the acupuncture group at week 8, although this improvement was too small to lead to differences between groups. Some review studies have provided evidence of the benefits of acupuncture to the autonomic response,[35,36] but few have evaluated the effects of

acupuncture on HRV of patients with high BP. Therefore, further research is required to use objective and clinically relevant outcomes such as HRV in combination with BP to understand the mechanism of acupuncture-induced lowering of BP.

In this study, there were no significant improvements in quality of life (Table 4). There might be two reasons. Firstly, baseline EQ-5D scores were high (Table 1; 0.93 in the acupuncture group and 0.97 in the control group). According to Korea Health Statistics 2012, the average score of EQ-5D in the healthy population is 0.96, and 0.91 in the hypertensive population.[2] Secondly, EQ-5D might not be appropriate to evaluate patients with prehypertension and stage I hypertension. In previous hypertension, general quality of life instruments such as the MOSSF-36 or EQ-5D were used to assess the health status.[37,38] However, there is no validated hypertension-specific instrument yet. It would be important to develop such an instrument.

At week 4, both SBP and DBP differed significantly between groups; however, at week 8, only DBP, but not SBP, was significantly different (Table 2, Fig. 3). Three factors, considered limitations of this study, might have influenced the results. Firstly, blinding of participants was not possible due to the non-treated control design of the study, so the effect of expectation and Howthorn effect might affect the participants in acupuncture group. In addition, even though we had trained researchers and acupuncturists not to over-communicate to participants in the treatment group, the interaction between researchers and participants might affect the result.[39] Secondly, change of researchers might affected the result. Due to the strict inclusion and exclusion criteria (untreated prehypertension and stage I hypertension), this trial took us 13 months to complete; inevitable situations such as the change in research coordinator occurred, that such changes might influence the interaction between participants and researchers even though we let them follow the SOP on interaction. Finally, the adherence of participants might not be consistent over the course of the trial. Many factors affect participant adherence, e.g., the inability of the participants to completely understand their responsibilities, the researcher's unfamiliarity with the protocol, and the long duration of trial.[40] In this study, although all the participants were asked to maintain their usual life style and to not use any type of antihypertensive treatment including diet or exercise, whether they complied with the request was not monitored suitably, and thus remains unclear. Further research is need to develop a self-report form that can be used to measure the adherence of participants. In addition, practitioners and research coordinators should be given a manual regarding revised or standard operating procedures, in order to prevent unnecessary bias.

10. Conclusion

The results of this study show that acupuncture might lower BP in patients with prehypertension and stage I hypertension, and further large-scale studies need 97 participants per group. The effect of acupuncture on prehypertension and mild hypertension should be confirmed in larger studies.

Conflict of interest

All the authors have declared that they had no competing interests.

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Authors' contributions

YL wrote the main draft; JEP performed the study and gave suggestions to improve the draft; KMS gave expert comments on the study design; ML took charge of the statistics; HJJ, ARK, and SYJ took charge of monitoring and managing the data, and played an essential role in study coordination; HRY performed the acupuncture and gave expert comments on acupuncture point selection; KOS performed the study and gave technical comments and suggestions; and SMC designed and performed the study, gave expert opinion on Oriental Medicine, and guided the researchers to successfully complete the study.

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