Complementary Therapies in Clinical Practice 30 (2018) 14–18

Contents lists available at ScienceDirect

Complementary Therapies in Clinical Practice

journal homepage: www.elsevier.com/locate/ctcp

Acupuncture therapy improves vascular hemodynamics and stiffness in middle-age hypertensive individuals

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ARTICLE INFO

Article history:
Received 16 October 2017
Accepted 7 November 2017

Keywords:
Acupuncture
Vascular hemodynamic
Arterial stiffness
Wave reflection

ABSTRACT

Acupuncture (ACU) is becoming a more common practice among hypertensive individuals. However, the reported therapeutic effects of ACU in lowering brachial blood pressure (BP) are ambiguous. Therefore, evaluating more sensitive markers of arterial functioning might unveil the protective effects of ACU on hypertension. We examined the effects of an 8-week ACU therapy intervention on vascular hemodynamics and stiffness in middle-age hypertensive individuals. Participants were randomly assigned to either ACU (n = 23) or a control group (n = 22). Brachial and aortic BP, wave reflection (AIx) and arterial stiffness (SI) were measured before and after 8 weeks. There was a significant group x time interaction ($P < 0.05$) for brachial and aortic BP, AIx and SI which significantly decreased ($P < 0.05$) following ACU but not after control. ACU led to reductions in brachial and aortic BP, wave reflection and arterial stiffness in middle-age hypertensive individuals. ACU might be effective in the prevention and treatment of hypertension.

1. Introduction

Hypertension (HTN), characterized by increased brachial blood pressure (BP), affects about one billion individuals worldwide and is considered the most important risk factor for premature cardiovascular disease (CVD) [1]. Current recommendations for the control of HTN include the use of pharmacological treatment as well as lifestyle changes such as diet and exercise training [2]. However, an effective decrease in brachial BP is limited by the cost, side effects and safety concerns of antihypertensive drugs [3]. Furthermore, long-term compliance with lifestyle modifications is difficult to maintain in most individuals. Therefore, modalities of complementary and alternative medicine, such as acupuncture (ACU), are becoming a more common practice among hypertensive individuals [4].

ACU has been used in both western and eastern countries for the management of many diseases, including HTN [5]. However, these therapeutic effects of ACU in lowering brachial BP are somewhat ambiguous. Recent systematic and meta-analytic reviews suggested that ACU can decrease brachial BP [5–7] while others have concluded that there is little or no effect [8,9]. Interestingly, brachial BP might underestimate the effects of ACU on HTN control, and hence the evaluation of other more sensitive markers of cardiovascular functioning might unveil the cardioprotective effects of ACU. For instance, aortic systolic BP (SBP), arterial stiffness and pulse wave reflection (augmentation index, AIx) more accurately reflect the health of the aorta and loading conditions of the heart's left ventricle and, thereby, are be better markers of cardiovascular risk [10–13] and therapeutic targets for HTN [14–16] than brachial BP. Yet, evidence on the effects of ACU on aortic hemodynamics and stiffness is limited and unclear. ACU has been shown to acutely decrease AIx without altering aortic BP in healthy individuals [17]. Previous studies reported that aortic stiffness shows a trend to decrease after a single session of ACU in healthy individuals [18,19]. There is also evidence that ACU can acutely enhance the nitric oxide (NO) generation, blood flow and distensibility of peripheral arteries in young individuals [20,21]. Thus, we hypothesized that ACU therapy, would improve aortic hemodynamics and arterial stiffness in hypertensive adults. Therefore, the aim of the study was to examine the effects of 8 weeks of ACU therapy on aortic BP, wave

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https://doi.org/10.1016/j.ctcp.2017.11.002
1744-3881/

reflection, and stiffness in middle-aged individuals with HTN.

2. Methods

2.1. Participants

Forty-five (age 47–63 years) middle-age individuals (men = 18, women = 27) with HTN [140–179 mmHg brachial SBP or 90–109 mmHg diastolic BP (DBP)] from the Magnitogorsk, Russia area participated in the present study. HTN was diagnosed by a physician prior to participation on the study. All women were postmenopausal, which was defined as the absence of menstruation for at least 1 year. Participants were excluded if they had pulmonary, renal, adrenal, pituitary, severe psychiatric, thyroid, or cardiovascular diseases other than HTN and the use medication or hormone replacement therapy during the 6 months prior the study. Participants were also excluded if they were smokers. In addition, those who attended psychological or physical therapy, had a history of steady exercise or received exercise training and dietary changes in the last year, were excluded to avoid potential confounders in the present trial. All participants received complete information about the study design and provided written informed consent. All protocols were approved by the Institutional Review Board and carried out in accordance with the Declaration of Helsinki.

2.2. Study design

We used a randomized controlled parallel experimental design. Following an initial screening and familiarization session of study tests and procedures, eligible individuals were randomly assigned to an ACU group or non-intervention control group (Fig. 1). Allocation was stratified for brachial SBP [>140 < 160 mmHg (n = 21 in ACU and n = 21 in control group) or ≥ 160 < 180 mmHg (n = 2 in ACU and n = 1 in control group)], and the sequence was generated by a computer-based number. Measurements were collected at baseline and after 8 weeks during the same time of day (±1 h) in the morning following an overnight fast, abstinence from caffeinated drinks and alcohol and between 48 and 72 h after the last ACU session. Cardiovascular measurements were collected in a quiet temperature-controlled room (22–24 °C) following at least 10 min of rest in the supine position. Participants were instructed not to alter their regular lifestyle habits during the study period (verified through food/physical activity logs).

2.3. Acupuncture intervention

Participants in the ACU group were treated with standardized ACU 3 x week for an 8-week period. We used disposable stainless steel needles (diameter: 0.20 mm, length: 30 mm). In each session, participants were given deqi sensation via manipulation right after inserting needle into the skin, plus 20 min of needle-retaining time. The ACU points used were bilateral ST36, ST37, PC 5, PC6, LR3, SP4, LI11 based on prior literature on hypertensive individuals [22].

2.4. Control intervention

Participants in the control group made no changes in their lifestyle, and were not provided any treatment during the study

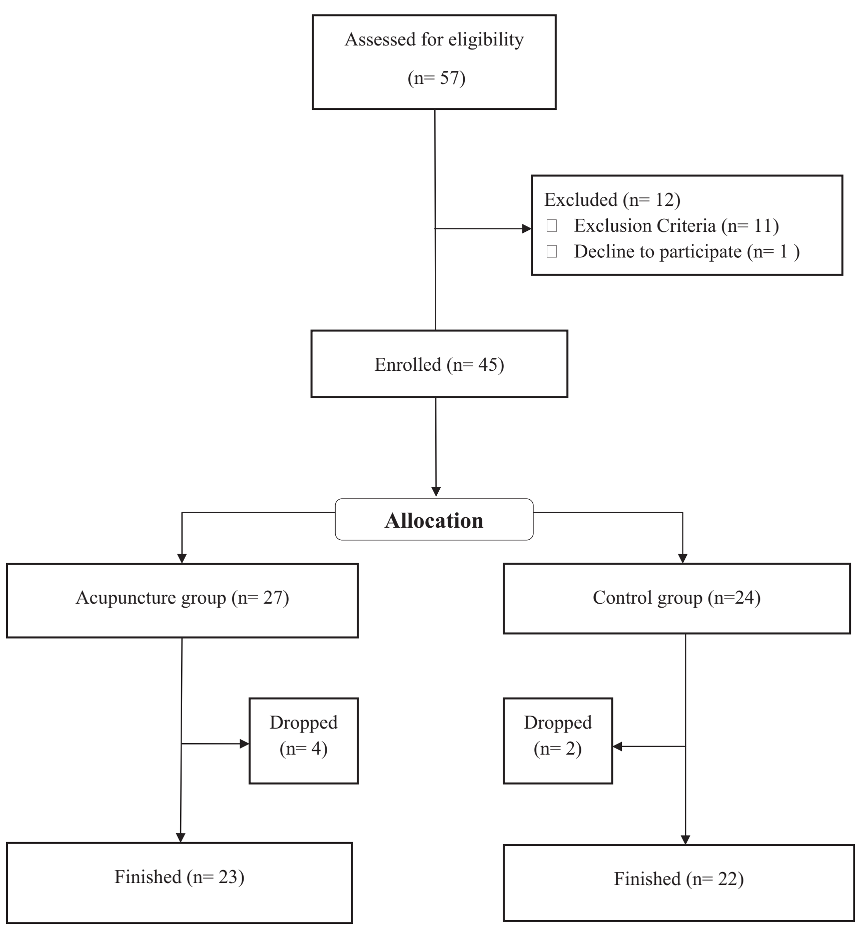

Fig. 1. Diagram for the experimental study.

period. We felt we had an ethical obligation to provide treatment to all individuals willing to participate in the study. Therefore, participants in the control group were offered ACU therapy for 2 months at the end of the study.

2.5. Hemodynamics and arterial stiffness

Brachial SBP and DBP were measured using a validated automatic device (A-PULSE CASPal, Healthstats International, Singapore, Republic of Singapore) and used to calibrate the radial waveforms obtained from a 10s epoch using a noninvasive tonometer included in the same device. Aortic SBP was obtained from aortic waveforms synthesized from the radial waveforms [23].

The digital volume pulse (DVP) was obtained by digital photoplethysmography on the index finger using a validated device (Angioscan-01, Angioscan-Electronics LLC, Russia). The photoplethysmographic device uses a signal conditioning circuit to obtain an accurate and noise-free signal at a sampling frequency of 130 Hz. The DVP signals obtained from a 5-min period capture a number of waveforms that are then averaged by the system to produce a single DVP waveform. The amount of light transmitted is indirectly proportional to the blood volume in the finger pulp and its changes due to pulse waves. The points of the waveform used for analysis are early systolic peak, caused by stroke volume ejection, and the late systolic peak that is formed by the pressure waves reflected back up to the aorta from peripheral sites [24]. The late systolic peak is modulated by reflection of the smaller sized distal arteries. The time interval (TI) between the early systolic and late systolic peaks is related to the transit time of pressure waves from the root of the subclavian artery to the apparent site of reflection and back to the subclavian artery [25]. This path length (length of the aorta) is related to the individual's height (h). An index of aortic stiffness (stiffness index, SI) is therefore derived similar to the calculation of pulse wave velocity (PWV), the gold standard for assessment of arterial stiffness [26], by the formula $= h/\text{TI}$. Indeed, SI has been shown to strongly correlate to aortic PWV [27,28].

Brachial SBP and DBP were used to calibrate DVP waveforms. The augmented pressure (AP) is the measure of the contribution that the wave reflection makes to the aortic SBP, and it is obtained by measuring the reflected wave coming from the periphery to the aorta. Reduced compliance of the elastic arteries causes an earlier return of the 'reflected wave', which arrives in systole rather than in diastole, causing a disproportionate rise in aortic SBP (late systolic peak) and an increase in pulse pressure, with a consequent increase in left ventricular afterload [24]. AP is the difference between the late and early systolic peaks. The AIx was defined as the AP expressed as a percentage of the pulse pressure. AIx was normalized to a HR of 75 beats/min (AIx@75), because it is influenced by HR [29]. The average of two measurements was used at each timepoint. The intraclass correlation coefficient for all measurements derived from DVP, calculated on 2 separate days in a subsample, was >0.90.

2.6. Statistical analysis

All parameters were normally distributed as shown by the Kolmogorov-Smirnov test. Student's t-test was used for group comparisons at baseline. A 2 X 2 ANOVA with repeated measures [group (control X ACU) x time (before X after 8 weeks)] was used to determine the effects of ACU and time on dependent variables. If a significant main effect or interaction was noted, paired t-test was used for *post hoc* comparisons. Pearson's correlations were used to analyze the relationship between changes in SI and hemodynamic parameters. Analyses were performed using SPSS 21.0 for Windows (IBM SPSS Analytics, Armonk, NY). Data are presented as mean ± SEM. Statistical significance was set at $P < 0.05$. A power analysis calculation determined a minimum sample size of 24 would allow the observation of a difference of 3%–5% between the groups (ACU versus control) on the primary study outcome variable of AIx with a power of 80% [17].

3. Results

Forty-five participants were included in the statistical analysis as 6 participants decided to discontinue their participation in the study because of time commitment (Fig. 1). Compliance to the ACU sessions was 99%. Importantly, none of the participants in the ACU group reported any unfavorable symptoms/signs or adverse side effects resulting from ACU.

Participant characteristics, hemodynamics and stiffness at baseline and after 8 weeks for the control and ACU groups are presented in Table 1. (Data are shown as means ± SEM). Baseline parameters between the two groups were not significantly different ($P > 0.05$). There were significant group x time interactions ($P < 0.05$) for SI, AIx, AIx@75, brachial SBP, brachial DBP, and aortic SBP which significantly decreased ($P < 0.01$). The changes in SI were correlated with changes in AIx ($r = 0.61$, $P < 0.05$) and AIx@75 ($r = 0.64$, $P < 0.05$). There were no significant changes in HR, weight and BMI after ACU or control.

4. Discussion

ACU has been used to treat symptoms related to HTN for centuries [5]. However, reliable evidence on the measurable effects of ACU on HTN has only been reported within the last several years [5,6]. The present study includes a new application of resting aortic parameters after ACU therapy, as all previous research involved acute responses to ACU. We found that 8 weeks of ACU therapy resulted in beneficial reductions of aortic hemodynamics and arterial stiffness. Our results indicate that ACU improves resting aortic vascular function in hypertensive middle-aged individuals. To our knowledge, this is the first study to evaluate the effects of ACU treatment on resting aortic hemodynamics and stiffness as was done in this study, as well as in this study population.

Pulse wave reflection, AIx, can be examined as the difference between the late and early systolic peak relative to aortic pulse pressure. The AIx observed in our participants before ACU may be explained by age and HTN [30]. The reduction in AIx found following ACU therapy in the present study agrees with a previous

Table 1
Participant's characteristics, hemodynamics and arterial stiffness before and after 8 weeks of ACU or control. Abbreviations: ACU, acupuncture; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AIx, augmentation index; AIx@75, augmentation index adjusted at heart rate of 75 beats/min. #P < 0.01 different than before. †P < 0.01 different than control. Data are mean ± standard error of the mean.

Variable	ACU		CONTROL	
	Before	After	Before	After
Age (years)	57 ± 1	–	57 ± 1	–
Height (m)	1.65 ± 2	–	1.66 ± 2	–
Body weight (kg)	81.9 ± 2.7	82.1 ± 2.6	80.3 ± 2.9	80.5 ± 2.8
BMI (kg/m^2)	30.5 ± 1.4	30.6 ± 1.4	29.8 ± 1.5	29.9 ± 1.4
Brachial SBP (mmHg)	150 ± 2	140 ± 3#†	150 ± 2	149 ± 2
Brachial DBP (mmHg)	85 ± 2	79 ± 3#†	84 ± 2	84 ± 2
Aortic SBP (mmHg)	144 ± 2	133 ± 3#†	144 ± 2	143 ± 3
AIx (%)	45 ± 2	38 ± 2#†	43 ± 2	42 ± 2
AIx@75 (%)	41 ± 2	34 ± 2#†	39 ± 2	38 ± 2
Stiffness Index (m/s)	10.9 ± 0.2	10.4 ± 0.2#†	11.1 ± 0.2	11.0 ± 0.2
Heart rate (beats/min)	68 ± 2	67 ± 2	68 ± 2	68 ± 2

study by Satoh et al. [17] that reported a decreased AIx after an acute session of ACU in young healthy individuals, which results from a decrease in the amplitude of the reflected wave from peripheral sites [21]. It has been proposed that stiffer aorta causes the reflected wave to travel back to the heart at a faster speed (low transient time), arriving during late systole, which increases the AIx. In the current study we observed a decreased SI, a surrogate marker related to aortic PWV [27,28], that was correlated to the decreased AIx; suggesting that a decreased aortic stiffness causes a decrease in the speed of the reflected wave (increase in transient time) back to the heart, which may be at least partially responsible for the decreased in AIx [31]. Therefore, a decrease in both the speed and amplitude of the reflected wave may explain the ACU mediated decrease in AIx. A recent meta-analysis revealed that increases in AIx by 10% would increase the risk for cardiovascular events by 31.8% [32]. We noted a 7% reduction in AIx after ACU. Thus, ACU therapy may reduce cardiovascular risk in middle-aged hypertensive individuals.

Aortic SBP is clinically more relevant than brachial SBP because it is the pressure exerted on the left ventricle [32] in addition to be shown as a more sensitive predictor of cardiovascular mortality [11,33]. Each 10 mm Hg increase in aortic SBP increases the risk for cardiovascular events by 8.8% [32]. Therefore, aortic SBP may be a treatment target for therapies intended to improve cardiovascular function. Our study demonstrated that ACU therapy reduced aortic SBP by approximately 10 mm Hg, in the absence of significant changes in HR; suggesting that the reduction in aortic stiffness (decreased SI) may influence the decrease in left ventricular afterload. This reduction in aortic SBP after ACU was greater than the increase in aortic SBP (7 mm Hg) observed in middle-aged women in a 10-year follow-up [34].

Recent meta-analyses have suggested that ACU therapy is associated with reductions of 8 mmHg and 4 mmHg in brachial SBP and brachial DBP, respectively [6]. In this study, ACU decreased brachial SBP and DBP by approximately 10 and 6 mmHg, respectively. Our study provides evidence that ACU helped lower BP in hypertensive middle-aged adults without medication. Our results are in agreement with the findings in previous studies in hypertensives in which resting [22,35] and 24-h ambulatory [36] brachial SBD and DBP decreased after 8 weeks of ACU treatments. Our observations contrast with those described in recent reviews, which concluded that ACU is effective only as an adjunct therapy to antihypertensive drug treatment [5,37]. Although the discussion of these discrepancies is beyond the scope of our study, it may be related to study population characteristics (age, sex, additional diseases other than HTN), duration of ACU therapy and different combination of antihypertensive medications in previous compared to the present study. Nevertheless, there is multiple evidence supporting the efficacy of ACU therapy in reducing brachial BP in both medicated and non-medicated hypertensives.

The possible mechanisms underlying the effects of ACU on aortic hemodynamics and stiffness may include an enhanced vasoactive balance between vasodilator and vasoconstrictor factors. Indeed, previous studies in hypertensive rats reported that plasma nitric oxide (NO) levels, a potent vasodilator, increased after ACU treatment [38,39]. Additionally, other studies in hypertensive rats have shown decrease plasma levels of endothelin-1 and angiotensin II, potent vasoconstrictors, following ACU treatment [40,41]. Furthermore, receptor expression for both endothelin-1 and angiotensin II decrease after ACU treatment in the aorta of hypertensive rats [40]. Another potential mechanism for the improved aortic hemodynamics and stiffness may be an improved autonomic activity. Previous animal studies have shown that ACU may modulate the autonomic nervous system [42,43]. This modulation appears to be related to the decreased sympathetic activity which can be shown by the inhibition of premotor sympathetic neural firing in the medulla oblangata [44] as well as maintenance of the bradycardic effect even after vagus nerve section [43]. Moreover, electroacupuncture at PC 5–6 and ST 36–37 acupoints (points also included in our current ACU protocol) have been shown experimentally to decrease elevated BP, and sympathetic outflow, including renal sympathetic nerve activity for prolonged periods [45]. Because high levels of sympathetic activity are associated with increased aortic hemodynamics and stiffness [46], and the current study showed decreases in these markers, it is possible that the effect of ACU on aortic BP, wave reflection and stiffness can be mediated, at least in part, by decreased sympathetic activity.

Potential limitations of this study include a small sample size. Our study evaluated aortic hemodynamics and stiffness in hypertensives and, hence, we cannot generalize our results to other populations. Vasoactive substances and sympathetic activity, were not measured in the present study; thereby, we cannot exclude them as potential mechanisms for our results. Finally, the study duration was relatively short and it is unclear whether a longer intervention period would result in greater reductions in aortic BP, wave reflection and stiffness.

5. Conclusion

In conclusion, our findings indicate that ACU therapy is effective for improving aortic BP, wave reflection and stiffness in middle-aged individuals with HTN. Our results support the use of ACU for the improvement of HTN beyond the brachial BP perspective.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

We are grateful to our participants.

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