Acupuncture

Stop Hypertension With the Acupuncture Research Program (SHARP)

Results of a Randomized, Controlled Clinical Trial

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Abstract—Case studies and small trials suggest that acupuncture may effectively treat hypertension, but no large randomized trials have been reported. The Stop Hypertension with the Acupuncture Research Program pilot trial enrolled 192 participants with untreated blood pressure (BP) in the range of 140/90 to 179/109 mm Hg. The design of the trial combined rigorous methodology and adherence to principles of traditional Chinese medicine. Participants were weaned off antihypertensives before enrollment and were then randomly assigned to 3 treatments: individualized traditional Chinese acupuncture, standardized acupuncture at preselected points, or invasive sham acupuncture. Participants received ≤12 acupuncture treatments over 6 to 8 weeks. During the first 10 weeks after random assignment, BP was monitored every 14 days, and antihypertensives were prescribed if BP exceeded 180/110 mm Hg. The mean BP decrease from baseline to 10 weeks, the primary end point, did not differ significantly between participants randomly assigned to active (individualized and standardized) versus sham acupuncture (systolic BP: −3.56 versus −3.84 mm Hg, respectively; 95% CI for the difference: −4.0 to 4.6 mm Hg; P=0.90; diastolic BP: −4.32 versus −2.81 mm Hg, 95% CI for the difference: −3.6 to 0.6 mm Hg; P=0.16). Categorizing participants by age, race, gender, baseline BP, history of antihypertensive use, obesity, or primary traditional Chinese medicine diagnosis did not reveal any subgroups for which the benefits of active acupuncture differed significantly from sham acupuncture. Active acupuncture provided no greater benefit than invasive sham acupuncture in reducing systolic or diastolic BP. (Hypertension. 2006;48:838-845.)

Key Words: acupuncture ■ blood pressure ■ hypertension ■ randomized clinical trial ■ traditional Chinese medicine

Hypertension affects ≈700 million individuals worldwide and is attributable each year for >7 million excess deaths and loss of 64 million disability-adjusted life years. Hypertension in most individuals remains untreated or uncontrolled. Effective control of hypertension is limited by availability, cost, and adverse effects of antihypertensive medications. Modalities of complementary and alternative medicine, including acupuncture, are being used by patients with increasing frequency, but these therapies lack demonstrated efficacy and safety for treating cardiovascular disease and hypertension.

Acupuncture has been used in traditional Chinese medicine (TCM) to treat symptoms related to hypertension for >2500 years. Today, acupuncture is commonly used to treat hypertension in China and the West. The efficacy of acupuncture is well supported for treating postoperative dental pain and nausea with few reported adverse effects. Acupuncture has been found effective for treating a number of other acute and chronic conditions in a growing number of randomized trials, although opinion differs on the role of placebo effects. Mechanistic studies have demonstrated effects of acupuncture on the activity and plasma concentrations of blood pressure modulators, including: renin, aldosterone, angiotensin II, norepinephrine, serotonin, enkephalins, and ß-endorphins. The efficacy of acupuncture for treating hypertension is suggested by a large number of published case series and uncontrolled trials. Three randomized trials reported significant reductions in BP relative to randomly assigned control groups treated for 4 to 8 weeks, whereas 3 others did not report significant effects of acupuncture relative to control subjects. They were all relatively small trials (n=10 to 68), and all but Yin et al were limited

Received February 22, 2006; first decision March 12, 2006; revision accepted August 8, 2006.

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Hypertension is available at http://www.hypertensionaha.org

DOI: 10.1161/01.HYP.0000241090.28070.4c

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by ≥ 1 of the following: incomplete descriptions of methods, incomplete blinding, and lack of peer review.

The Stop Hypertension with the Acupuncture Research Program (SHARP) pilot trial\(^9\) overcomes these limitations by combining rigorous methodology, adherence to principles of TCM acupuncture, and a large sample size. We investigated whether acupuncture administered according to principles of TCM more effectively controlled hypertension than invasive sham acupuncture and whether acupuncture individualized to each participant’s TCM diagnosis was more effective than acupuncture at preselected acupuncture points.

### Methods

#### Trial Design

The SHARP trial was a prospective, double-blind, randomized, sham-controlled, parallel-group clinical trial testing the efficacy of 6 weeks of twice-weekly TCM acupuncture for treating moderate essential hypertension without use of antihypertensive medications. The complete study design has been published.\(^9\)

The trial protocol was approved by applicable institutional review boards and was monitored by an independent data and safety monitoring board. Prospective study participants were recruited from outpatient clinics, referrals from Boston-area physicians, via advertising in periodicals and on public transportation, and through mass mailings to age-eligible Boston residents. All of the participants provided written informed consent. The eligibility criteria included: (1) essential hypertension with stable blood pressure (BP) after suspension of any antihypertensive medications between 140/90 mm Hg and 179/109 mm Hg over 3 qualifying visits spanning 8 to 31 days; (2) age ≥ 18 years; (3) no acupuncture in the previous 6 months; and (4) no medical contraindications to acupuncture or suspension of antihypertensive medications if prescribed previously (including: history of cerebrovascular events, endocrine disorders, and renal insufficiency). Participants were randomly assigned with equal allocation to each of 3 treatments: TCM individualized (IND), TCM standardized (STD), or control (CNTL) acupuncture (Table 1).

IND and STD acupuncture, based on TCM principles, were considered active treatment. CNTL acupuncture was an invasive sham control with insertion of acupuncture needles at non-TCM sites. Randomizations were stratified according to use of antihypertensive medications in the previous 6 months and were supplied by a centralized computer just before first treatment.

Participants were weaned off antihypertensives, screened for trial eligibility, and followed for 1 year after random assignment for BP, physical exams, electrocardiograms, quality of life (QoL), and adverse events at Massachusetts General Hospital. Antihypertensive medications were suspended individually with ≥ 7 days between each suspension conditional on BP remaining < 180/110 mm Hg. At each visit, 3 or 5 replicate measurements of seated BP were made after at least a 5-minute rest period using manual mercury sphygmomanometers by trained staff masked to participant random assignment. The same size of arm cuff, determined individually for each participant, was used at all of the visits. At 2 visits during the 6- to 8-week treatment interval, BP was measured immediately before and immediately after treatment. Antihypertensive drugs were initiated between random assignment and week 10 under the following conditions: (1) either systolic or diastolic BP exceeded 180 mm Hg or 110 mm Hg, respectively, at a single visit; (2) either systolic or diastolic BP exceeded 170 mm Hg or 105 mm Hg, respectively, on 2 sequential visits; or (3) an adverse event required treatment to lower BP. Criteria for initiating antihypertensive drugs were relaxed after week 10 with drugs initiated if either systolic or diastolic BP exceeded 140 mm Hg or 90 mm Hg, respectively, or to treat an adverse event.

Participants received acupuncture diagnoses and treatment from a team of licensed acupuncturists in a clinic established at Massachusetts General Hospital. Diagnoses and treatment followed TCM principles as described by Cheng.\(^40\) With full follow-up, treatment consisted of ≤ 12 generally twice-weekly 30-minute acupuncture sessions provided over 6 to 8 weeks. At visits 1, 5, 9, and 12, a diagnosing acupuncturist trained in China and with ≥ 12 years of clinical experience, masked to random assignment, established each participant’s TCM differential diagnosis\(^6\) based on evaluation of history and symptoms and examination of pulses, face, and tongue using a 32-point standardized diagnosis inventory. A separate team of treating acupuncturists, masked to BP, administered the most recently prescribed treatment for IND participants or substituted STD or CNTL acupuncture for participants randomly assigned to those treatment groups. Details of the criteria used for TCM diagnoses, acupuncture point definitions, including depth and duration of needle insertion, needle stimulation, elicitation of de qi (a dull aching and irradiating sensation indicative of effective needle placement), and locations of control points are provided in Kalish et al.\(^9\)

Blood chemistries, lipid profiles, complete blood cell counts, and urinalysis were performed at baseline, 10 weeks, 6 months, and 12 months. QoL data were collected using self-administered Medical Outcomes Study Short Form questionnaires\(^41\) at baseline, 10 weeks, and 12 months. Maintenance of participant masking to their treatment randomization was assessed at 4 months using a self-administered instrument that asked participants to guess their treatment assignment and state their confidence on a 5-point scale.

In addition to changes in BP, adverse events were recorded when participants presented with complaints at any time and based on asking participants if they had been well at each visit. Serious adverse events were recorded as defined by the International Conference on Harmonization Guideline E2A.\(^42\)

#### Statistical Analysis

The primary end point was change in systolic BP (SBP) from baseline to week 10. Ten-week change in diastolic BP (DBP) was a secondary end point. The primary comparison was between participants randomly assigned to active (IND and STD) versus sham (CNTL) acupuncture. To evaluate the efficacy of acupuncture for treating hypertension, BP observations made after the initiation of antihypertensives were censored.

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**TABLE 1. Treatment Definitions**

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Treatment Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>IND</td>
<td>Corporal acupuncture at 10 to 12 points (median: 12, counting bilateral points twice) selected and stimulated as individually prescribed. Auricular acupuncture at the 2 most active points identified with a point detector at the start of each treatment session.</td>
</tr>
<tr>
<td>STD</td>
<td>Corporal acupuncture at 5 bilateral points with neutral stimulation: GB 20, LI 11, LR 03, SP 06, and ST 36. Auricular acupuncture at Heart and Jiāng Ya Gōu. Points selected a priori by an expert panel.</td>
</tr>
<tr>
<td>CNTL</td>
<td>Corporal acupuncture at 5 bilateral points that do not fall along any TCM meridian with no stimulation. Auricular acupuncture in Darwin’s tubercle and the posterior ear lobe. All corporal and auricular acupuncture points in areas considered inactive according to TCM.</td>
</tr>
</tbody>
</table>
The primary analysis was a linear mixed model of change in BP between randomization and weeks 2 through 10 controlling for baseline BP, use of antihypertensives in the 6 months before baseline, and gender. Treatment group, days since first treatment, and their 2-way interaction were included as fixed and random terms modeling within-participant residuals as compound symmetric over visits. Unstructured and autoregressive covariance models fit less well. Comparisons among treatment groups were tested using linear contrasts evaluating differences at week 10. Reported point estimates are least-square means.

Subgroup analyses for age, race, gender, baseline BP, history of antihypertensive use, obesity, and primary TCM diagnosis were tested by including each classification and its 2- and 3-way interactions with treatment and time in the primary model. Significance of the 3-way interaction provided evidence that treatment-specific differences in the rates of BP change varied among subgroups. Differences among treatment groups at baseline were tested by Fisher’s exact test and 1-way ANOVA. Univariate changes in SBP and DBP between measurements taken immediately before and after an acupuncture treatment were tested by ANCOVA. Differences among treatment groups in the rate of antihypertensive initiation were tested by log rank test. Differences among treatment groups at baseline were tested by Fisher’s exact test and 1-way ANOVA. Differences in the number of antihypertensives required were tested by the Jonckheere–Terpstra test. Changes in laboratory values were assessed by ANCOVA. Effects on QoL were tested as the change from baseline of the Medical Outcomes Study Short Form physical and mental component scores by univariate and multivariate ANCOVA. Adequacy of masking was tested by Fisher’s exact test comparing true assignments to participant guesses, including “don’t know.” Confidence scores were tested by ordinal logistic regression. Differences in adverse event rates were analyzed in a negative-binomial generalized linear model. For all of the tests, significance was accepted for $P < 0.05$ for 2-tailed tests. Analyses were performed using SAS (version 9.1.2, SAS Institute).

Results

Participants and Treatment

Between March 2001 and July 2002, 424 individuals provided written, informed consent and were screened for trial eligibility, of whom 192 individuals were determined eligible and interested (Figure 1). Baseline characteristics of the 192 randomly assigned participants did not differ significantly among treatment groups, except for racial profile, with more minority subjects represented in the CNTL group by chance (Table 2). Four participants lacked any follow-up data and were excluded from the primary analysis. Sample sizes are somewhat lower for data from self-administered instruments.

Of the 188 participants with follow-up, nearly all (96%) received 12 treatments over an average of 42 days (range: 35 to 65 days). IND participants received a wide range of...
treatments. The most common combination of points prescribed included 3 of the 5 bilateral points used in the STD treatment (GB20, LI11, and SP06). The number of STD corporeal points prescribed for IND participants was distributed as follows: 1% received acupuncture at 0 STD points, 9% at 2 STD points, 28% at 4 STD points, 41% at 6 STD points, 20% at 8 STD points, and 2% at all 10 STD points (the sum is >100% because of rounding error). Participants received the wrong treatment on 3 occasions of 2219 treatments administered (1 CNTL participant received an IND treatment, 1 CNTL participant received a STD treatment, and 1 IND participant received an IND treatment).

Primary and Secondary End Points
Mean SBP and DBP declined between randomization and week 10 (Figure 2). At 10 weeks, BP declines did not differ between participants randomly assigned to active (IND and STD) versus sham (CNTL) acupuncture (SBP [mean±SE]: −3.56±1.92 mm Hg versus −3.84±1.93 mm Hg; \( P=0.90 \); DBP: −4.32±1.01 mm Hg versus −2.81±0.99 mm Hg; \( P=0.16 \)). The 95% CIs on the estimated benefit of active versus sham acupuncture were within 4 mm Hg (active versus sham: SBP: −4.00 to 4.56 mm Hg; DBP: −3.65 to 0.62 mm Hg). BP declines did not differ between participants receiving IND versus STD acupuncture or IND versus CNTL acupuncture (Table 3). No treatment effects were evident after 12 months. Categorizing participants by age, race, gender, baseline BP, history of antihypertensive use, obesity, or primary TCM diagnosis did not identify any subgroups for whom the benefits of TCM acupuncture differed significantly from sham acupuncture.

On average, BP increased modestly between measurements taken before and after an acupuncture session (by 2.1/0.8 mm Hg for a participant with preacupuncture BP of 143/88 mm Hg), although individual responses were quite variable (SD: ±8.9/5.5 mm Hg). The median interval between preacupuncture and postacupuncture measurements was 75 minutes. No significant difference was found in the immediate effect of active versus sham acupuncture (SBP [mean±SE]: −0.10±0.13 mm Hg; 95% CI: −2.13 to 1.92; \( P=0.92 \); DBP: −1.04±0.61 mm Hg; 95% CI −2.24 to 0.15; \( P=0.09 \)).

The risk of developing BP levels that required initiation of antihypertensive drugs did not differ significantly among participants randomly assigned to the 3 treatment groups (\( P=0.97 \); Figure 3). By 10 weeks, 11% of IND participants, 19% of STD participants, and 12% of CNTL participants were on antihypertensives. The number of distinct classes of antihypertensives required to control hypertension at 10 weeks among participants using antihypertensives did not differ among the 3 treatment groups (\( P=0.51 \)). Ten-week change in physiological parameters other than BP differed significantly among treatment groups only in the case of fasting blood glucose, with a significant decrease among participants receiving sham acupuncture (IND and STD mean±SE: CNTL mean±SE: fasting glucose (mg/dL): 2.33±0.85, −1.33±1.23; \( P=0.015 \)). The treatment groups did not differ with respect to changes in weight, blood urea nitrogen, creatinine, fasting triglycerides, total cholesterol, high-density lipoprotein, or low-density lipoprotein. STD participants reported a significant decline in mental QoL.
between baseline and 10 weeks relative to IND and CNTL participants (mean±SE: IND: 0.59±1.01; STD: −2.49±0.98; CNTL: 1.17±1.09; P=0.025). Mean 10-week change in physical QoL did not differ among participants (IND: 0.27±0.73; STD: 0.81±0.70; CNTL: 0.27±0.78; P=0.83). Overall mean change in QoL did not differ between participants receiving active versus sham acupuncture (P=0.35).

Among the 141 participants who completed the masking assessment instrument at 4 months, the association between true random assignment and participants’ guessed random assignment was nearly significant (P=0.06). Although participants in all of the groups were equally likely to make a guess about their treatment assignment (67%; P=0.53) and were equally confident in their guesses (P=0.92), IND participants were more likely to guess IND assignment (59%) than STD (19%) or CNTL (41%) participants among those guessing. Similarly, STD participants were more likely to guess STD assignment (52%) than IND (22%) or CNTL (38%) participants.

Three study-related serious adverse events occurred over 165 patient years of follow-up: 2 STD participants experienced hypertensive urgencies, and 1 CNTL participant experienced congestive heart failure. No deaths occurred. The risk of any (n=98) or study-related (n=50) adverse events did not differ among treatment groups (P>0.68).

**Discussion**

The results of the SHARP pilot trial did not indicate any differential benefit of active acupuncture relative to invasive

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### TABLE 3. BP Change From Baseline to 10 Weeks

<table>
<thead>
<tr>
<th>Treatment Groups and Comparisons</th>
<th>N</th>
<th>SBP, mm Hg</th>
<th>DBP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>IND</td>
<td>60</td>
<td>−3.57 (−7.33 to 0.18)</td>
<td>−4.67 (−6.63 to −2.70)</td>
</tr>
<tr>
<td>STD</td>
<td>64</td>
<td>−3.55 (−7.33 to 0.24)</td>
<td>−3.97 (−5.95 to −1.99)</td>
</tr>
<tr>
<td>CNTL</td>
<td>64</td>
<td>−3.84 (−7.62 to −0.05)</td>
<td>−2.81 (−4.75 to −0.87)</td>
</tr>
<tr>
<td>IND and STD vs CNTL</td>
<td>64</td>
<td>0.28 (−4.00 to 4.58) P=0.90</td>
<td>−1.51 (−3.65 to 0.62) P=0.16</td>
</tr>
<tr>
<td>IND vs STD</td>
<td></td>
<td>−0.03 (−4.90 to 4.85) P=0.99</td>
<td>−0.70 (−3.12 to 1.72) P=0.57</td>
</tr>
<tr>
<td>IND vs CNTL</td>
<td></td>
<td>0.27 (−4.64 to 5.18) P=0.91</td>
<td>−1.86 (−4.30 to 0.58) P=0.14</td>
</tr>
</tbody>
</table>

All values are least-square means and 95% CIs from the primary analysis.
Our results suggest that 6 weeks of twice-weekly sessions of fully individualized TCM acupuncture are unlikely to achieve clinically meaningful reductions in SBP or DBP for the average patient with mild-to-moderate hypertension relative to invasive sham acupuncture. Although the estimated 95% CIs cannot be interpreted directly as bounds on the true efficacy of active acupuncture, it is unlikely that active acupuncture reduces SBP or DBP >5 mm Hg. Twice-weekly acupuncture is unlikely to be cost-effective relative to available pharmacological treatments for hypertension nor is it likely to be widely embraced by patients solely on the basis of any mild antihypertensive effect given the significant time required for acupuncture therapy. Nevertheless, it is possible that active acupuncture may yield larger benefits if the treatment is extended beyond 6 weeks. In addition, given that the diagnosing acupuncturists were prescribing holistic treatments tailored to a subject’s specific presentation. The use of separate diagnosing and treating acupuncturists may represent an antihypertensive effect of invasive acupuncture not along TCM-defined meridians or treatment in environments unrelated to needle placement. Middlekauff et al reported that invasive sham acupuncture at a non-TCM point in the anterior deltoid resulted in a significant attenuation of the acute increase in BP induced by a mental stress test. Con-versely, other researchers have not observed an improvement in hemodynamics from invasive sham acupuncture.

A number of factors limited interpretations from the SHARP trial. Although larger than any previous study, the SHARP pilot trial was not designed to detect small effects. The conclusion of no active acupuncture effect would be stronger if the CIs of the estimated differences between treatments were narrower. Use of sham acupuncture for controlling SBP, avoiding need for antihypertensive medications, or improving QoL or other comorbidities of hypertension, including dyslipidemia, renal function, or glucose control. No subgroups of subjects were identified that experienced a differential benefit of one treatment over another in controlling BP. The average magnitude of BP declines (SBP: −3.5 to −3.8 mm Hg; DBP: −2.8 to −4.7 mm Hg) achieved by SHARP participants was no greater than the magnitude of decrease observed in the placebo arms of 7 pharmaceutical trials analyzed by the Individual Data Analysis of Antihypertensive Intervention trials (INDANA) research committee (SBP: −6.8 to −14.6 mm Hg; DBP: −2.8 to −7.2 mm Hg; S. Pocock, unpublished data, 2003). These reductions are consistent with regression to the mean. They may also reflect changes in diet or lifestyle or other nonspecific effects of participating in clinical research. Alternatively, the observed BP reductions may represent an antihypertensive effect of invasive acupuncture unrelated to needle placement. Middlekauff et al reported that invasive sham acupuncture at a non-TCM point in the anterior deltoid resulted in a significant attenuation of the acute increase in BP induced by a mental stress test. Conversely, other researchers have not observed an improvement in hemodynamics from invasive sham acupuncture.

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acupuncture without complementary use of antihypertensives does not reflect the usual practice among acupuncturists for subjects with stage 2 hypertension. Twelve treatment sessions spread over 6 to 8 weeks may be inadequate to reduce systolic hypertension reliably. The small magnitude of any immediate antihypertensive effect of active acupuncture may suggest that acupuncture treatments were not adequately administered given that most published work and practicing acupuncturists report sizeable reductions in both SBP and DBP immediately after treatment. Lastly, use of an invasive sham control group prevented estimation of nonspecific effects of acupuncture, which may constitute an important component of clinical acupuncture.

**Perspectives**

Twelve sessions of TCM acupuncture do not appear to control hypertension better than invasive sham acupuncture when used as monotherapy. Some participants experienced substantial improvements in their hypertension, but no subgroups of participants could be identified from baseline characteristics that experienced a differential benefit of active acupuncture. Further research is required to determine whether acupuncture can enhance clinical management of hypertension if used in combination with antihypertensive agents, over longer periods, or among specific subgroups of patients.

**Acknowledgments**

Thanks are expressed to the participants of the SHARP trial for their time and commitment, to our acupuncture consultants (Jian Kong, Jing Liu, Weidong Lu, and Zhen-zhen Zhang); the staff at the Hypertension Center (Sharon Maginnis, Jean Sullivan, and Mildred Wasilecki), the Acupuncture Clinic (Kate Billings, Edward Chiu, Christian Connors, Amy Hull, Diane Iuliano, Zhi Ping Li, and Nicole Stockholm), and the Data Coordinating Center (Patricia Connell, Allison Gemmel, and Julie Miller); to Chang Shik Yin and Yun-ju Kim for sharing prepublished manuscripts and bibliographic suggestions; and to Stuart Pocock for sharing data from the INDANA database.

**Source of Funding**

This work was supported by Cooperative Agreement U01 AT00210, awarded to New England Research Institutes, Inc, by the National Center for Complementary and Alternative Medicine, National Institutes of Health.

**Disclosures**

None.

**References**


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_Hypertension_. 2006;48:838-845; originally published online October 2, 2006; doi: 10.1161/01.HYP.0000241090.28070.4c

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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