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A Randomized, Controlled Pilot Study of Acupuncture Treatment for Menopausal Hot Flashes

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## Abstract and Introduction

### Abstract

**Objective:** To investigate the feasibility of conducting a randomized trial of the effect of acupuncture in decreasing hot flashes in peri- and postmenopausal women.

**Design:** Fifty-six women ages 44 to 55 with no menses in the past 3 months and at least four hot flashes per day were recruited from two clinical centers and randomized to one of three treatment groups: usual care (n = 19), sham acupuncture (n = 18), or Traditional Chinese Medicine acupuncture (n = 19).

Acupuncture treatments were scheduled twice weekly for 8 consecutive weeks. The sham acupuncture group received shallow needling in nontherapeutic sites. The Traditional Chinese Medicine acupuncture group received one of four treatments based on a Traditional Chinese Medicine diagnosis. Usual care participants were instructed to not initiate any new treatments for hot flashes during the study. Daily diaries were used to track frequency and severity of hot flashes. The mean daily index score was based on the number of mild, moderate, and severe hot flashes. Follow-up analyses were adjusted for baseline values, clinical center, age, and body mass index.

**Results:** There was a significant decrease in mean frequency of hot flashes between weeks 1 and 8 across all groups ( $P = 0.01$ ), although the differences between the three study groups were not significant. However, the two acupuncture groups showed a significantly greater decrease than the usual

care group ( $P < 0.05$ ), but did not differ from each other. Results followed a similar pattern for the hot flash index score. There were no significant effects for changes in hot flash interference, sleep, mood, health-related quality of life, or psychological well-being.

**Conclusions:** These results suggest either that there is a strong placebo effect or that both traditional and sham acupuncture significantly reduce hot flash frequency.

## Introduction

Hot flashes and/or night sweats are the most common and troubling symptoms associated with menopause.<sup>[1,2]</sup> Hot flashes generally begin early in the menopausal transition and peak just before a woman's last menstrual period.<sup>[3,4]</sup> Although some women report going through the menopausal transition without experiencing any hot flashes,<sup>[5]</sup> for other women, these symptoms can be frequent and severe enough to become debilitating and interfere with daily activities and quality of life.<sup>[6-12]</sup> Relief from hot flashes and night sweats has been shown to be the primary reason that women begin hormone therapy (HT).<sup>[13-15]</sup>

Estrogen therapy, alone or in combination with progesterone, is currently the gold standard for treatment of vasomotor symptoms. HT, however, is associated with a number of risks such as thromboembolic events and breast cancer, and some troublesome side effects such as breast tenderness and irregular bleeding.<sup>[16-18]</sup> The wide publicity of the Women's Health Initiative results has heightened women's concerns about taking HT. Given the risks and side effects associated with HT, many women either cannot or choose not to take HT and have sought alternatives.<sup>[19-22]</sup> These alternatives include other pharmaceutical agents, herbal or dietary remedies, and behavioral therapies. Unfortunately, many of these agents have a high incidence of side effects or have not been shown to be effective.<sup>[21,23-26]</sup>

Modern theories of neurophysiologic and neurohumoral mechanisms as well as concepts of Traditional Chinese Medicine (TCM) suggest that acupuncture may be an effective method to control hot flashes.<sup>[27]</sup> Evidence suggests that changes in levels of  $\beta$ -endorphins and other neurotransmitters affect the thermoregulatory center in the hypothalamus and that acupuncture alters these central neuromodulators.<sup>[28-30]</sup> TCM differential diagnosis and treatment strategies for menopausal syndrome are currently taught in TCM colleges in China and in nationally accredited acupuncture schools in the United States.

Studies of acupuncture and hot flashes have been conducted with mixed results. Several uncontrolled studies have shown positive effects of acupuncture.<sup>[31-33]</sup> Studies that include sham acupuncture controls have shown beneficial effects in both true and sham acupuncture groups<sup>[34,35]</sup> or in the true acupuncture group only.<sup>[36]</sup>

Except for Nir et al,<sup>[36]</sup> most studies use a set of standard acupuncture points. The TCM approach, however, tends to rely on more individualized treatments. This article describes the results of a randomized clinical trial pilot study to test the effectiveness of acupuncture for treating menopausal hot

flashes. A three-group design was used that compared usual care (UC) to both sham acupuncture (SA) and standardized individual acupuncture based on TCM principles. The primary outcomes were a decrease in hot flash frequency and severity. Secondary outcomes included improvement in hot flash interference, sleep, mood, and overall quality of life.

## **Methods**

### **Study Design**

We conducted a two-site clinical trial using a three-arm prospective, randomized, single-blind, sham-control design in peri- and postmenopausal women experiencing four or more hot flashes per day. Recruitment occurred between August and November 2004 at the University of North Carolina at Chapel Hill and between September 2005 and January 2006 at Massachusetts General Hospital. Participants were in the study for a total of 18 weeks, including a 2-week pretreatment diary collection period, 8 weeks of acupuncture treatment, and 8 weeks of follow-up after treatment was completed. The study was approved by the institutional review boards at both sites.

### **Study Participants**

Participants eligible for the study were peri- or postmenopausal women ages 42 to 55 with at least four moderate to severe hot flashes per day. Perimenopause was defined as 3 or more months of self-defined amenorrhea and postmenopause was defined as amenorrhea for 12 or more months. Participants were excluded for the following reasons: had used HT, a selective estrogen-receptor modulator, an aromatase inhibitor, clonidine, Bellergal, antidepressant therapy, or gabapentin in the past 12 weeks; had received chemotherapy; had a significant psychiatric disorder; had used acupuncture treatment for any reason within the past 4 weeks; had any previous acupuncture treatment for hot flashes; had untreated thyroid disease; had been diagnosed with a bleeding or clotting problem other than heavy periods; or were currently taking any prescribed medications that increase the risk of bleeding (Coumadin, Enoxaparin, or Plavix).

### **Procedures**

Women were recruited through newspaper advertisements, radio announcements, and hospital postings. Initial eligibility was determined by a telephone screener. Eligible women were scheduled for an initial clinic visit where they completed a self-administered baseline questionnaire and received instructions on keeping a 2-week hot flash diary, which was then mailed back to the clinic and used to verify eligibility. Women who met the criteria of an average of at least four hot flashes per day were randomized to one of the three study groups. Those in the two treatment groups were scheduled for acupuncture visits. Those in the UC group were scheduled for a clinic visit in 4 weeks. Women who were not eligible were called, thanked, and informed that they were not eligible for the study. All study participants completed questionnaires 4 weeks after baseline and at the end of treatment.

Participants assigned to acupuncture (both TCM and sham) were seen twice a week for 8 weeks (a total of 16 treatment sessions) by a trained acupuncturist. Study staff who administered questionnaires were blinded to which form of acupuncture that the women received. All study participants were instructed not to take hormonal medications or initiate other treatments for their hot flashes during treatment. All study participants (including those in the UC group) were paid \$10 for each clinic visit (baseline, mid-treatment, and end of treatment). Those who completed all three visits were paid an additional \$20.

## Randomization

Eligible women were randomized to one of the three groups stratified by clinical center (Massachusetts General Hospital and University of North Carolina). Randomization sequences were prepared at Wake Forest University. Participants were considered to have been randomized when the group membership was made known, even if the woman did not actually attend any treatment sessions. We used a block randomization with block size unknown to the investigator and staff to ensure equal accrual to each arm of the study.

## Acupuncture Groups

All treatments were performed by experienced acupuncturists trained in TCM. At the first treatment session, women received a TCM diagnosis and prescription based on standard acupuncture points. This prescription was maintained throughout the treatment period. Participants assigned to the TCM acupuncture group (TA) received needling at sites based on a standardized individual approach, a combined approach that maximized therapeutic benefits by customizing points based on a woman's presentation and use of standardized core points. Women assigned to the SA group received needling at sites thought to have minimal effects on hot flashes. The acupuncturists were blinded to the participant's treatment group until after making the TCM diagnosis.

**TA Group.** According to TCM theory, menopausal symptoms are mainly caused by a decline in kidney essence leading to a yin/yang imbalance. Women in the TA group received a standard acupuncture treatment designed to tonify or reinforce the kidney essence, balance yin/yang, and control hot flashes and night sweats. The standard treatment involved the following acupuncture points: CV-4, KI-3, SP-6, BL-23, HT-6, and KI-7. Except for CV-4, which is located in the midline, all standard treatment points were needled bilaterally, for a total of 11 acupuncture points (Figure 1). In addition to the standardized treatment that all participants received, additional points were needled based on a person's TCM diagnostic category or based on the acupuncturist's clinical judgment. No more than 16 acupuncture points were needled during any treatment. The diagnostic categories and the associated acupuncture points are summarized in [Table 1](#). We anticipated that most of the women's symptoms and clinical presentations would be consistent with one of four different TCM diagnostic categories: kidney yin deficiency; kidney yin deficiency and kidney yang deficiency; kidney yin and liver yin deficiency leading to liver yang rising, and kidney and heart not harmonized.



## Figure 1.

True and sham acupuncture points. True acupuncture points were located in specific acupuncture point locations thought to have an effect on hot flashes. Sham acupuncture points were located in sites away from the points and meridian pathways thought to have an effect on hot flashes.

Sterile, single-use, Vinco 34-gauge, 1-inch (0.22 x 25 mm) and 30-gauge, 1.5-inch (0.30 x 40 mm) needles were used. Needles were inserted through the skin to a depth of from 0.5 to 3 cm based on anatomical location. Acupuncturists attempted to achieve a *de Qi* sensation upon insertion of acupuncture needles (a sensation of soreness, numbness, heaviness, or distention around the needled acupuncture point), whenever possible. The duration of each treatment was approximately 30 minutes: 20 minutes for anterior points and 10 minutes for posterior points.

**SA Group.** This group was included to assess effects that may be related to attention, relaxation, anticipation of benefit, and the needling process itself, but which are not secondary to physiologic changes that may be induced by needling locations on the body that correspond to conventional acupuncture points. The sites in which the SA needles were placed are believed to have minimal possible effects on hot flashes. Each woman assigned to the SA group had six needles on the right side of the body and six on the left: nonacupuncture point sites needled shallowly, without attempting to elicit the *de Qi* sensation ( [Table 1](#) and Figure 1).

## UC Group

The participants in this group did not receive any form of acupuncture needling. They were instructed not to initiate any new treatments for their hot flashes over the next 2 months, but could continue with any nonpharmacologic treatments that they were currently using.

## Measures

The primary study outcomes were frequency and severity of hot flashes as measured by the Daily Diary of Hot Flashes. This diary records the frequency and severity of hot flashes and allows the investigator to calculate hot flash frequency and a hot flash index score (the sum of the number of hot flashes multiplied by severity).<sup>[37]</sup> Women were asked to record the number and severity of hot flashes each day during the treatment phase of the trial. Women were provided counters to help them keep track of the number of hot flashes throughout the day. We modified the severity rating scale, using 1 to 3 (1 = mild, 2 = moderate, 3 = severe) in place of 1 to 4 as used in the studies of Loprinzi et al.<sup>[25,38,39]</sup> The simplified scale is easier to understand. Our modified scale also distinguishes between daytime and nighttime vasomotor symptoms.

Secondary study outcomes were hot flash interference, sleep, symptoms bothersomeness, mood, and general quality of life.

**Hot Flash Interference.** The 10-item Hot Flash Related Daily Interference Scale measures the degree that hot flashes interfere with daily life or overall quality of life and nine specific domains within the past week (work, social activities, leisure activities, sleep, mood, concentration, relation with others, sexuality, and enjoyment of life).[40]

**Sleep.** The Women's Health Initiative Insomnia Rating Scale was used to measure sleep patterns and quality.[41] This 6-item scale is designed to measure sleep initiation and maintenance in the past 4 weeks. The scale assesses sleep problems including, but not limited to, the ability to fall asleep, sleep quality, and fatigue.

**Symptoms.** In addition to assessing frequency and severity of vasomotor symptoms with the daily diaries, we administered the Menopause-specific Quality of Life Questionnaire to measure bothersomeness of vasomotor symptoms and other menopause-related symptoms. This questionnaire contains 30 symptoms categorized into four domains, vasomotor, physical, psychological, and sexual, and a global quality-of-life-item.[42]

**Mood.** The Psychological General Well-Being Index was used to assess the following moods: vitality, self-control, well-being, general health, depressed mood, and anxiety and a composite score that ranges from 0 (most negative affective experience) to 110 (most positive effective experience).[43,44]

**Health-related Quality of Life.** Two measures of quality of life were included: a single global 100-mm visual analogue scale with which women rated their overall quality of life along a line where 0 is the lowest possible quality of life and 100 is the highest, and the Medical Outcomes Study 36-Item Short Form Health Survey.[45]

Study covariates included sociodemographics (age, education, marital status, employment status), medical information (body mass index, blood pressure, past HT use, other complementary alternative medicine use), and the Somatosensory Amplification Scale.[46] This scale is a 10-item questionnaire that assesses sensitivity to a range of uncomfortable bodily sensations and physiologic states that are not typically symptoms of disease. The scale has been shown to prospectively predict the persistence of hypochondriacal symptomatology in transient hypochondriacal patients[46] and frequency of hot flashes.[4]

## Statistical Analysis

All analyses were conducted using the intent-to-treat approach. Descriptive and regression analyses were performed using SAS software (SAS Institute Inc., Cary, NC). Repeated-measures models were used to describe the relationship between hot flash frequency and the index score with treatment and

time. The dependent variable was the log of the ratio of the follow-up measures divided by baseline (ie,  $\log_e [\text{follow-up} + 1 / \text{baseline} + 1]$ ). The independent variables included intervention group and week. Results were adjusted for baseline values and clinical center. The addition of the constant (1) to baseline and follow-up measures was necessary because some participants had hot flash frequency and index equal to zero for some weeks. In further analyses the two acupuncture groups were combined as they did not differ significantly.

## Results

Participant data are shown in Figure 2. Of the 246 women screened, 141 (57%) were ineligible. Primary reasons for ineligibility at the time of screening were not enough hot flashes and taking antidepressants. Of the 105 eligible women, 41 women declined participation. Of the 64 women seen for baseline visits, eight did not have enough hot flashes after the diary completion. Fifty-six women were entered into the study and randomized. Overall, we found that 39% (97) of women who were reached in response to the advertisements were eligible and that 58% (56/97) of these eligible women were enrolled in the study. Study retention was excellent with all women remaining in the study. However, not all women completed all study procedures. Eight (42%) of the women in the TA group and 10 (56%) in the SA group completed at least 80% of the 16 treatments. Furthermore, two women in the UC group did not complete any follow-up diaries, one in the SA group, and three in the TA group.



**Figure 2.**

CONSORT figure.

## Sample Characteristics

Sample characteristics by group assignment are shown in [Table 2](#). Thirty-six percent of women had an average of four to six hot flashes per day, whereas 64% had an average of more than seven hot flashes per day. Fourteen percent of the women were perimenopausal, 48% were naturally postmenopausal, and 38% had undergone surgical menopause. There were no significant differences by group. The majority of women had a TCM diagnosis of kidney deficiency ( $n = 14$ ) or kidney and heart not harmonized ( $n = 10$ ).

At baseline, the mean frequency of hot flashes was between 7.4 in the UC group and 8.5 in the SA and TA groups. These differences were not statistically significant ( $P = 0.63$ ). Differences in the mean index scores were also not statistically significant ( $P = 0.80$ ): UC, 16.3, SA, 18.1 and TA, 15.7.

## Hot Flash Change

The percentages of change in hot flash frequency (including daytime and nighttime) are shown in Figure 3. There was a significant week effect ( $P = 0.01$ ) with hot flash frequency declining over time for all three groups. There were no significant differences in hot flash frequency between the treatment groups ( $P = 0.15$ ). However, when the two acupuncture groups were combined, there was a significant difference between acupuncture and UC ( $P < 0.05$ ), with both acupuncture groups showing greater decline than the UC group. By the third week of treatment, women in both acupuncture groups were reporting a decrease of approximately 40% in hot flash frequency. The UC group showed a decrease of approximately 10% until week 7, when hot flash frequency decreased more. One participant in the UC group had a particularly greater decrease at weeks 7 and 8, which is reflected in the figure, but the significance of the results is similar with and without this participant. When daytime frequency and nighttime frequency were looked at separately, these effects were only seen for daytime frequency (data not shown).



### Figure 3.

Percentage of change in hot flash frequency in the daytime and nighttime. UC, usual care; SA, sham acupuncture; TA, Traditional Chinese Medicine.

Figure 4 shows the results using the hot flash index, which takes into account both frequency and severity. This figure follows a pattern similar to that for frequency alone, although neither the week effect ( $P = 0.08$ ) nor treatment effect ( $P = 0.07$ ) was significant. There was a significant decrease ( $P = 0.02$ ) over time in both of the acupuncture groups compared with the UC group, with no difference between the acupuncture groups. Both acupuncture groups decreased to approximately 40% to 50% of their index score by week 3.



### Figure 4.

Percentage of change in hot flash severity index in the daytime and nighttime. UC, usual care; SA, sham acupuncture; TA, Traditional Chinese Medicine.

## Other Outcomes

We did not find any significant results in hot flash interference, sleep, mood, or health-related quality of life. Although this small pilot study was not powered to find statistical significance, these variables did not show any consistent trends. However, women in the two acupuncture groups reported that their vasomotor symptoms were less bothersome than women in the UC group reported ( $P < 0.02$ ).

## Discussion

This pilot study showed a significant decrease in hot flash frequency and index score for both TA and SA groups despite not having been powered for statistical significance. However, there were no observed clinical differences between the two acupuncture groups, as we had hypothesized. These results are remarkably consistent with those of Vincent et al,<sup>[34]</sup> who also found that hot flash frequency decreased in both TA and SA groups. Vincent et al,<sup>[34]</sup> however, did not have a UC group and were thus unable to determine whether both acupuncture treatments were equally effective or whether improvement was a result of time. The inclusion of the UC group in our study suggests that the decrease in hot flashes in both acupuncture groups was not due to time alone. The important question remains as to whether SA provides some benefit from the needling or whether the hot flash decrease was due largely to a placebo effect. Because we did not have an attention control group, a placebo effect cannot be ruled out.

Future research might use sham needling that does not penetrate the skin and/or include a placebo control group that does not receive any form of acupuncture, but receives an intervention that controls for attention and expectations, such as a psychoeducation group. It is possible that different acupuncture points might be more effective, but we do not think this is the case. Our acupuncture points were different from those used by Vincent et al,<sup>[34]</sup> yet our results were remarkably consistent. Future research might also include an objective measure of hot flashes to help determine whether sham acupuncture has a physiologic effect.

This study has several limitations. The time commitment for treatments was difficult for some women who had to travel, and less than half of the women in the TA group received at least 80% of the targeted treatments. To achieve better adherence to treatment, future research needs to make treatments more convenient for women and perhaps provide more incentives for adherence. Second, as a pilot study, the sample size was relatively small and was not powered to find significance on secondary outcomes (nor was it powered to find significance on primary outcomes). Our data, however, do not suggest any consistent trends in these outcomes. In addition, the small sample did not allow for analyses to examine characteristics of women who might benefit most from acupuncture.

The strengths of this study are the inclusion of both the SA and UC groups as controls, a wide range of secondary outcomes, and acupuncture based on TCM diagnosis.

## Conclusions

In this three-arm randomized trial of acupuncture for menopausal hot flashes, both TA and SA produced a significant decrease in hot flashes compared with a no-treatment, UC group. Whether this result was due to the effectiveness of sham needling or a placebo effect could not be determined.

## Table 1. TCM Diagnoses and Anticipated Treatments

Table 1: TCM Diagnoses  
and Anticipated Treatments

## Table 2. Sample Characteristics

Table 2: Sample  
Characteristics

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