Menopause: The Journal of The North American Menopause Society
Vol. 14, No. 1, pp. 45-52
DOI: 10.1097/01.gme.0000227854.27603.7d

Acupuncture for hot flashes: a randomized, sham-controlled clinical study

Ann Vincent, MBBS, MD,[1] Debra L. Barton, PhD, RN,[1] Jayawant N. Mandrekar, PhD,[1] Stephen S. Cha, MS,[1] Teresa Zais,[1] Dietlind L. Wahner-Roedler, MD,[1] Marina A. Keppler, LAc, MA, DiplAc,[1] Mary Jo Kreitzer, PhD, RN,[2] and Charles Loprinzi, MD[1]

ABSTRACT

Objective: Hot flashes are a significant problem in women going through the menopausal transition that can substantially affect quality of life. The world of estrogen therapy has been thrown into turmoil with the recent results of the Women's Health Initiative trial report. Pursuant to a growing interest in the use of alternative therapies to alleviate menopausal symptoms and a few pilot trials that suggested that acupuncture could modestly alleviate hot flashes, a prospective, randomized, single-blind, sham-controlled clinical trial was conducted in women experiencing hot flashes.

Design: Participants, after being randomized to medical versus sham acupuncture, received biweekly treatments for 5 weeks after a baseline assessment week. They were then followed for an additional 7 weeks. Participants completed daily hot flash questionnaires, which formed the basis for analysis.

Results: A total of 103 participants were randomized to medical or sham acupuncture. At week 6 the percentage of residual hot flashes was 60% in the medical acupuncture group and 62% in the sham acupuncture group. At week 12, the percentage of residual hot flashes was 73% in the medical acupuncture group and 55% in the sham acupuncture group. Participants reported no adverse effects related to the treatments.

Conclusions: The results of this study suggest that the used medical acupuncture was not any more effective for reducing hot flashes than was the chosen sham acupuncture.

Key Words: Hot flashes – Acupuncture.

A hot flash is a transient episode of flushing, sweating, and sensation of heat often accompanied by palpitations, feelings of anxiety, and chills.[1] Cross-sectional and longitudinal studies reveal that 50% to 70% of postmenopausal women suffer from hot flashes and night sweats.[2,3] The prevalence of hot flashes has been reported to be 60% at 52 to 54 years of age, declining to 30% at age 60 and 9% at age 72.[4] Symptoms have been reported to be more severe in women with surgical menopause compared with women with intact ovaries.[5]

Hot flashes affect quality of life. Symptoms associated with hot flashes include a sensation of moderate to severe warmth, sweating, weakness, feeling of faintness, change in heart rate or rhythm, anxiety, feelings of a panic attack, and disturbances with sleep.[6] Sleep deprivation has been reported to occur with repeated nocturnal hot flashes and has been reported to lead to decreased attention span, fatigue, an inability to concentrate, and cognitive difficulties.[6]

Estrogen has been the long-standing treatment of choice for hot flashes and decreases hot flashes by 80% or more.[7] Nonetheless, there has been renewed concerns about this

Received February 22, 2006; revised and accepted April 11, 2006.

From the [1]Mayo Clinic College of Medicine, Rochester, MN; and the [2]Center for Spirituality and Healing, University of Minnesota, Saint Paul, MN.

Funding/support: This trial was funded by a Mayo Foundation Award.

Financial disclosure: None reported.

Address correspondence to: Charles L. Loprinzi, MD, 200 First Street SW, Rochester, MN 55905. E-mail: cloprinzi@mayo.edu.

therapy based on the recent results of the Women's Health Initiative, which found that conjugated equine estrogens and medroxyprogesterone acetate increased the risk of breast cancer, coronary heart disease, strokes, blood clots, and dementia and that conjugated equine estrogens alone increased stroke risk.[8,9] As a result, many women have stopped estrogen and even more are fearful to initiate it. Thus, although estrogen is still indicated for hot flashes, the reluctance of patients to take it, and physicians to prescribe it, limits its utility.

Megestrol acetate, a synthetic progesterone, decreases hot flashes to a similar degree as estrogen.[10] Nonetheless, progesterone is a hormone, and the precise relationship of progesterone therapy alone to breast cancer is yet to be determined.

Antidepressants, including venlafaxine, paroxetine, and fluoxetine, and the antiseizure medication gabapentin have all been studied for hot flashes and appear to decrease hot flashes by about 50% to 60%.[11] These medications are limited by costs, some toxicities, and the refusal of some women to take antidepressants or anticonvulsant medications.[11]

Clonidine decreases hot flashes by about 30% to 40%, compared with a 20% to 30% reduction seen with placebo.[12] This limited efficiency and its toxicity limit its use.

Acupuncture is a rapidly growing complementary health modality that originated in Asia approximately 2,500 years ago. In November 1997 the National Institutes of Health conducted a consensus conference to review scientific evidence regarding acupuncture.[13] The panel concluded that acupuncture was a safe and effective treatment for various conditions, including addiction, chronic pain, and postoperative and chemotherapy-induced nausea and vomiting.[13] Although hot flashes are not yet a proven indication for acupuncture, several pilot reports have suggested that acupuncture decreases hot flashes.[14-16] One advantage of this modality is that the risk profile is low.

In one small uncontrolled pilot study, acupuncture was associated with an improved quality of life and decreased luteinizing hormone levels in menopausal women. However, no changes were seen in follicle-stimulating hormone, prolactin, estradiol, or progesterone levels.[14] In another study, both electroacupuncture and standard acupuncture were associated with an approximately 50% reduction in hot flashes in 24 healthy postmenopausal women.[15] In the electroacupuncture group, the results persisted 3 months after treatment. Also seen was a significant decrease in calcitonin gene-related peptide, a neuropeptide with endothelium-dependent vasodilator properties. In another study, 15 postmenopausal women with breast cancer on tamoxifen treated with weekly acupuncture for 3 months reported improvements in mood, somatic, and vasomotor symptoms.[16]

TABLE 1. *Acupuncture points*

Point	Meridian	Needling	Location
SP 4	Spleen	Perpendicular 1-2 cm, unilateral right	In the depression distal to and below the base of the first metatarsal bone, on the medial side of the foot
SP 6	Spleen	Perpendicular 1-3 cm, bilateral	3 cun above the medial malleolus, dorsal to the posterior border of the tibia
He 7	Heart	Perpendicular 0.5 cm, from the ulnar side 1 cm, bilateral	On the transverse crease of the wrist, radial to the tendon of medial flexor carpi ulnaris
L1 11	Large intestine	Perpendicular 1-2 cm, bilateral	With elbow flexed at 90 degrees the point is on the anterolateral elbow joint in the midpoint between the radial side of the skin crease of the elbow and lateral epicondyle humerus
Liv 2	Liver	Oblique 0.5-1.5 cm, bilateral	Dorsum of foot in the fossa between the first and the second proximal phalanges and proximal to the margin of the toe web
Ki 6	Kidney	Perpendicular 0.5-1 cm, unilateral left	1 cun directly below the tip of the medial malleolus
LU 7	Lung	Oblique 1-2 cm, unilateral right	On the radial side of the forearm on the border of the radius, 1.5 cun proximal to the transverse crease of the wrist
PC 6	Pericardium	Perpendicular 1-2 cm, unilateral left	Between the tendons of the tendons of palmaris longus and flexor carpi radialis 2 cun proximal to the transverse crease of the wrist
GB 34	Gallbladder	Perpendicular 2-3 cm, bilateral	At the point of intersection of lines from anterior and inferior borders and head of fibula
Liv 3	Liver	Perpendicular 1-2 cm, bilateral	Between the first and second metatarsal bones, 2 cun proximal to the margin of the web
Ren 4	Ren mai	Perpendicular 2-3 cm	On the midline 3 cun below the umbilicus
GB 20	Gallbladder	Perpendicular 1 cm, bilateral	Between the origins of the medial border of sternocleidomastoid and the trapezius

A cun is a relative body measure in Traditional Chinese Medicine. It is the distance between the transverse creases of the interphalangeal bone of the thumb when the finger is slightly flexed.[17]

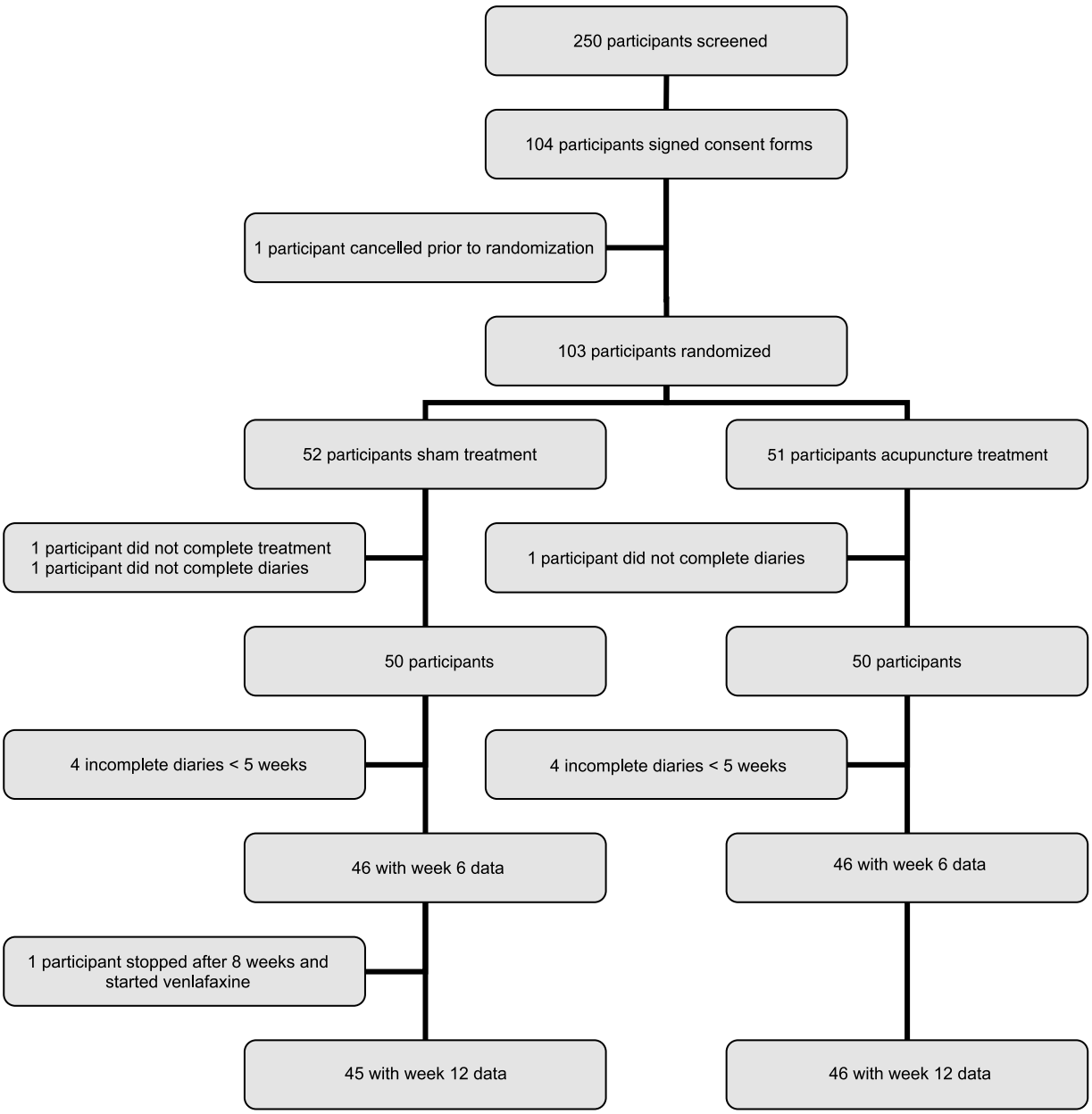

FIG. 1. Consort diagram representing participant activity in this study.

Because pilot studies are inadequate to draw clinically relevant conclusions, this randomized, controlled clinical trial was conducted.

MATERIALS AND METHODS

Study design and participant selection

This study was a clinical trial that used a prospective, randomized, single-blind, sham-controlled design in perimenopausal and postmenopausal women experiencing five or more hot flashes a day. Recruitment occurred between January and July 2004, and acupuncture treatments occurred between January and October 2004 in the Mayo Clinic General Clinical Research Center. Participants were in the study for a total of 13 weeks, including a week before acupuncture treatments (baseline week), 5 weeks of acupuncture treatments, and 7 weeks of follow-up after the acupuncture

TABLE 2. *Baseline median values with minimum and maximum values*

Variable	Sham (n = 52)			Medical (n = 51)			*P* (rank sum test)
	No.	Median	Range	No.	Median	Range	
Age, y	52	52	45-59	51	52	44-58	0.12
Height, cm	51	163	151-175	48	166	152-180	0.02
Weight, kg	51	72	49-101	49	69	50-109	0.84
Body mass index	51	27	18-41	48	26	19-41	0.65
Daily hot flash score	52	14	4-64	51	13	1-47	0.42

treatments were completed. Information about the study was provided to potential participants, and those who chose to participate signed a consent form per US federal guidelines. The study was approved by the Mayo Foundation Institutional Review Board.

Participants eligible for this study were perimenopausal and postmenopausal women aged 45 to 59 with a reported average of five or more hot flashes a day. Perimenopausal status was defined as 3 or more months of self-reported menstrual irregularity or amenorrhea, and postmenopausal status was defined as amenorrhea for 12 or more months. Participants were not eligible if they used estrogen, soy, progesterone, vitamin E, or black cohosh. They could not be using over-the-counter products, gabapentin, or antidepressants specifically for the treatment of hot flashes within the previous month. Use of coumadin, skin disorders with skin breakdown like eczema or psoriasis, the presence of pacemaker or prosthetic joints, diabetic neuropathy, and active chemotherapy were other exclusion criteria. This was to avoid unwanted side effects or possible infections from needles in this group. In designing this study, decisions regarding point selection and duration of acupuncture were based on pilot data and expert opinion.[14,15]

Randomization

Participants were randomized to medical or sham acupuncture using a stratified randomization schedule. Stratification was done using menopausal status to ensure equal distribution of peri- and postmenopausal women among the two groups. A block size of four was used.

Medical and sham acupuncture

A single acupuncturist with more than 5,000 hours of experience and licensed by the Minnesota Board of Medical Practice provided acupuncture treatments. Medical acupuncture was defined as needling administered in 12 acupuncture points, listed in Table 1.[17] All participants received acupuncture in the preselected 12 acupuncture points at each visit. After the needle was put into the correct anatomic position, de qi sensation was obtained, and the needles were left untouched for 30 minutes.[18] Participants came in for twice-weekly acupuncture treatments for a total of 5 weeks. Sham acupuncture was defined as needling administered in nonacupuncture, nonnmeridian areas, whenever possible 5 cm or more away from the actual acupuncture point.

Study outcome

The primary outcome of the study was the hot flash score, which is the product of hot flash frequency and hot flash severity. Using this formula, the mean daily hot flash score was calculated for each individual. The advantage of a hot flash score, as opposed to just using hot flash frequency, is that it takes into account hot flash severity. A self-report prospective hot flash diary was used to collect data. The hot flash diary is a reliable and valid tool that has been used in multiple previous hot flash clinical studies.[19]

Statistical methods

For each participant, we calculated the percentage of residual daily hot flash scores from baseline to two

TABLE 3. *Hot flash scores*

Variable	Sham (n = 52)		Medical (n = 51)		*P* (rank sum test)
	Median	Range	Median	Range	
Baseline score	14	4-64	13	1-47	0.42
Week 6 score	8	0-39	8	0-56	0.79
Week 12 score	8	0-47	8	0-31	0.72
Week 6: % residual hot flashes	62	0-185	60	0-123	0.71
Week 12: % residual hot flashes	55	0-231	73	4-250	0.21

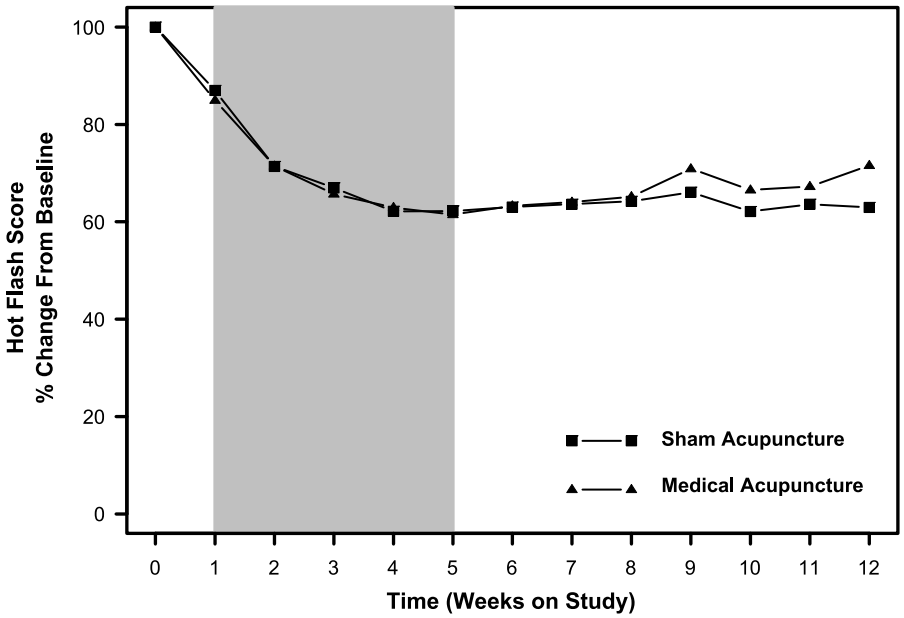

FIG. 2. Hot flash score changes over time for the two protocol arms. The shaded area represents the time the sham and medical acupuncture treatments were administered.

time points (weeks 6 and 12). The percentage of residual hot flash score is defined as 100 times the mean daily score at the time point divided by the baseline score. The last observation carried forward was used for imputing missing data per an intention-to-treat model. Comparison of the percentage of daily residual hot flash scores between the two groups at weeks 6 and 12 was made using the Wilcoxon rank sum test because of the nonnormal distribution of the data. The sample size available for analysis was large enough to detect a medium effect size of 0.6 with 90% power. Analysis was done using SAS software (version 8.0).[20]

RESULTS

Participation data for this trial are illustrated in Figure 1, and baseline characteristics and baseline hot flash scores are presented in Table 2, indicating that both study arms were well balanced.

Residual hot flash scores at weeks 6 and 12 for the medical acupuncture arm were 60% (decrease of 40%) and 73% (decrease of 27%) of baseline, respectively and for the sham acupuncture arm they were 62% (decrease of 38%) and 55% (decrease of 45%) of baseline, respectively. The percentage of residual hot flashes at weeks 6 and 12 did not differ significantly between the two groups (illustrated in Table 3 and Fig. 2). The stream plots of daily hot flash scores and changes in hot flash score from baseline to 12 weeks for individual participants receiving sham and medical acupuncture are displayed in Figures 3 and 4. Data using hot flash frequency changes, as opposed to hot flash score changes, reveal virtually identical-appearing results for all of the efficacy analyses.

Although participant numbers preclude any reasonable power for subset analyses, the results did not suggest any benefit of acupuncture for perimenopausal women, postmenopausal women, or women with baseline hot flash scores above or below the median.

No adverse effects were encountered as a result of the acupuncture treatment used in this study. Specifically, no participants reported substantial discomfort with the treatment, and there were no signs or symptoms of infection.

At the completion of the study, 52 participants were randomly surveyed to assess their perception of whether they were receiving actual versus sham acupuncture treatment. Fifty-one percent of the participants in the sham group believed they received the medical acupuncture treatment, whereas 43% in the actual treatment group believed they received the sham treatment.

DISCUSSION

The results of this study failed to suggest that the medical acupuncture used was any more effective for reducing hot flashes than the chosen sham acupuncture therapy.

This lack of efficacy is likely not related to the study methodology because it was virtually identical

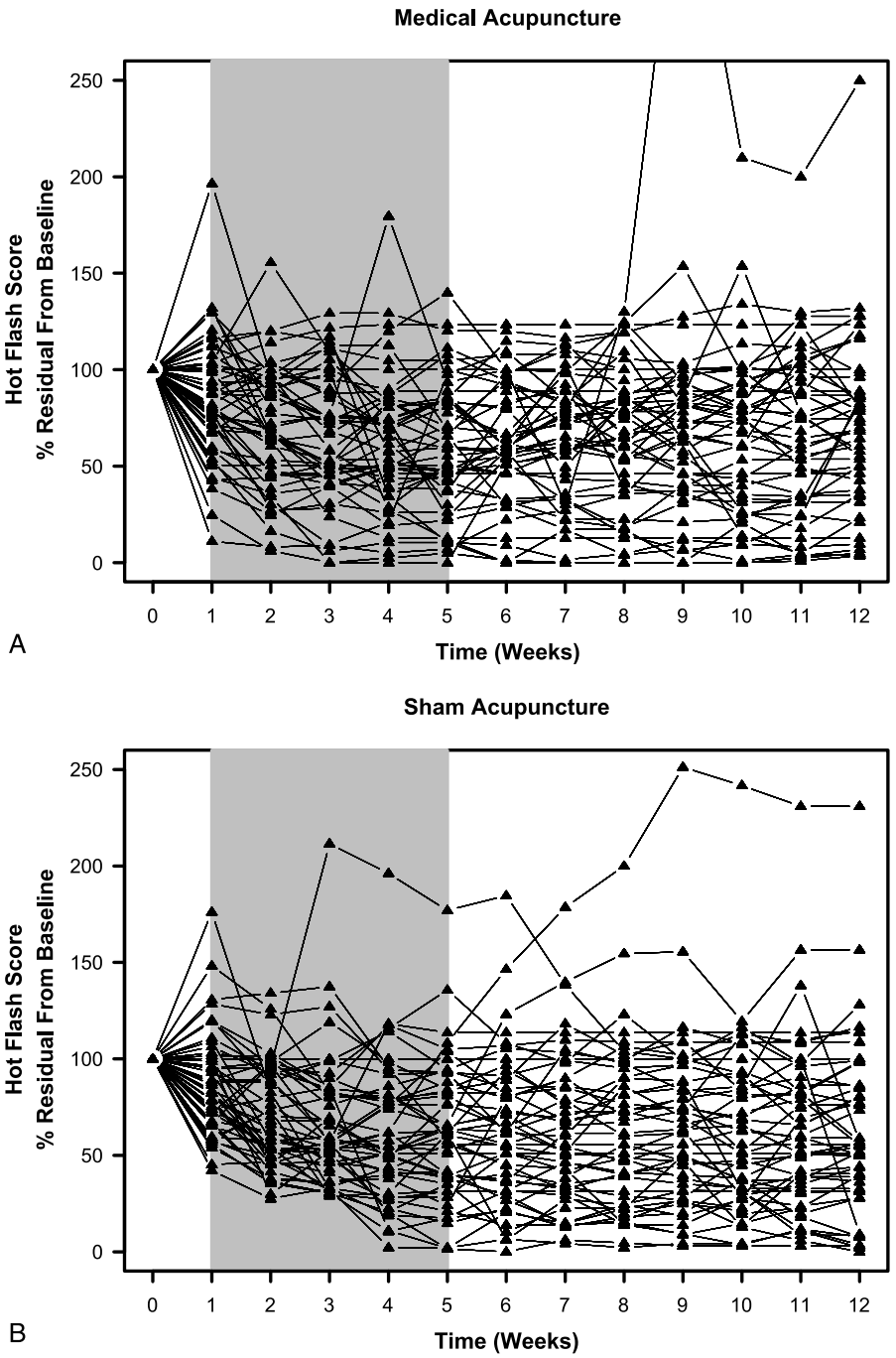

FIG. 3. Hot flash score changes (percentage of residual) over time for individual participants, segregated by medical acupuncture treatment (**A**) versus sham treatment (**B**). The shaded areas represent the time the sham and medical acupuncture treatments were administered.

to the methodology used in multiple previous trials, some of which have had negative results and others that have had positive outcomes.[19]

It is reasonable to ask whether the negative results of this trial are at odds with the data from the pilot trials that suggested that acupuncture was efficacious. However, it does not appear so. There is a prominent placebo effect seen in multiple prior randomized, double-blind clinical trials, ranging from 20% to 35%.[19,21] In some randomized trials, the placebo effect has been even higher and therefore quite variable and substantial.[22] In addition, there are other substances (eg, soy products and black cohosh) that looked promising in pilot trials but then did not show benefit over placebo in properly conducted randomized clinical trials.[23,24] Last, the study design is

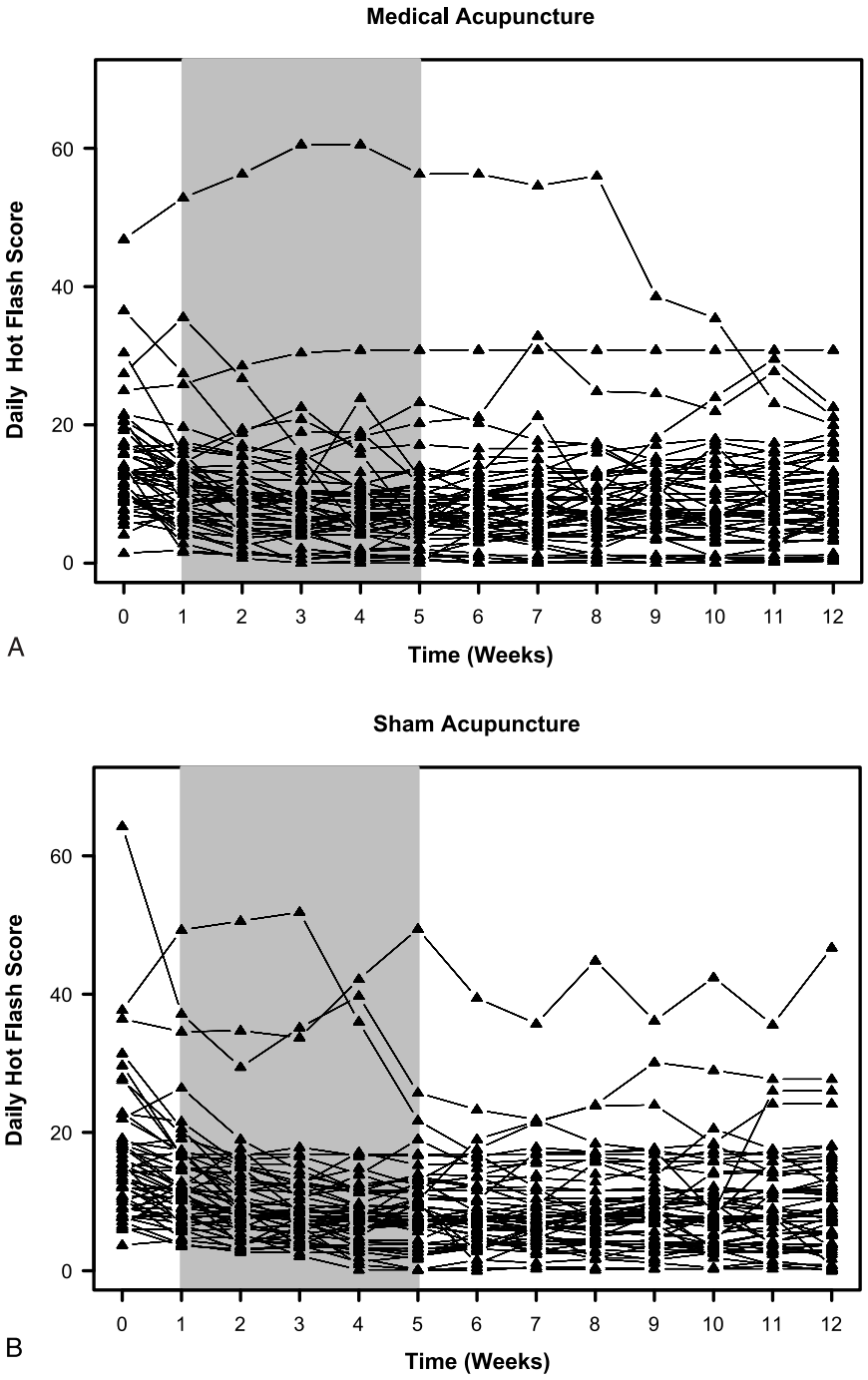

FIG. 4. Hot flash score changes (actual changes from baseline) over time for individual participants, segregated by medical acupuncture treatment (**A**) versus sham treatment (**B**). The shaded areas represent the time the sham and medical acupuncture treatments were administered.

substantiated by noting that participants, at the end of the study, were appropriately blinded.

CONCLUSION

Although it is clear that the acupuncture procedure used in this study was no better than the sham procedure, one should be careful not to conclude that this study proves that all forms of acupuncture will not work against hot flashes. It is hypothetically possible that another acupuncture program will work or that the sham procedure used in this trial actually helped hot flashes. Although one of these might actually be true, such a conclusion would need to be clinically tested in a properly designed clinical trial to be confident of such.

To the best of our knowledge, this is the first report of a randomized, controlled clinical trial of acupuncture for hot flashes. Other such trials have been initiated, the results of which are eagerly awaited.

REFERENCES

1. Kronenberg F. Menopausal hot flashes: randomness or rhythmicity. *Chaos* 1991;1:271-278.
2. Berg G, Gottwall T, Hammar M, Lindgren R. Climacteric symptoms among women aged 60-62 in Linkoping, Sweden, in 1986. *Maturitas* 1988;10:193-199.
3. Stadberg E, Mattsson LA, Milsom I. The prevalence and severity of climacteric symptoms and the use of different treatment regimens in a Swedish population. *Acta Obstet Gynecol Scand* 1997;76:442-448.
4. Rodstrom K, Bengtsson C, Lissner L, Milsom I, Sundh V, Bjorkelund C. A longitudinal study of the treatment of hot flushes: the population study of women in Gothenburg during a quarter of a century. *Menopause* 2002;9:156-161.
5. Bachmann GA. Vasomotor flushes in menopausal women. *Am J Obstet Gynecol* 1999;180:S312-S316.
6. Kronenberg F. Hot flashes: phenomenology, quality of life, and search for treatment options. *Exp Gerontol* 1994;29:319-336.
7. Chung TK, Yip SK, Lam P, Chang AM, Haines CJ. A randomized, double-blind, placebo-controlled, crossover study on the effect of oral oestradiol on acute menopausal symptoms. *Maturitas* 1996;25:115-123.
8. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-333.
9. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;291:1701-1712.
10. Loprinzi CL, Michalak JC, Quella SK, et al. Megestrol acetate for the prevention of hot flashes. *N Engl J Med* 1994;331:347-352.
11. Shanafelt TD, Barton DL, Adjei AA, Loprinzi CL. Pathophysiology and treatment of hot flashes. *Mayo Clin Proc* 2002;77:1207-1218.
12. Goldberg RM, Loprinzi CL, O'Fallon JR, et al. Transdermal clonidine for ameliorating tamoxifen-induced hot flashes. *J Clin Oncol* 1994;12:155-158.
13. NIH Consensus Conference. Acupuncture. *JAMA* 1998;280: 1518-1524.
14. Dong H, Ludicke F, Comte I, Campana A, Graff P, Bischof P. An exploratory pilot study of acupuncture on the quality of life and reproductive hormone secretion in menopausal women. *J Altern Complement Med* 2001;7:651-658.
15. Wyon Y, Lindgren R, Lundeberg T, Hammar M. Effects of acupuncture on climacteric vasomotor symptoms, quality of life, and urinary excretion of neuropeptides among postmenopausal women. *Menopause* 1995;2:3-12.
16. Porzio G, Trapasso T, Martelli S, et al. Acupuncture in the treatment of menopause-related symptoms in women taking tamoxifen. *Tumori* 2002;88:128-130.
17. Stux G, Hammerschlag R. *Clinical Acupuncture: Scientific Basis*. Berlin, Germany: Springer-Verlag, 2001:198-209.
18. Bossy J. Morphological data concerning the acupuncture points and channel network. *Acupunct Electrother Res* 1984;9:79-106.
19. Sloan JA, Loprinzi CL, Novotny PJ, Barton DL, Lavasseur BI, Windschitl H. Methodologic lessons learned from hot flash studies. *J Clin Oncol* 2001;19:4280-4290.
20. SAS Institute. SAS User's guide, version 8.0. Cary, NC: SAS Institute, 2000.
21. National Institutes of Health. National Institutes of Health State-of-the-Science Conference statement: management of menopause-related symptoms. *Ann Intern Med* 2005;143:845-846.
22. Suvanto-Luukkonen E, Koivunen R, Sundstrom H, et al. Citalopram and fluoxetine in the treatment of postmenopausal symptoms: a prospective, randomized, 9-month, placebo-controlled, double-blind study. *Menopause* 2005;12:18-26.
23. Quella SK, Loprinzi CL, Barton DL, et al. Evaluation of soy phytoestrogens for the treatment of hot flashes in breast cancer survivors: a North Central Cancer Treatment Group trial. *J Clin Oncol* 2000;18:1068-1074.
24. Pockaji B, Gallagher J, Loprinzi CL, et al. Phase III double-blinded, randomized trial to evaluate the use of black cohosh in the treatment of hot flashes: a North Central Cancer Treatment Group study [abstract]. *Proc Am Soc Clin Oncol* 2005;23(Suppl 16 pt 1):732S.