



A randomized trial of acupuncture for vasomotor symptoms in post-menopausal women

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KEYWORDS

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Summary

Objective: The goal of this study was to determine whether acupuncture would relieve the vasomotor symptoms of post-menopausal women.

Design: A randomized, single-blind trial.

Setting: A small city in a rural area of Eastern Oregon.

Interventions: Women were recruited into the study from the community by advertising or physician referral. All study subjects were in non-surgical menopause and medically stable. Study subjects were randomly assigned to receive 12 weeks of treatment with either Chinese Traditional Medicine (TCM) acupuncture ($n=27$) or shallow needle (sham) acupuncture ($n=24$).
Outcome measures: Study participants kept a diary recording their hot flashes each day. At baseline, study participants filled out Greene Climacteric Scales and the Beck Depression and Anxiety Inventories. These same outcomes were also measured at week 4 of treatment and at 1 week and 12 weeks after treatment. The number of hot flashes and the numeric scores on the Climacteric Scales and the Beck inventories were compared between the verum and shallow needling groups using two-way repeated measures.

Results: Both groups of women showed statistically significant improvement on all study parameters. However, there was no difference between the improvement in the shallow needle and verum acupuncture groups. Study subjects were not able to guess which group they had been assigned to.

Conclusions: This study showed that both shallow needling and verum acupuncture were effective treatments of post-menopausal vasomotor symptoms. Study subjects were not able to distinguish shallow needling from real TCM acupuncture. Shallow needling may have therapeutic effects in itself reducing its utility as a ‘‘placebo’’ control for verum acupuncture. This result is consistent with other published studies.

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Introduction

The transition between the reproductive and post-menopausal years occurs in women between the ages of 40 and 58 (average age at onset 52, mean age at onset 48) and lasts 4–5 years⁴⁴ although symptoms of menopause may

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Table 1 Complementary and alternative treatments for menopausal transitional symptoms.

Bioidentical hormone therapy	Uses plant products with estrogenic activity, such as estrone, estradiol, estriol, and others	Some evidence that these products treat symptoms, but no evidence they are safer than standard HRT ¹⁰
Dietary supplements with no known estrogenic activity	Don quai, chastetree, wild yam, evening primrose, ginkgo, ginseng, kava, motherwort, valerian, St. John wort, black cohosh	Anecdotal evidence and a few small trials indicate that some relief of symptoms may occur, especially with black cohosh and St. John's wort, but safety has not been systematically assessed ^{16,17,19,26}
Dietary soy	Usually mixed with other botanicals	Several small trials suggested some benefit but a large RCT showed a significant worsening of menopausal symptoms ^{41,26}
Exercise		Numerous anecdotal studies indicating relief of symptoms with exercise. ^{8,51} Cochrane review found no evidence to support exercise for treatment of menopausal symptoms ¹²
Relaxation or stress management therapy	Very commonly used for treatment of menopausal symptoms ⁴⁰	Only a few small trials of relaxation have been conducted but they did show a positive effect ^{28,38,60}
Massage or chiropractic	Used by a small number of women for treatment of menopausal symptoms	Very limited evidence but one RCT was negative ⁵⁷

last long after the menopausal transition is complete.⁵ Many women go through this transition with minimal symptoms, but over half of women in menopause transition experience symptoms such as hot flashes, night sweats, vaginal dryness and painful intercourse, sleep problems, mood and cognitive problems, somatic symptoms, bleeding symptoms, and sexual dysfunction.^{37,39,46,40}

Hormone Replacement Therapy (HRT) is effective in the treatment of the symptoms of the menopause transition and was an accepted treatment for many years.^{36,39} However, the Women's Health Initiative (WHI), a study of 16,600 women with results released in 2002, identified increased rates of myocardial infarction, stroke and breast cancer in women treated with combined estrogen and progesterone therapy during the menopause transition, leading the investigators to suggest that the risks of such therapy exceed the benefits for many women.^{47,55,2} Although the WHI has been criticized and many physicians have expressed skepticism about the results,^{52,42} reluctance on the part of physicians and women alike to take risks of life-threatening illness to treat menopausal symptoms has led to reduced use of HRT^{18,23,24} and an increased interest in alternative therapy for treatment of menopausal symptoms.^{29,11} An Australian study showed that half of women surveyed had sought care from a CAM practitioner for menopausal symptoms⁵³ while an American study showed that 23% of women in menopause transition were actively using a CAM treatment.⁴⁰ Some of

the commonly used complementary and alternative treatments for menopause other than acupuncture are described in Table 1.

Acupuncture is becoming increasingly popular in the United States and offers an important alternative or complement to standard medical care. It is one of the more common non-pharmacological therapies used by menopausal women to mitigate menopausal symptoms^{26,53,40,9} and detailed treatment protocols as well as anecdotal data can be found in the acupuncture literature.^{34,58,13}

The results of published RCTs of the use of acupuncture to treat symptoms of menopausal transition have been contradictory. A recent study by Vincent et al. used a methodology similar to ours in which sham acupuncture was compared to genuine acupuncture using a single-blind design. While both groups showed improvement, there was no difference between the two groups in relief of hot flashes.⁵⁴ Another recent study by Zaborowska et al., randomized patients to receive estrogen, relaxation therapy, acupuncture or placebo acupuncture. In that study, all treatments, including acupuncture, were statistically superior to placebo acupuncture.⁶⁰ In a 2002 study Sandberg et al.⁴⁸ compared placebo versus genuine acupuncture in a small single-blind trial and found, again, that both groups improved but that the two groups were not statistically different.

An earlier small study by Wyon et al. compared deep needling with needling sensation (de qi) and elec-

troacupuncture (EA) at 4 points with superficial needling. The number of hot flashes decreased by 50% in both groups but the superficial needling group experienced a greater increase of hot flashes at 3 months follow-up.⁵⁹

In another small study men with prostatic carcinoma experienced a 70% decrease of hot flashes after receiving manual acupuncture in combination with EA to 4 points for 12 weeks.²²

Based on these reports we believed it would be worthwhile to conduct a larger trial, using placebo or non-invasive sham treatment to control for any specific or non-specific physiological effects activated by invasive sham treatments such as superficial needling or non-acupuncture point needling.⁹

The objective of this study was to determine whether real acupuncture (RA) was more effective than placebo acupuncture (PA) for the treatment of vasomotor symptoms in naturally menopausal women. We expected that participants in the RA group would experience a 50% decrease of vasomotor symptoms as measured by the Greene Climacteric Scale²⁰ and subjective symptom logbooks.

Prior to the introduction of non-piercing placebo acupuncture needles in 1998,^{50,25} acupuncture trials compared no treatment to acupuncture treatment, making blinding of studies impossible. We used non-piercing placebo needles to more clearly define acupuncture's usefulness in reducing the number of hot flashes. To facilitate future technical comparisons, we chose Traditional Chinese Medicine (TCM) as the single discipline on which needle prescriptions would be based.

This study was designed as a single-blind, randomized, controlled clinical trial.

Subjects

The setting of the study was the Klamath River basin, a rural area in south-central Oregon including the small city of Klamath Falls. After receiving approval from the Institutional Review Board of Sky Lakes Medical Center, the local hospital, participants were recruited between September 2000 and August 2002 through advertisements in the local newspaper, brochures displayed at local physician's offices and by word of mouth. Women without a menstrual period for at least 6 months and with FSH levels above 30 IU, who had not been on HRT for at least 3 months and who were experiencing vasomotor symptoms of any severity more than 14 times per week or moderate to severe events more than 5 times per week were eligible.

Participants had to have had no acupuncture treatment for at least 6 months and had to be able to keep regular appointments. Patients were excluded if they had surgically or chemically induced menopause, anemic amenorrhea, a cardiac pacemaker, fibromyalgia, HIV disease, untreated thyroid disease, untreated hypertension, or if they had a history of substance abuse within the previous year. The inclusion and exclusion criteria for the study are summarized in Table 2.

Subjects were informed that they had a 50% chance to be in the RA group and a 50% chance of being in the placebo group. If they agreed, informed consent regarding study participation and acupuncture treatment was obtained.

Table 2 Inclusion and exclusion criteria.

Inclusion criteria

- No menstrual period for at least 12 months
- Natural menopause
- No ERT/HRT or herbal treatment for menopausal symptoms for at least 3 months before enrollment
- Vasomotor symptoms (hotflashes, night sweating)—more than 14 events of any severity per week or more than 5 moderate to severe events (waking up soaked, needed to change clothing)
- No acupuncture treatments within the last 6 months
- Able to keep regular appointments

Exclusion criteria

- Artificial menopause (due to surgery, radiation, or medication)
- Pacemaker
- History of heart disease
- History of active alcohol or drug abuse within the last year before enrollment
- HIV disease
- Fibromyalgia
- Uncontrolled thyroid disease
- Uncontrolled hypertension
- Any systemic illness, condition, or personal situation (such as an unstable living situation) which might render the patient unable to complete the study, fulfill the demands of the study, interfere with data interpretation, or create undue risk

Materials and methods

Prior to entering the study each study subject received a physical examination from her own physician including assessment of follicle stimulating hormone to determine that the subjects were physiologically menopausal, and serum thyroid stimulating hormone to determine that thyroid dysfunction was not a confounding variable. A hemoglobin level was also done to rule out anemia as a cause of symptoms.

Those who qualified to enter the study received a menopause symptom log with instructions 4 weeks prior to treatment. This log was maintained before and throughout the study period, so that the frequency of hot flashes could be followed longitudinally.

At the start of the study, randomization was then accomplished by asking study subjects to draw an envelope. In each envelope there was a small piece of paper with the typed letter 'A' or 'B'. Subjects who drew an 'A' were randomized to the PA group; subjects who drew 'B' were randomized to the RA group.

At the baseline visit subjects were given the Greene Climacteric Scale,²⁰ the Beck Depression Inventory⁴ and the Beck Anxiety Scale³ as well as diagnosed according to Traditional Chinese Medicine (TCM) criteria, as discussed below.

The three written assessment tools were performed before treatment started and repeated form weeks into treatment and within 1–2 weeks after the last treatment (13–14 weeks after first treatment) and again 12 weeks after the last treatment (study week 24). Entries from the

Table 3 Demographic characteristics of the real and sham acupuncture groups were not statistically different.

	Real acupuncture (N = 27)	Sham acupuncture (N = 24)
Age (years)	54.1 (SD 4.665)	52.6 (SD 2.873), $p = 0.1$
Married	24 (89%)	24 (100%), $p = 0.2$
Non-White ethnicity	0	3 (6%), $p = 0.1$
Education high school	26 (96%)	20 (83%), $p = 0.1$
Education college	1 (4%)	4 (17%), $p = 0.1$
Employed	23 (85%)	21 (87%), $p = 0.4$

menopause logs were also entered at each of these time intervals. During the final visit study subjects were asked to guess whether they had received placebo or real acupuncture, and at what stage they came to that conclusion. This helped us assess how successful our blinding method was.

Treatment

Treatment length and frequency were a modification of the regimen adopted by Wyon et al.⁵⁹ Women received two 25-min treatments a week for 4 weeks followed by one treatment a week for 8 weeks (total of 16 treatments over 12 weeks). We adopted the longer treatment course to ensure that any failure to show results would not be due to a treatment course that was too brief to be effective. The treatment interval of 25 min is standard clinical practice.

A licensed acupuncturist (LV), who was trained in TCM style acupuncture and had experience treating hot flashes in menopausal women and women with breast cancer, provided acupuncture and placebo treatment. During treatment subjects of both groups were positioned prone to limit opportunities to observe placebo needling. Advice regarding diet and exercise was given to women in both study groups.

Real acupuncture (RA)

TCM pattern differentiation and selection of acupuncture points were based on several TCM sources.^{35,58,34,13} In TCM menopausal hot flashes correspond primarily to the pattern of Kidney Yin Deficiency, but additional patterns can occur as well and include Kidney and Liver Yin Deficiency with Liver Yang rising, Kidney Yin and Yang Deficiency, Kidney yin and Spleen deficiency, Kidney and Heart not communicating, Heart Blood Deficiency and Liver Qi Stagnation.

Subjects were treated with a point prescription according to their TCM diagnosis. Acupuncture points were selected from a core group of acupuncture points that included treatment points for each of the TCM patterns listed above and which would be accessible on a prone patient. During each treatment 6–12 acupuncture points were selected from this group which included UB 23 (Shenshu), UB 20 (Pishu), UB 15 (Xinshu), UB 17 (Geshu), Du 9 (Zhiyang), Du 4 (Mingmen), Sp 9 (Yinlingquan), Sp 6 (Sanyinjiao), right Lu 7 (Lieque), left Ki 6 (Zhaohai), Ki 3 (Taixi), Ki 7 Fuli, H 6 (Yinxi), H 7 (Shenmen), Liv 3 (Taichong), Du 24 (Shenting), GB 20 (Fengchi).

Disposable Hwato needles (1 in./34 gauge and 1.1/2 in./32 gauge) without tubes were used. The skin at the needling sites was cleaned with alcohol. After insertion of needles they were manipulated to achieve

De Qi, a sensation of heaviness or soreness around the needle experienced by the subject. Four needles, bilateral UB 23 (Shenshu) and SP 6 (Sanyinjiao), were connected to an electroacupuncture device (ITO, model IC 1107) and stimulated at a frequency of 2 Hz. The intensity was adjusted to be just above the threshold of subjects' perception. The remaining needles were stimulated again manually after 15 min. Needles were retained for a total for 25 min.

Placebo acupuncture (PA)

For the PA group placebo acupuncture needles developed by Streitberger and Kleinhenz⁵⁰ were used. The blunted needle does not penetrate the skin and retreats into the handle. After cleaning the skin with alcohol, 6 small plastic rings were taped to the skin at sites away from any of the acupuncture meridians, 2 on the back, 2 on the lower legs and 2 on the forearms. The placebo needles were inserted through the tape into the small plastic ring. This enabled them to remain in an upright position. Four of the placebo needles were connected to a disabled acupuncture device (ITO, model IC 1107). The other two placebo needles were rotated slightly after placement and again after 15 min. The placebo needles were removed after 25 min.

Statistics

A two-way repeated measures design was used to evaluate the differences between groups over time. Hot flash score pair wise comparisons between groups over treatment times were determined using the Duncan test. The SAS System for Windows, release 8.0 (SAS Institute, Cary, NC) was used to perform calculations; $p < 0.05$ was defined as statistically significant. Means are expressed \pm the standard deviation (SD).

Results

A total of 80 women were assessed for entry into the study. Of these, 24 were considered ineligible based on the exclusion criteria or decided against participation once they understood the time commitment. A total of 56 subjects were randomized and 51 of these completed the study. Of the five subjects who dropped out of the study, one did not receive acupuncture, one had three treatments, one six treatments and two received 16 treatments but quit keeping a hot flash diary about half way through. All but one drop out had received PA. RA was given to 27 and PA to 24 of the 51 subjects who completed the study. Study subjects did not

Table 4 Medical and behavioral factors at start of study.

	Real acupuncture <i>n</i> = 27	Sham acupuncture <i>n</i> = 24
Taking no medications	2 (8%)	2 (11.1%), <i>p</i> = 0.5
Prior hysterectomy	6 (22%)	6 (25%), <i>p</i> = 0.6
Age at last menstrual period	45.7 (\pm 8.4)	45.5 (\pm 9.6), <i>p</i> = 0.9
Number of children	2.1 (SD 2.1)	2.2 (SD 1.3), <i>p</i> = 0.6
Regular exercise	13 (48%)	10 (42%), <i>p</i> = 0.6
Smoker	4 (15%)	2 (8%), <i>p</i> = 0.5
Taking antidepressants at start of study	0	4 (15%), <i>p</i> = 0.00

Table 5 Results. Baseline results were not different between groups except for the baseline flash scores. Similarly, no 20 week scores were different between groups. However, other than the Green sex score, scores improved significantly between baseline and 16 weeks for all tests in both groups. The number in parenthesis is the standard deviation.

	Real acupuncture <i>n</i> = 27		Sham acupuncture <i>n</i> = 24	
	Baseline	16 weeks	Baseline	16 weeks
Depression scores (BDI)	11.1 (8.0) ^a	7.2 (5.8) ^{a,b}	13.9 (9.9)	7.0 (4.0) ^b
Anxiety scores (BAI)	12.6 (10) ^a	7.7 (6.8) ^b	12.8 (7.9) ^a	7.8 (5.3) ^b
Flash scores	4.0 (2.4) ^c	2.6 (3.1) ^{a,b}	4.5 \pm 2.2	2.5 (2.6) ^b
Green psych score	9.1 (5.0) ^a	6.5 (5.0) ^{a,b}	9.1 (5.4)	6.5 (3.8) ^d
Green soma score	5.1 (3.2) ^a	3.6 (3.6) ^{a,b}	4.6 (3.1)	2.8 (2.7) ^b
Green vasomotor score	4.0 (1.1) ^a	2.4 (1.6) ^{a,b}	4.0 (1.1)	2.4 (1.8) ^b
Green sex score	1.4 (1.0) ^a	1.0 (0.7) ^{a,d}	1.3 (0.8)	1.0 (0.7) ^d
Total green score	28.7 (12.8) ^a	20.7 (12.8) ^{a,b}	28.1 (13.2)	19.5 (9.2) ^b

^a No difference between sham and real acupuncture groups (*p* > 0.05).

^b Significant difference between baseline and 16 week values (*p* < 0.05).

^c Significant difference between sham and real acupuncture groups (*p* < 0.05).

^d No difference between baseline and 16 week values (*p* > 0.05).

report any adverse events or side effects as a result of the treatment given.

Table 3 illustrates that the two groups had similar population demographics. Table 4 shows that participants did not differ in factors that might influence hot flash scores. Two study volunteers had used acupuncture in the past before study participation; one was randomized to the RA group and one to the PA group. Two study subjects were taking

SSRI antidepressants at the start of the study and continued them during the study. Both were randomized to the PA group.

Table 5 gives the study results. As shown in the table, there were no baseline differences between the two groups in their test scores. Both groups improved significantly between baseline and the follow-up after treatment was completed (13–14 weeks) with respect to almost every

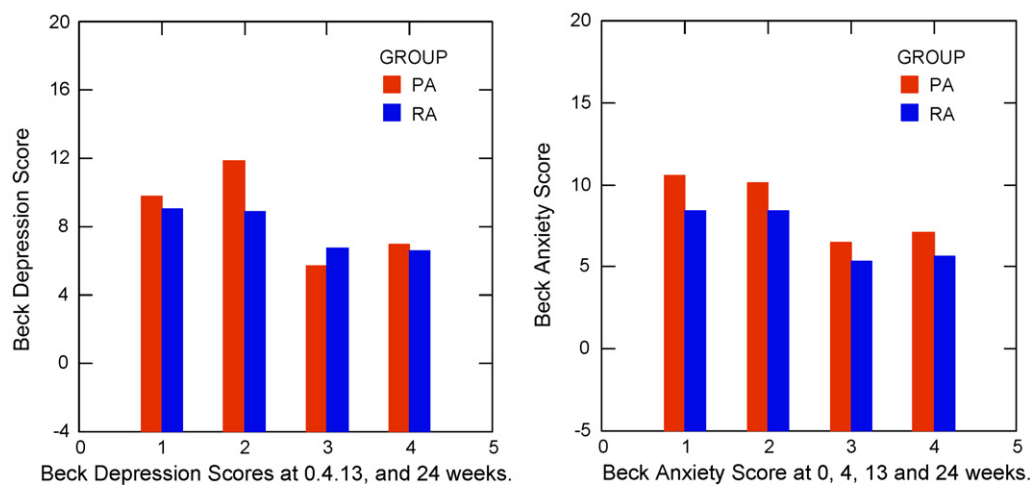


Figure 1 Depression and anxiety scores trended towards improvement over time. Test cluster 1 is baseline, cluster 2 is at 4 weeks, 3 is at 1 or 2 weeks after the end of treatment (13–14 weeks after start of study), and point 4 is 12 weeks after the end of treatment (24 weeks into the study). Lower Beck Depression and Anxiety scores indicate less depression or anxiety.

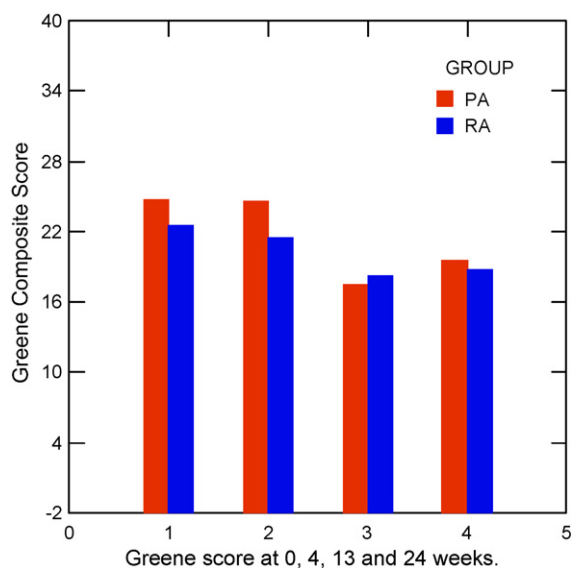


Figure 2 Greene Scales trended towards improvement over time. Test cluster 1 is baseline, cluster 2 is after 4 weeks of treatment, 3 is 1–2 weeks after the end of treatment (13–14 weeks after first treatment), and point 4 is 12 weeks after the end of treatment (24 weeks into the study). A lower Greene score indicates a lower level of menopausal symptoms.

measurement. Of the 51 participants who completed the last follow-up visit, 39 (76.5%) reported some diminution of hot flashes and 12 (23.5%) did not experience improvement. Figs. 1 and 2 show that this trend towards improvement progressed steadily over time for depression and total Greene scores.

Although there were no significant differences between the shallow needling and verum acupuncture groups in our measured parameters, study subjects clearly obtained benefit from either acupuncture treatment.

At the last follow-up visit each participant was asked to guess her treatment group and the reason for the guess. The majority (37, 73%) of study subjects in both groups thought they were receiving RA, while 14 (27%) of the total sample guessed they were in the PA group. Of the 27 in the RA group, 7 (26%) guessed they were in the PA group and 20 (74%) in the RA group. Of the 24 in the PA group, 7 (29%) guessed they were in PA group and 17 (71%) in the RA group, the guess percentages were not statistically different between the two groups ($p=0.7$). When asked why they picked the group they did, 30 of the 37 persons who picked the RA group said that they picked that group because their symptoms improved during the study, while 9 of the 14 who picked PA felt that their symptoms did not improve. The remainder picked various other reasons or were not sure.

Discussion

Most of the subjects who participated in this study experienced a significant decrease in hot flashes, depression and anxiety. However, being in the verum acupuncture treatment group as opposed to the shallow needle group did not predict improvement.

In the interests of developing an evidence base for acupuncture treatment, a number of recent trials have been conducted comparing verum acupuncture to non-invasive needling for various conditions such as back pain,^{21,6,7} fibromyalgia,^{43,31,32} and migraine.²⁷ One trial of non-invasive versus verum acupuncture for in vitro fertilization therapy actually showed a superiority for the shallow needling treatment.⁴⁹ All these studies showed benefit for study subjects from both non-invasive and verum acupuncture, with most showing no statistical differences between verum and non-invasive acupuncture, consistent with our study. Most studies did not include a treatment group with no intervention, but used non-invasive needling as a “placebo”; the problem being, as discussed above, that non-invasive needling is perhaps not equivalent to no treatment or placebo treatment.

We expected that using non-piercing needles would produce outcomes that were simpler to interpret in part because shallow needling is not rare in clinical practice.^{6,7} Shallow needling is the hallmark of Japanese style acupuncture. Wyon et al.⁵⁹ conducted a small trial comparing Japanese style acupuncture to electrostimulated acupuncture. Again, both groups showed benefit, with some non-statistical trends favoring the electrostimulation group.

Lundberg and Lund^{33,30} have commented that no sham acupuncture procedure is truly inert; they cite studies showing that light touch or sham acupuncture has central nervous system and endocrine effects similar to those seen in verum acupuncture.⁵⁶ They conclude that there is evidence that sham acupuncture is of benefit in many conditions and that to conclude that trials showing equality between sham and verum acupuncture disprove the effectiveness of acupuncture could potentially encourage practitioners to withhold safe and cost-effective treatment from patients. Alfaily et al.,¹ in an extensive literature review, make a similar point and also point out that acupuncture trials currently published lack adequate control groups and sufficient numbers of patients to draw definitive conclusions.

Our study shares a limitation of many of those cited above in having an insufficient sample size to determine at the 0.05 alpha level whether a difference between verum and shallow needling (sham) acupuncture exists. For example, showing a difference in depression scores would have required 50 study subjects in each group and even larger samples would have been needed to show differences for some of the other variables (see Table 5). Other limitations in our study were the rural setting, which might make generalizing to other settings problematic, and the fact that since the study consisted of volunteers from the community, it is possible that study participants had an interest in acupuncture or a positive feeling about acupuncture before the study. Another limitation is that we did all our acupuncture in the prone position in order to make detection of sham needling more difficult. It is possible that more effective acupuncture could have been performed in other than the prone position.

The fact that our study subjects were unable to guess which group they were in also suggests that sham (shallow needling) acupuncture had a similar effect to verum acupuncture. Thus, the absence of an untreated control group may be a limitation of our study, as discussed above. However, it may be reasonable to assume that study

subjects would have had little change in symptoms during the brief study period with no intervention; many had been in menopause for a number of years.

It is possible that coming in for acupuncture treatment twice a week and regular contact with a sympathetic acupuncturist had a therapeutic effect related to relaxation beyond that obtained from acupuncture alone, improving symptoms of depression and anxiety so that hot flashes were perceived as less worrisome.^{31,32} It is also possible that study subjects may have had a desire, conscious or unconscious, to improve their scores to fulfill perceived goals of the study.

The relatively high prevalence of depression (higher Beck scores) in our study population is consistent with findings in larger populations of women in the transitional or menopausal condition.^{15,5,14} Our study showed that improvements in the Green score and Beck depression index tended to correlate (see figures). This finding is consistent with epidemiologic studies showing a strong association between menopausal symptoms and depression; whether menopausal symptoms cause depression to increase or whether the reverse is true is difficult to determine.^{45,5}

Conclusion

Subjects in this study reported fewer hot flashes and improved in other parameters whether given real or shallow needle acupuncture, showing that both treatments were beneficial. The study lacked sufficient power to prove equivalence or non-equivalence of the two treatments compared.

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