PRESS RELEASE

The effect of acupuncture on postmenopausal symptoms and reproductive hormones: a sham controlled clinical trial

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ABSTRACT

Background Acupuncture is commonly used to treat menopausal symptoms and other gynaecological conditions. In this study, the authors aimed to investigate whether acupuncture has an effect on menopausal symptoms and to explore whether this effect is related to changes in hormone levels.

Materials and methods A total of 53 postmenopausal women were alternately assigned into two treatment groups: acupuncture (n=27) and sham acupuncture (n=26). Menopausal symptoms were assessed using the Menopause Rating Scale (MRS). The serum oestradiol, follicular stimulating hormone (FSH) and luteinising hormone (LH) levels were measured at baseline and again after the first and last sessions. The Student t test was used for normally distributed data and the Wilcoxon signed rank test for not normally distributed data. The group differences in MRS scores were assessed using non-parametric Mann–Whitney U test.

Results After treatment, total MRS, and the somatic and psychological subscale scores were significantly lower in the acupuncture group than the sham group (all p=0.001). The severity of hot flushes was found to be significantly decreased after treatment in acupuncture group (p=0.001). In the acupuncture group LH levels were lower and oestradiol levels were significantly higher than sham group (p=0.046 and p=0.045, respectively) after treatment, but there was no difference in FSH levels.

Conclusion Acupuncture was effective in reducing menopausal complaints when compared to sham acupuncture and can be considered as an alternative therapy in the treatment of menopausal symptoms.

INTRODUCTION

Perimenopause syndrome, referred also as climacteric syndrome, results from the changing of relationship among the hypothalamus, pituitary and ovary during women's ageing process. Those changes take place first in the ovary, then in the hypothalamus and pituitary, which are reflected as the functional changes in the endocrinological and central nervous system, accompanied with a series of psychological symptoms.[1] Oestrogen, either by itself or with progestins is the most consistently effective therapy for these symptoms.[2] However, the Women's Health Initiative and Million Women Study have identified important risk factors (coronary heart disease, stroke, breast and endometrial cancer) associated with hormone replacement therapy (HRT).[3–6] Those findings have led to an expanded interest in non-hormonal therapies for managing menopausal symptoms. However, there are only limited data to support their use. The common conclusion in reviews regarding to complementary and alternative therapies for the management of menopause related symptoms was that the data were insufficient to recommend any alternative therapy and further investigation was still needed.[7 8] In the area of complementary and alternative therapies, acupuncture and acupressure treatments are promising, however, the results of published randomised controlled trials of the effect of acupuncture on hormone levels and symptoms in postmenopausal women have been contradictory.[9–15]

Many studies in animals and humans have demonstrated that acupuncture can cause multiple biological responses.[16 17] These responses can occur at or close to the site of application, or at a distance, mediated mainly by sensory neurons to many structures within the central nervous system. This can lead to activation of pathways affecting various physiological systems in the brain as well as in the periphery. Stimulation by acupuncture may also activate the hypothalamus and the pituitary gland, resulting in a broad spectrum of systemic effects. Alteration in the secretion of neurotransmitters and neurohormones and changes in the regulation of blood flow, both centrally and peripherally, have been documented.[18]

In the present sham controlled study we aimed to investigate whether acupuncture has an effect on menopausal symptoms and to explore whether this effect is related to changes in levels of reproductive hormones.

MATERIALS AND METHODS

After obtaining approval of the local ethical committee, 56 postmenopausal women (50 naturally and six surgically), who had been referred to the outpatient clinic of menopause at Ankara Training and Research Hospital, Ankara, Turkey, between October 2009 and December 2009, for follow-up or treatment and who agreed to participate were included in this, single-blind, sham-controlled study. All participants were informed about the study and written consents were received. Participants were alternately assigned into two treatment groups: acupuncture (n=28) and sham acupuncture (n=28). The age, menopausal age, body weight and height of all participants were recorded. Body mass index (BMI) was calculated by the formula body weight (kg)/height (m^2).

The term postmenopausal was defined as: 12 months spontaneous amenorrhea for women who still had a uterus, and serum oestradiol (E2) levels lower than 50 pg/ml and serum follicular stimulating hormone (FSH) levels higher than 40 IU/ml for women who had surgical menopause and had no uterus. None of the participants had taken HRT previously.

The primary outcome of the study was an assessment of improvement in menopausal symptoms. Hence, menopausal symptoms were assessed using an 11 item Turkish version of the Menopause Rating Scale (MRS).[19 20] Three aspects were assessed from the menopausal symptoms: somatic (four items), psychological (four items) and urogenital (three items) symptom complexes. A 5-point rating scale allowed the women to describe the perceived severity of symptoms for each item (severity: 0=no complaints to 4=very severe symptoms). The composite scores for each dimension (subscale) are based on adding the item scores in the respective dimensions. The composite score (total score) is the sum of the dimension scores.

The secondary outcome measures were hormone levels. Hence, the baseline serum E2 (E2b), FSH (FSHb) and luteinising hormone (LH; LHb) levels were recorded. These parameters were measured again after the first (E2fs, FSHfs, LHfs) and last sessions (E2ls, FSHls, LHls) to evaluate whether the effect of intervention was cumulative. The first session of interventions was applied 2–7 days after the baseline measurements.

The acupuncture group received traditional Chinese medicine acupuncture twice a week for a total of 10 sessions by a licensed acupuncturist with 6 years experience. Sterile, disposable, silver needles with a length of 0.25×25 mm (Wujiang Jia Chan, Wujiang City, China) were used. The needles were inserted bilaterally at four acupuncture points (ST36, depth 1 *cun*; LI4, 0.5 *cun*; KI3, 0.2 *cun*; LR3, 0.3 *cun*) and also in the points EX-HN3 at 0.1 *cun* depth and CV3, 0.5 *cun*; *de qi* sensation was obtained with manipulation and the needles were then left for 20 min without any manual or electrical stimulation. The points were located by the acupuncturist according to WHO Standard Acupuncture Point Locations in the Western Pacific Region.[21]

Sham acupuncture was performed on the sham group twice a week for a total of 10 sessions at the same points by the same acupuncturist. Sham acupuncture needles developed by Streitberger and Kleinhenz[22] (Asia Med, Munich, Germany) were used. The blunted needles were inserted by using an O ring and adhesive dressing to avoid penetration to the skin. No other interventions were administered to the groups.

In relation to the reproductive hormones, we hypothesised that the interventions would be considered effective if FSH and LH levels decreased and oestradiol levels increased.

Data were analysed using SPSS V.12. G-Power V.3.1 software was used to evaluate sample size and power of

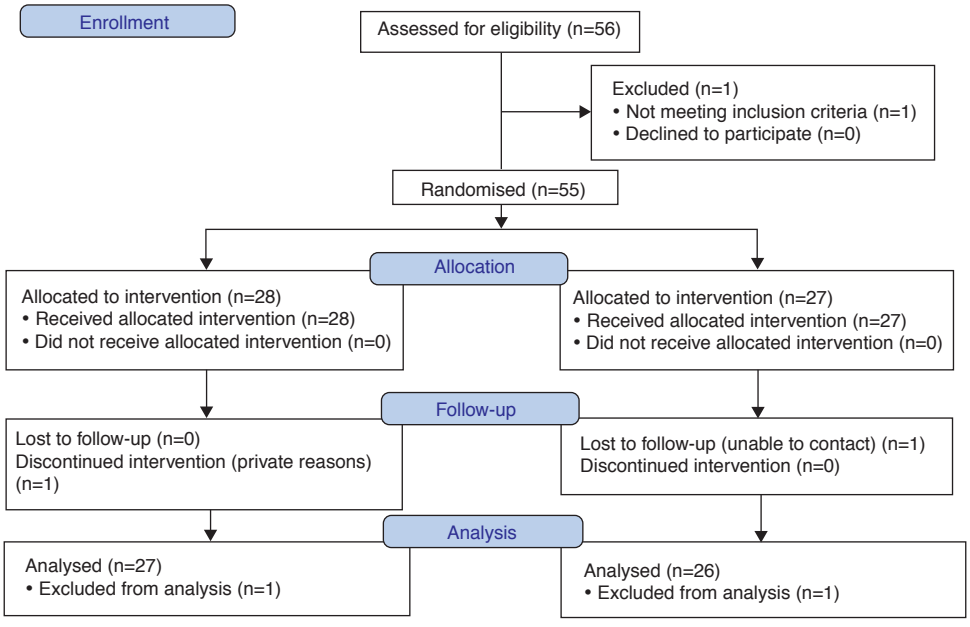

Figure 1 Flow diagram of the progress through the phases of the randomised trail.

the present study. Theoretical power was taken as 0.80 in planning the study and the power actually achieved was calculated to be 0.71 at the end of the study. Descriptive statistics were expressed as mean±SD for continuously measured variables. Student t test was used for normally distributed data, and Wilcoxon signed rank test for not normally distributed data for comparisons in dependent groups. The group differences in MRS scores were assessed using non-parametric Mann–Whitney U test. Multivariate analysis with Bonferroni correction was used posthoc to explore changes in FSH levels. A p value of 0.05 was considered significant.

RESULTS

In the acupuncture group, one patient left the study for personal reasons, in the sham group, one patient did not come to follow-ups and one patient did not meet the inclusion criteria (she had surgical menopause with FSH levels lower than 40 IU/ml). Hence, the study was completed with 53 participants (27 in the study group, 26 in the sham group) analysed (figure 1). No adverse effects were observed in any of the patients.

The groups were similar in terms of mean age, mean menopausal age and mean duration of menopause (p=0.633, p=0.991 and p=0.760, respectively). Mean BMI of the groups were also similar (p=0.186) (table 1).

The MRS scores for the two groups are shown in table 2. When total MRS scores of the groups were compared, no differences were found between the total scores of the groups after the first session (p=0.115), but the total score of the acupuncture group after the last treatment was significantly lower than the sham group (p=0.001). The urogenital subscale and hot flush severity scores were significantly different between groups at baseline, which was considered a random finding. Somatic subscale scores after the first and last sessions were significantly lower in acupuncture group than the sham group (both p=0.001). The psychological subscale scores after the first session were similar in the two groups (p=0.626) whereas the scores after the last session were significantly lower in acupuncture group than placebo group (p=0.001). Urogenital subscale scores of the groups were no different after the first and last sessions (p=0.447 and p=0.153, respectively).

When the scores were compared before and after the interventions (within groups), no significant differences were found in sham group in terms of somatic, psychological and urogenital subscale scores (p=0.132, p=0.066 and p=0.461, respectively). However, all subscale scores were significantly decreased after therapy in the acupuncture group (all p=0.001).

When the severity of hot flushes in somatic subscale was evaluated alone, a significant difference was found between groups, with scores in the acupuncture group significantly lower than the sham group (p=0.001) after the last session. For the within group changes in severity of hot flushes no significant difference was observed in the sham group (p=0.317), but there was a significant decrease in acupuncture group (p=0.001).

The comparisons of hormone levels (baseline, after the first and last sessions) of groups are shown in table 3. In the acupuncture group, FSHb levels were higher than sham group before treatment (p=0.002), which was considered to be a chance occurrence.

FSH levels of the acupuncture group were higher than the sham group (p=0.009) after the first treatment but not at the end of the course of acupuncture (p=0.659). LH levels in the acupuncture group were significantly lower after the first treatment (p=0.036) and also at the end of the course (p=0.046). Oestrogen levels were significantly higher than in the sham group at the end of treatment (p=0.045).

Considering the changes within the groups before and after interventions, no significant differences were found between FSHbs and FSHls, LHb and LHls, E2b and E2ls levels in acupuncture and sham groups (p=0.853, p=0.245, p=0.138, p=0.043, p=0.904 and p=0.695, respectively).

DISCUSSION

In the present study, total MRS scores as well as somatic and psychological (but not urogenital) subscale scores of acupuncture group were lower than sham group after

Table 1 The mean age, menopausal age, duration of menopause and mean body mass index (BMI) of the groups

	Acupuncture	Sham
	Mean±SD (Min–Max)	Mean±SD (Min–Max)
Age	50.3±4.5 (39.0–58.0)	48.5±7.9 (40.0–56.0)
Menopausal age	45.6±5.5 (38.0–55.0)	46.4±3.2 (40.0–52.0)
Menopause duration (year)	4.7±4.5 (1.0–12.0)	4.1±3.4 (0.0–14.0)
BMI	29.1±3.9 (23.5–37.6)	30.6±5.1 (21.8–39.0)

Table 2 Menopause Rating Scale scores of the two groups

	Acupuncture	Sham	
	Mean±SD (Min–Max)	Mean±SD (Min–Max)	p Value
Somatic			
Somatic bs	8.9±2.5 (2.0–13.0)	9.1±2.3 (5.0–12.0)	0.931
Somatic fs	6.1±2.8 (0.0–11.0)	9.1±2.3 (5.0–13.0)	0.001
Somatic ls	3.2±2.1 (0.0–7.0)	8.8±2.3 (5.0–12.0)	0.001
Psychological			
Psychological bs	9.8±3.9 (1.0–16.0)	8.6±3.1 (4.0–15.0)	0.154
Psychological fs	7.9±3.6 (1.0–15.0)	8.5±3.2 (3.0–15.0)	0.626
Psychological ls	4.1±2.3 (1.0–9.0)	8.3±3.3 (2.0–15.0)	0.001
Urogenital			
Urogenital bs	5.2±2.9 (0.0–12.0)	3.7±2.6 (0.0–11.0)	0.038
Urogenital fs	4.2±2.7 (0.0–12.0)	3.8±2.7 (0.0–11.0)	0.447
Urogenital ls	2.3±1.9 (0.0–7.0)	3.5±2.8 (0.0–11.0)	0.153
Total			
Total bs	23.9±6.5 (10.0–36.0)	21.4±6.2 (12.0–35.0)	0.155
Total fs	18.2±6.7 (7.0–36.0)	21.3±6.8 (10.0–35.0)	0.115
Total ls	9.6±4.7 (1.0–22.0)	20.5±6.8 (9.0–35.0)	0.001

bs, baseline; fs, first session; ls, last session.

Table 3 Hormone levels of groups at baseline and after the first and the last sessions

	Acupuncture	Sham	
	Mean±SD (Min–Max)	Mean±SD (Min–Max)	p Value
Follicular stimulating hormone (FSH)			
FSH bs	87.1±29.2 (41.9–167.5)	64.8±16.0 (41.4–99.9)	0.002
FSH fs	82.7±30.3 (30.7–164.4)	63.0±15.3 (40.2–98.2)	0.009
FSH ls	80.6±37.0 (17.8–171.6)	63.1±15.8 (40.3–100.3)	0.053*
Luteinising hormone (LH)			
LH bs	37.2±13.9 (18.5–68.8)	41.4±11.0 (14.6–63.3)	0.272
LH fs	33.8±14.0 (16.1–68.6)	42.4±12.6 (17.1–65.3)	0.036
LH ls	33.7±14.6 (10.4–63.3)	42.7±11.1 (18.9–61.9)	0.046
Oestradiol			
Oestradiol bs	14.2±8.2 (10.0–42.0)	17.9±11.9 (6.6–47.5)	0.136
Oestradiol fs	20.9±35.1 (10.0–192.0)	16.9±9.1 (5.7–35.2)	0.186
Oestradiol ls	22.9±34.8 (10.0–147.0)	18.8±11.6 (6.5–56.0)	0.045

*Multivariate analysis: no significant effect of time (p=0.464) or group × time interaction (p=0.659).
bs, baseline; fs, first session; ls, last session.

treatment. LH levels were reduced and oestradiol levels were raised after treatment with acupuncture group, but those we believe that those changes in hormone levels are not sufficiently large to explain the changes in symptoms. Most acupuncture studies in this topic have used similar time frames for acupuncture sessions, but it is not clear whether the length of time chosen for treatment was sufficient to reflect acupuncture's complete effect. Therefore we assessed MRS scores and the hormone levels after the first session of interventions, to explore whether the effect of acupuncture was cumulative: we found that the differences were greater after the last session than the first session.

It was suggested in 1976 that acupuncture stimulation in normal ovulatory women may affect endocrine functions.[23] Later, the effect of acupuncture on ovulation induction was investigated by Yu *et al*[24] who found that ovulation was induced in five of 11 women with chronic anovulatory cycles, three of whom conceived. However, different results have been reported in studies examining the effect of acupuncture on postmenopausal hormone levels. In some studies, where different acupuncture techniques and different HRT procedures were applied, significantly decreased FSH and LH levels and increased oestradiol levels were reported with acupuncture[10–12 15] while in some, a significant decrease in menopausal symptoms but no change in hormone levels were reported.[9] Especially in studies with electroacupuncture, more significant results were obtained in hormone levels.[12 25] Since we observed small changes in hormone levels similar to some studies, we speculate that acupuncture might have an effect on reproductive hormones through some mechanisms that we could not explain. It is certain that further studies are needed for definitive results.

In the present study somatic, psychological and urogenital symptom subscale scores of MRS decreased with acupuncture therapy. In studies that have investigated the effect of HRT in treatment of menopausal symptoms, it was reported that HRT relieved some menopausal symptoms, such as vasomotor symptoms and vaginal or genital dryness, but also contributed to treatment-related effects, such as bleeding and breast tenderness.[26 27] Also different results have been reported in studies comparing HRT with acupuncture for the treatment of menopausal symptoms. In some of those, it was reported that symptoms decreased significantly with both treatments,[11 28] in some of them better results with HRT,[10] and in others with acupuncture[12 13] have been reported.

Among menopausal symptoms, the most prominent symptom—and the one on which most studies have been conducted—is hot flushes. The symptoms are characteristic of a heat-dissipation response and consist of sweating on the face, neck and chest, as well as peripheral vasodilation. Although hot flushes clearly accompany oestrogen withdrawal at menopause, oestrogen alone is not responsible since levels do not differ between symptomatic and asymptomatic women. Until recently, it was thought that hot flushes were triggered by a sudden, downward resetting of the hypothalamic thermoregulatory set-point, since there was no evidence of increased core body temperature. Evidence obtained using a rapidly responding ingested telemetry pill indicates that the thermoneutral zone, within which sweating, peripheral vasodilation and shivering do not occur, is virtually non-existent in symptomatic women but normal in asymptomatic women. The results suggest that small temperature elevations preceding hot flushes acting within a reduced thermoneutral zone constitute the triggering mechanism. Central sympathetic activation is also elevated in symptomatic women, which reduces the thermoneutral zone in animal studies. Oestrogen virtually eliminates hot flushes but its mechanism of action is not known.[29] Acupuncture has been suggested as an alternative to HRT, based on the fact that acupuncture increases central β-endorphin activity and therefore may make the thermoregulation more stable and decrease hot flushes and sweating.[28] In some studies significant decrease has been reported not in frequency but in severity of hot flushes with acupuncture.[14 30] Like

several other studies, in this study the severity of hot flushes was significantly decreased in the acupuncture group after treatment. However, in the acupuncture group, significant changes in hormone levels (especially in oestrogen) were not observed and this suggests that other factors are activated in the causing hot flushes. In another study,[9] vasomotor and physical symptoms were found to be improved with acupuncture, although no changes were found in sexual symptoms and reproductive hormones.

In some studies comparing sham acupuncture to real acupuncture, both forms of acupuncture therapy were effective in the treatment of postmenopausal symptoms.[25 28] Recently, Venzke *et al*[31] reported that the subjects obtained benefit from either form of acupuncture treatment and they suggested that non-invasive needling might not be equivalent to no treatment or true placebo treatment. However, in the present study, real acupuncture treatment was superior to sham acupuncture in the relief of somatic, and psychological symptoms in postmenopausal women.

Despite the importance of the current findings, several limitations must be mentioned. First the sample size was very small. Next, as we did not follow-up the patients after the treatment we could not know whether the positive effects of acupuncture especially on symptoms continue. More reliable results can be obtained in the studies with larger sample size and longer follow-up.

CONCLUSION

The current data indicate that acupuncture can be considered as an alternative therapy in the treatment of menopausal symptoms particularly in hot flushes, in women who have contraindications for HRT.

Summary points

- Evidence is mixed on whether acupuncture is superior to sham in the treatment of hot flushes.
- We compared acupuncture with non-penetrating sham.
- Acupuncture was superior for menopause symptom scores.

Competing interests None.

Ethics approval This study was conducted with the approval of the local ethical committee.

Provenance and peer review Not commissioned; externally peer reviewed.

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