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Acupuncture for treating menopausal hot flushes: a systematic review

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ABSTRACT

Objective To assess the effectiveness of acupuncture as a treatment option for menopausal hot flushes.

Design We have searched the literature using 17 databases from inception to October 10, 2008, without language restrictions. We included randomized clinical trials (RCTs) of acupuncture versus sham acupuncture. Their methodological quality was assessed using the modified Jadad score.

Results In total, six RCTs could be included. Four RCTs compared the effects of acupuncture with penetrating sham acupuncture on non-acupuncture points. All of these trials failed to show specific effects on menopausal hot flush frequency, severity or index. One RCT found no effects of acupuncture on hot flush frequency and severity compared with penetrating sham acupuncture on acupuncture points that are not relevant for the treatment of hot flushes. The remaining RCT tested acupuncture against non-penetrating acupuncture on non-acupuncture points. Its results suggested favorable effects of acupuncture on menopausal hot flush severity. However, this study was too small to generate reliable findings.

Conclusion Sham-controlled RCTs fail to show specific effects of acupuncture for control of menopausal hot flushes. More rigorous research seems warranted.

INTRODUCTION

Hot flushes are the most frequent and troublesome symptoms related to menopause[1]. The much publicized risks of hormone replacement therapy on postmenopausal women often motivate patients to try complementary medicine[2–4]. Acupuncture is one of the most popular forms of complementary medicines used by women in menopause[5–7]. It can be defined as the insertion of needles into the skin and underlying tissues at particular sites, known as acupoints, for therapeutic or preventive purposes[8]. Acupuncture points can be stimulated by needle insertion, with electricity, lasers, pressure, heat or ultrasound waves. Acupuncture is now a widely accepted

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intervention for the treatment of a variety of conditions. It is frequently recommended for menopausal symptoms but relatively few rigorous clinical trials have tested its efficacy. Currently, no systematic review is available (only a Cochrane protocol[9]). Hence, the objective of this systematic review was to summarize and critically assess the evidence from randomized clinical trials (RCTs) for or against the effectiveness of acupuncture for treating menopausal hot flushes.

METHODS

Data sources

Databases searched from their respective inceptions through to 10 October, 2008 were: Medline, AMED, British Nursing Index, CINAHL, EMBASE, PsycInfo, The Cochrane Library 2008 (Issue 4), six Korean Medical Databases (Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, Research Information Centre for Health Database, KoreaMed, and Korean National Assembly Library), and four Chinese Medical Databases (China Academic Journal, Century Journal Project, China Doctor/Master's Dissertation Full Text DB, and China Proceedings of Conference Full Text DB). The search phrase used was '(acupuncture AND climacteric) OR (acupuncture AND menopause) OR [acupuncture AND (hot flash OR hot flush)]'. In addition, our own files and relevant journals (FACT – Focus on Alternative and Complementary Therapies) were manually searched. Hard copies of all articles were obtained and read in full.

Study selection

All articles were included that reported an RCT in which women with hot flushes due to perimenopausal, menopausal or postmenopausal status or surgical menopause of any age were treated with needle acupuncture, with or without electrical stimulation. Perimenopause was defined as the period immediately prior to menopause and the first year after menopause. Only studies with women experiencing hot flushes at baseline were included. Acupuncture was defined as the insertion of needles into the skin and underlying tissues at particular sites, known as acupoints, for therapeutic or preventive purposes. Trials testing other forms of acupuncture, such as laser acupuncture or moxibustion, were excluded. We also excluded studies of women with induced menopause through radiation or chemotherapy or women with breast cancer. To be included, trials had to compare needle acupuncture with various forms of sham acupuncture in parallel or cross-over design. No language restrictions were imposed. Dissertations and abstracts were included provided they contained sufficient detail.

Data extraction, quality and validity assessment

All articles were read by two independent reviewers (M.S.L. and B.-C.S.), who extracted data from the articles according to predefined criteria. Allocation concealment was assessed using the Cochrane classification[10]. The modified Jadad score was calculated by assessing three criteria: description of randomization, blinding, and withdrawals, with the score ranging from 0 to 5 points[11]. Taking into account that it is impossible to blind therapists to the use of acupuncture, one point was given for blinding if the outcome assessor was blinded. Disagreements were resolved by discussion between the two reviewers (M.S.L. and B.-C.S.), with the opinion of a third reviewer (E.E.) being sought if necessary. There was no disagreement between the two reviewers about the Jadad scores.

Outcome measures and data synthesis

The mean change of hot flush (with or without night sweats) and frequency or severity or hot flush index (frequency × severity), compared with baseline, was defined as the primary outcome measure. These variables were evaluated subjectively with the help of a daily diary or validated scoring systems, including the Kupperman index or other generic measures of vasomotor symptoms. The differences between the intervention groups and the control groups were assessed. Weighted mean differences and 95% confidence intervals were calculated using the Cochrane Collaboration's software (Review Manager (RevMan) Version 5.0 for Windows, Copenhagen, The Nordic Cochrane Centre). The variance of the change was imputed using a correlation factor of 0.5. The χ^2 test for heterogeneity was used to test whether the distribution of the results was compatible with the assumption that inter-trial differences were attributable to chance variation alone. Homogeneous datasets were statistically pooled using a random effects model.

RESULTS

Study description

The searches identified 106 potentially relevant articles; 100 studies were excluded, 23 of which were RCTs (Figure 1). Among these, four RCTs were excluded because the participants in these trials were breast cancer patients[12–15]. One RCT that did not report outcomes related to hot flushes was excluded[16]. Three RCTs were excluded because they were duplicates[17–19]. Nine RCTs tested acupuncture compared with drug therapy[20–28]. The majority of these trials reported favorable effects of acupuncture. Six further RCTs were excluded because they tested acupuncture in combination with other treatments[29–34]. Key data of the six included RCTs are summarized in Table 1a and b[35–40]. A total of 309 participants were included in these trials. Two RCTs originated from Sweden[35,39], three studies were conducted in the USA[36,37,40], and one trial was from Korea[38]. Four RCTs[35,38–40] included only subjects with postmenopausal problems, while the other studies[36,37] included peri- and postmenopausal women. Manual acupuncture alone was used in four trials[36–38,40], and electroacupuncture combined with acupuncture was employed in two trials[35,39]. The acupuncture methods were classical Chinese acupuncture[35,37–40] and Western formula acupuncture[36] (Table 2). Four RCTs[35–38] employed penetrating sham acupuncture on non-acupuncture points, one RCT[39] used penetrating

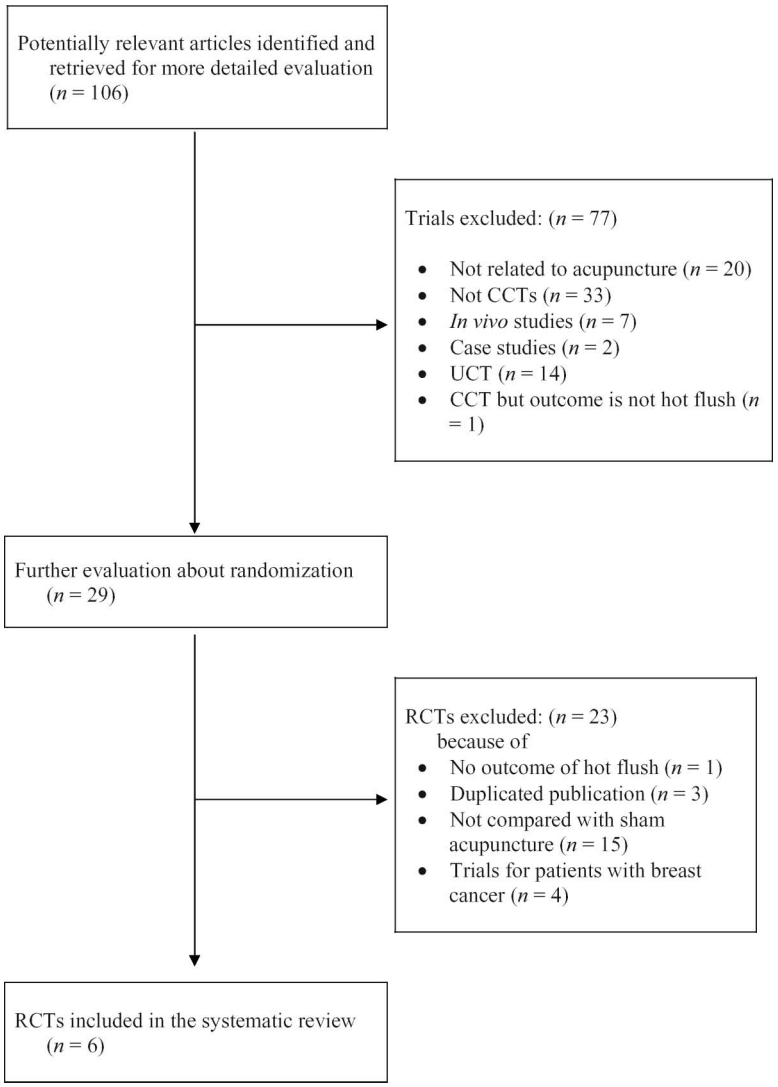

Figure 1 Flowchart of trial selection process. RCT, randomized clinical trial; CCT, controlled clinical trial; UCT, uncontrolled clinical trial

Table 1a Summary of randomized, placebo-controlled clinical trials of acupuncture for menopausal hot flushes

First author	*Quality score**	*Allocation concealment*	*Sample size and included subjects*	*Age range* (years)
Wyon[35]	5 (1+1+1+1+1)	adequate	45 women with vasomotor symptoms and a spontaneous menopause of at least 6 months (include surgical menopausal)	48–63
Vincent[36]	4 (1+1+1+1+0)	not reported	103 peri- or postmenopausal women experiencing ≥5 hot flushes a day (moderate to severe hot flushes, surgical menopausal not reported)	45–59
Avis[37]	4 (1+1+1+1+0)	not reported	56 peri- or postmenopausal women with no menses in the past 3 months experiencing ≥4 moderate to severe hot flushes per day (include surgical menopausal)	44–55
Kim[38]	4 (1+1+1+1+0)	not reported	52 postmenopausal women experiencing hot flushes ≥14 times a week and scored severity at 50 of 100 mm VAS (include surgical menopausal)	43–53
Wyon[39]	3 (1+0+1+1+0)	not reported	24 women with natural menopause for at least 1 year	47–62
Nir[40]	4 (1+1+1+1+0)	not reported	29 postmenopausal women experiencing ≥7 moderate to severe hot flushes per day (include surgical menopausal)	45–65

*Quality score: modified Jadad score (randomization 1 point + appropriate randomization method 1 point + describing withdrawals and dropouts 1 point + patient blinding 1 point + assessor blinding 1 point), maximum 5 points; VAS, Visual analog scale

Table 1b Summary of randomized, placebo-controlled clinical trials of acupuncture for menopausal hot flushes

First author	*Intervention (regimen)*	*Control (regimen)*	*Hot flush measurement tools*	*Intergroup difference*
Wyon[35]	AT (8 points used, 5–20 mm depth), plus electrical stimulation (2 Hz, 4 points used), (de-qi, 30 min, 2 times weekly for first 2 weeks and 1 time weekly for 10 weeks, $n = 15$) 24 weeks follow-up	Sham AT (superficial penetrating, non-acupuncture point, 0.5–1 mm depth, no de-qi, other same as AT group, $n = 15$)	Daily diary (calculated from 7 days of values of severity) 1) Mean frequency/24 h 2) Mean severity (10 points scale)/24 h	1) Frequency: intergroup, NS; within-group, $p < 0.01$ in all groups 2) Severity: intergroup, NS; within-group, $p < 0.01$ in all groups
Vincent[36]	AT (de-qi, 30 min, 2 times weekly for 5 weeks, $n = 51$) 7 weeks follow-up	Sham AT (penetrating, non-acupuncture point and non-meridian area, de-qi (n.r.), other same as AT group, $n = 52$)	Daily diary (hot flush score = frequency × severity)	Percentage change in hot flush score: Intergroup, NS Within-group, not reported
Avis[37]	AT (individualized, de-qi, 0.5–3 cm depth, 30 min, 2 times weekly for 8 weeks, $n = 19$) 8 weeks follow-up (however, there were no reported data)	Sham AT (minimal penetrating, non-acupuncture point, no de-qi, other same as AT group, $n = 18$)	Daily diary of hot flush (hot flush index = frequency × severity) 1) Percent changes in hot flush frequency 2) Hot flush index score	1) Intergroup: AT vs. sham, NS; within-group, $p = 0.01$ in all groups 2) Intergroup, NS; within-group, $p = 0.02$ in both AT groups with no difference between groups
Kim[38]	AT (de-qi, 20 ± 3 min, 2 times weekly for 8 weeks, $n = 26$) 4 weeks follow-up	Sham AT (minimal penetrating, non-acupuncture points, 1 mm depth, no de-qi, other same as AT group, $n = 26$)	VAS	Severity: intergroup, NS; within-group, significant reduction in both groups (p values were not reported)
Wyon[39]	AT (1.25–2.5 cm depth) plus electrical stimulation (2 Hz, 4 points used), (de-qi, 30 min, 2 times weekly for first 2 weeks and 1 time weekly for 6 weeks, $n = 11$) 3 month follow-up	Sham AT (superficial penetrating subcutaneously, 2 mm depth, same acupuncture points, no de-qi, other same as AT group, $n = 10$)	Daily diary 1) Number of flush/day 2) Severity of symptoms (VAS)	1) Intergroup, NS; within-group, $p < 0.01$ compared with baseline in both groups 2) Intergroup: not reported; within-group, EA: $p < 0.05$, sham: $p > 0.05$ compared with baseline
Nir[40]	AT (de-qi, 20 min, 2 times weekly for first 2 weeks and 1 time weekly for 5 weeks (total 9 sessions), $n = 12$) 4 weeks follow-up	Sham AT (non-penetrating, non-acupuncture points (5–7 sham points), $n = 17$)	Daily diary Hot flush index (frequency × severity)	1) Percentage reduction in severity: intergroup, $p = 0.042$; within-group, significant reduction in AT ($p = 0.003$), but not in sham AT ($p = 0.15$) 2) Percentage change in frequency: intergroup, NS; within-group, significant reduction in both groups ($p \leq 0.001$)

NS, not significant; VAS, Visual analog scale; AT, acupuncture treatment; EA, electroacupuncture; n.r., not reported

Table 2 Summary of treatment points and other information related with treatment

First author	*Acupuncture method*	*Total sessions*	*Acupuncture points*	*Rationales*	*Adverse events*	*Comments*
Wyon[35]	Classic acupuncture (1 physiotherapist)	12	Fixed points (12) Bilateral: BL15, BL23 (EA), BL32 (EA) Unilateral: GV20, HT7, PC6, LR3, SP6, SP9	TCM theory	Unwanted bleeding (estradiol therapy: 1)	
Vincent[36]	Medical acupuncture (1 acupuncturist)	10	Fixed points (19) Bilateral: SP6, HT7, LI11, LR2, GB34, LR3, GB20 Unilateral: SP4(R), KI6(L), LU7(R), PC6(L), CV4(M)	Pilot data and expert opinion	None	Test the success of blinding
Avis[37]	Classic acupuncture (more than 2 TCM acupuncturists)	16	Individualized acupuncture points used Standard points (11): CV4(M), bilateral: KI3, SP6, BL23, HT6, KI7 Possible additional points (individualized): Kidney deficiency: KI6, KI10; Kidney yin and yang deficiency: KI6, KI10, GV4, CV6, BL52; Kidney and liver yin deficiency with liver yang rising: LR3, LR8, GB20, BL18, PC7, GB13, GV20, taiyang (Extra); Kidney and heart not harmonized: HT7, HT8, PC7, Yintang (Extra); CV15, BL15, GV20	TCM theory	Not reported	Reported the acupuncturist blinding
Kim[38]	Classic acupuncture (1 traditional Korean medical doctor)	16	Fixed points (13) Bilateral: PC6, HT8, HT7, LI4, ST36, SP6, unilateral: CV4	Previous study and clinical experiences	Temporary skin rash and pruritis (sham AT: 1)	Test the success of blinding (successive)
Wyon[39]	Classic acupuncture (1 physiotherapist)	8	Fixed points (12) Bilateral: BL15, BL23 (EA), BL32 (EA) Unilateral: GV20, HT7, PC6, LR3, SP6, SP9	TCM theory	Not reported	
Nir[40]	Classic acupuncture (5 acupuncturists)	7	Individually tailored acupuncture Bilateral: KI3, SP6 Unilateral: CV4, BL23, plus individual pattern points (total 5–7 points)	TCM theory	Bleeding/bruising (AT: 8, sham: 1); discomfort (AT: 7, sham: 6); insomnia (AT: 2, sham: 2); irritability (sham: 3); pain (AT: 1, sham: 1); itchiness (AT: 1); twitching (AT: 1); low energy (sham: 1); resentment (sham: 1); gas (sham: 1)	Test the success of blinding (successive)

TCM, traditional Chinese medicine; AT, acupuncture treatment

acupuncture on acupuncture points, and one RCT[40] employed non-penetrating acupuncture on non-acupuncture points. Five[35,36,38–40] of the included trials adopted a two-armed, parallel-group design, and one used a three-armed, parallel group design[37]. Four RCTs[35,36,38,39] used a fixed selection of acupuncture points for all patients, while two trials[37,40] employed individualized acupuncture points. Two RCTs[37,40] employed more than two acupuncturists for treatment and the other four RCTs employed one physiotherapist[35,39], one traditional Korean medical doctor[38], or one acupuncturist[36]. Five trials used a daily diary[35–37,40] while the sixth study[38] employed a visual analog scale (VAS). The follow-up duration ranged from 4 to 24 weeks.

Study quality

The methodological quality of the trials was high (from 3 to 5 points on the 5-point scale). Five RCTs described the methods of randomization[35–38,40]. Details of drop-outs and withdrawals were described in all six trials. One study reported details about allocation concealment and employed adequate methods[35]. One RCT adopted both subject blinding and assessor blinding[35]. None of the other RCTs employed assessor blinding. Adverse events were mentioned in four studies[35,36,38,40].

Outcomes

Four RCTs[35–38] tested the effects of manual or electroacupuncture on hot flush frequency, severity and hot flush index (frequency × severity), compared to penetrating sham acupuncture on non-acupuncture points. All of these RCTs failed to show effects of acupuncture on hot flushes. One RCT[39] compared the effects of manual acupuncture plus electroacupuncture on hot flush frequency and severity of hot flush measured with a VAS with penetrating sham acupuncture on acupuncture points that were irrelevant for hot flushes. They failed to show favorable effects of acupuncture in both frequency and severity. The sixth RCT[40] tested manual acupuncture with non-penetrating sham acupuncture on non-acupuncture points. Its results suggested favorable effects of acupuncture on percentage reduction in severity but not in frequency. The follow-up periods ranged from 4 to 24 weeks. One RCT[40] reported favorable effect of acupuncture on the frequency and severity of hot flush after 4 weeks follow-up, while the other five RCTs[35–39] demonstrated no such effects.

We had originally intended to submit these data to formal meta-analyses. However, statistical and clinical heterogeneity prevented us from doing so.

DISCUSSION

Few sham-controlled RCTs have tested the effects of acupuncture on menopausal hot flushes. Collectively, the results of the existing studies failed to show specific effects of acupuncture on this symptom. Only one of the six RCTs suggested positive effects. However, this study was too small to generate reliable findings. Overall, our findings provide no convincing evidence that acupuncture is beneficial for women suffering from menopausal hot flushes.

We assessed the methodological quality of the primary studies using a modified Jadad scale. It allocates one point for subject blinding and assessor blinding separately. Of the six RCTs, only one trial[35] was both patient-blinded and assessor-blinded. The other five trials failed to incorporate patient- or assessor-blinding and were therefore open to performance and detection bias. The concealment of treatment allocation was reported in one trial[35]. Trials with inadequate blinding and inadequate allocation concealment may be subject to selection bias and are likely to generate exaggerated treatment effects[41,42]. Details of drop-outs and withdrawals were described in all of the included RCTs. A power calculation was performed in none of them. Most of the RCTs had a small sample size; their results were therefore prone to a type II error. Four RCTs reported checks on the success of blinding[36–38,40].

Several placebo or sham acupuncture methods have been proposed for trials of acupuncture. They range from penetrating needling of non-acupuncture points[35–38], superficially puncturing the skin on acupuncture points[39], and non-penetration on non-acupuncture points[40]. In the present systematic review, no evidence of the superiority of real acupuncture was found compared with sham acupuncture, regardless of the acupuncture technique employed. Non-penetrating sham acupuncture was reported to be superior to placebo tablets for subjective pain outcomes[43]. This may suggest that most of the effects of needle acupuncture are non-specific by nature.

The rationale for the selection of acupuncture points was stated in all of the included RCTs. The authors quoted traditional Chinese theory[35,37,39,40] or pilot studies[36,38] to justify their

point selection. Needle stimulation causing a typical needle sensation has been claimed to be important for reaching maximum effects. This needle sensation (de-qi) was considered in all of the six included RCTs. In the present data set, we found no evidence that the presence or absence of de-qi exerted an important influence on the clinical outcome.

The fact that, overall, there is no good evidence could have three possible interpretations. First, acupuncture could be ineffective for treating hot flushes. Alternatively, it could be effective, but was administered sub-optimally. For instance, the number of treatment sessions could have been too small to generate a significant effect, stimulation could have been insufficient, or the protocol applied in the acupuncture group might not have been suitable for treating hot flushes. The third interpretation is that sham acupuncture is also effective and thus no inter-group differences could be demonstrated. Penetrating acupuncture could induce physiological modulations which might influence symptoms, including pain and autonomic nervous systems. The observed effects of penetrating sham acupuncture on non-acupuncture points might be due to a physiological effect of needling or the therapeutic relationship[44,45].

One argument for using acupuncture for the management of hot flushes might be that it is safer than drug treatment. Four RCTs[35,36,38,40] assessed adverse events of acupuncture treatment and two RCTs did not. Mild adverse effects of acupuncture were noted with both real and sham acupuncture. Relative to those of hormone replacement therapy, these are mild, infrequent and perhaps even negligible.

Our review has a number of important-limitations. Although strong efforts were made to retrieve all RCTs on the subject, we cannot be absolutely certain that we succeeded. Moreover, selective publishing and reporting are other major causes for bias, which have to be considered. It is conceivable that several negative RCTs remain unpublished and thus the overall picture may be distorted[46,47]. Further limitations include the paucity and the often suboptimal methodological quality of the primary data. In total, these facts limit the conclusiveness of this systematic review considerably.

In conclusion, the evidence from sham-controlled RCTs for the effects of acupuncture for treating menopausal hot flush is not convincing. The number, size and quality of the RCTs are too low to draw firm conclusions. Further rigorous RCTs seem warranted but need to overcome the many limitations of the current evidence.

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Conflict of interest Nil.

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