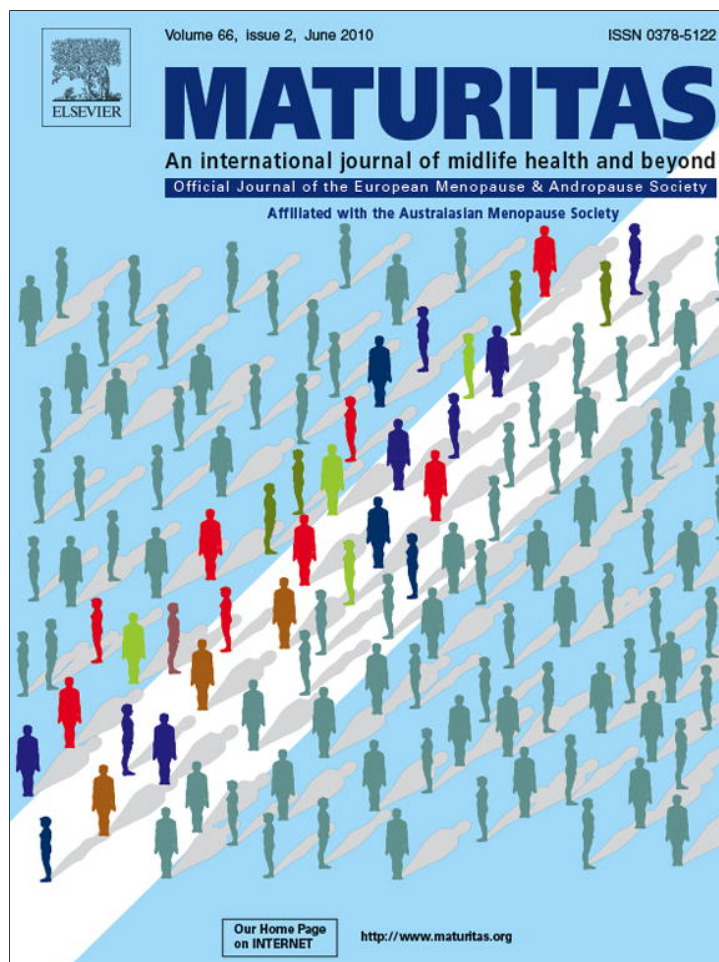


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## Review

## A review of acupuncture for menopausal problems

Einar Borud, Adrian White\*

*The National Research Center in Complementary and Alternative Medicine, University of Tromsø, N-9037 Tromsø, Norway*

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## ABSTRACT

Acupuncture is one of the complementary therapies that are increasingly used by women with menopausal hot flushes. Acupuncture can be understood as a form of neurological stimulation. Clinical trials of acupuncture use different control groups according to whether they wish to provide practical information on the role of acupuncture in health care, or theoretical information on the specific needle effect. Controls for the latter research question are highly problematic, and no convincingly inert 'placebo' needle has yet been designed. For natural menopause, one large study has shown acupuncture to be superior to self-care alone in reducing the number of hot flushes and improving the quality of life; five small studies have been unable to demonstrate that the effect of acupuncture is limited to any particular points, as traditional theory would suggest; and one study showed acupuncture was superior to blunt needle for flash frequency but not intensity. For flushes associated with induced menopause, clearly acupuncture is useful for reducing flushes in clinical practice, but there is mixed evidence on the nature of the effect: one trial found genuine acupuncture superior to control needling, but another showed no significant difference between acupuncture and blunt needle. The possible mechanisms of acupuncture for hot flushes are discussed. Current evidence clearly justifies further research into the most cost effective form of acupuncture for treating hot flushes.

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## 1. Introduction

Women are increasingly rejecting the use of oral hormone replacement for treating hot flushes because of the risk of adverse effects, and many instead are turning to complementary therapies. Among women attending a tertiary menopause clinic, nearly 70%

have used some form of complementary therapy, mostly with a high degree of satisfaction [1].

One common form of complementary therapy is acupuncture, which has its origins in Chinese medicine approximately 2000 years ago, and evolved over time in different cultures and contexts. Acupuncturists have explained acupuncture according to the prevailing world views of their own time. A number of different traditional approaches are still used, the common features being concepts of Yin and Yang, circulation of *qi*, and the existence of meridians. More recently, the understanding of acupuncture involves a rigorous, evidence based approach called Western medical acupuncture [2]. Since there is no evidence to support the value

\* Corresponding author. Permanent address: Peninsula Medical School, University of Plymouth, UK. Tel.: +44 1752 764448.

E-mail addresses: [Einar.Borud@fagmed.uit.no](mailto:Einar.Borud@fagmed.uit.no) (E. Borud), [Adrian.white@pms.ac.uk](mailto:Adrian.white@pms.ac.uk) (A. White).

of Yin/Yang, or the existence of *qi* or the meridians, these concepts have been replaced by the concept of acupuncture as a form of neurophysiological (sensory) stimulation.

This approach argues that acupuncture needling has local effects through local antidromic axon reflexes, releasing neuropeptides such as calcitonin gene-related peptide and increasing local nutritive blood flow; and reflex effects involving the release of neurotransmitters such as opioid peptides and serotonin in the spinal cord, brain stem and brain [3]. Not all effects of acupuncture observed clinically can be fully explained yet, which is not surprising when we consider that the mechanisms of conditions such as chronic pain and menopausal hot flushes have yet to be fully elucidated.

This modern, scientific approach to acupuncture underpins current clinical practice in the West, where points are chosen for their neurophysiological effects. The approach is also highly relevant for choosing suitable control procedures for acupuncture, as discussed below. We are here limiting the discussion to acupuncture in which needles are inserted and stimulated either by hand or electrically (EA), thus excluding acupressure, laser 'acupuncture' and so on.

In this article, we review the current state of evidence of effectiveness of acupuncture for hot flushes both in natural and induced menopause, and consider the possible mechanisms by which acupuncture might have an effect.

## 2. Natural menopause: overviews of evidence on acupuncture for hot flushes

There have been two recent systematic reviews of acupuncture for hot flushes [4,5]. The first included six trials with 309 patients, and the second adds five more trials from the Chinese literature. Three of these additional Chinese trials are not directly relevant to our discussion, as they use forms of therapy rarely offered in the West—embedding of catgut in the acupuncture point, and auricular acupressure. The other two RCTs found positive effects of long courses of acupuncture (manual and electroacupuncture (EA) in which the needles are stimulated by low voltage electrical currents respectively) compared with hormone therapy.

The conclusions of the first review only focussed on studies of acupuncture compared with sham acupuncture, and found no effect. The second review made the same conclusion but added that 'some studies have shown that acupuncture is better than hormone therapy for reducing vasomotor symptoms'. Both reviews point to lack of rigour in the studies.

One particular area of weakness is small sample sizes. The variance of hot flush frequency is large, and sample sizes need to be large. In estimating the size of our study of acupuncture compared with usual care, we calculated that 100 analysable women would be required in each group based on a baseline daily flush rate of 7.0 (SD 3.0), and the assumption that the difference of interest is 20 percentage points (i.e. equivalent to reductions of 50% and 30%) [6]. A much larger sample would be needed to reliably identify a difference between acupuncture and control acupuncture. Only two studies in these reviews included 100 women. Moreover, neither of these reviews combined study results in a meta-analysis to reduce the risk of a type II error.

Unreliable evidence from primary studies does not become reliable simply by inclusion in a systematic review. Therefore the results of these reviews should be regarded as inconclusive, and we shall discuss the evidence in a little more detail, starting with comments on the control group.

### 2.1. Choice of acupuncture control group

Different control groups are selected to address different research questions. Studies with usual care control groups address

the (pragmatic) question that women might ask: Is it worth trying acupuncture for my hot flushes?

Clinicians are more likely to want to know the answer to the question of how acupuncture compares with existing treatments, in terms of effect, safety and cost.

Scientists, regulators and those not directly involved in patient care are more likely to be interested in the more theoretical question: Do acupuncture needles have a specific, biological effect on hot flushes? This type of question is usually addressed in a placebo controlled trial.

The need for some form of control procedure that replicates acupuncture but is an inactive placebo is rather obvious, but so far has not been satisfied in practice. For control arms, many studies use acupuncture needles inserted at locations that are not generally regarded as acupuncture points. These needles are often inserted superficially, compared with intra-muscular insertion in the verum group. However, this assumes that 'acupuncture points' exist. The Western, neurophysiological understanding of acupuncture [2] holds that any needle stimulation of nerves may have an effect on the activity of the central nervous system, and their location may be almost irrelevant, particularly for non-local effects such as influencing the temperature regulation mechanism. Thus, needles inserted in non-specific locations might have significant effects on the central nervous system, and one might expect 'verum' acupuncture to show very little difference in outcome from 'sham' acupuncture.

In recent years, several versions of a blunted needle have been developed which seem to provide somewhat convincing placebos for control [7,8]. Generally the needle handle is loose and, when the needle is applied to the skin, the handle slides over the needle giving the impression that the needle is being inserted. A recent novel design seems to allow blinding of the practitioner as well as the patient [9]. These innovations are somewhat technical and difficult to use without considerable amounts of training, and have not been widely adopted. In addition, there is doubt whether even these needles are truly inert since they stimulate the C-tactile nerve fibres in the skin, which can have biological effects [10].

We shall refer to these controls as 'needle controls' or 'blunt needle controls' in this paper, to avoid the confusion of terms such as sham or placebo acupuncture.

## 3. Acupuncture versus no acupuncture for hot flushes in natural menopause

The largest controlled trial in this area is that of our own group, the ACUFLASH study [11]. This multicenter, pragmatic, randomized, controlled trial recruited 267 postmenopausal women experiencing, on average, seven or more hot flushes per 24 h during seven consecutive days. The acupuncture group received 10 acupuncture treatment sessions (traditional acupuncture) and advice on self-care, and the control group received advice on self-care only. The frequency and severity (0–10 scale) of hot flushes were registered in a diary. Urinary excretion of calcitonin gene-related peptide was assessed at baseline and after 12 weeks. The primary endpoint was change in mean hot flash frequency from baseline to 12 weeks, and the secondary endpoint was change in health-related quality of life measured by the Women's Health Questionnaire.

The results show that hot flash frequency at baseline was about 12 per day, which decreased by 5.8 per day in the acupuncture group ( $n=134$ ) and 3.7 per day in the control group ( $n=133$ ), a difference of 2.1 ( $P<0.001$ ). Hot flash intensity decreased by 3.2 units in the acupuncture group and 1.8 units in the control group, a difference of 1.4 ( $P<0.001$ ). The acupuncture group experienced statistically significant improvements in the vasomotor, sleep, and somatic symptoms dimensions of the Women's Health

Questionnaire compared with the control group. Urinary calcitonin gene-related peptide excretion remained unchanged from baseline to week 12. No serious adverse events were reported.

The acupuncture used in this trial was individualised by traditional Chinese medicine (TCM) diagnosis and acupuncture point selection. A subsequent analysis was made of whether the response rate varied with different syndrome groups, and found no such effect [12]. In addition, a core of common acupuncture points was used in all the syndromes, and no individual points were more likely to be associated with a response than any other, supporting the concept that any effect of acupuncture in this condition is generalised and not point-specific.

In another rigorous comparison of acupuncture and usual care, Avis et al. conducted a three-arm study also including a control needle acupuncture group [13]. For both frequency and severity of flushes, the usual care group responded significantly worse than the combined acupuncture groups. This three-armed study provides evidence that the effects seen in acupuncture groups are not due to time alone.

Two Chinese studies included in one systematic review [5] showed significantly positive effects of acupuncture compared with oral oestrogens. It is interesting to note that the studies used long courses of acupuncture treatment, with 24 and 36 sessions.

Studies such as these leave little room for doubt that acupuncture can mitigate the symptoms of hot flushes in natural menopause, though they cannot answer the question about how much of this effect is due to a 'biological' effect of the needle directly on the nervous system, and how much due to patients' enhanced beliefs, expectations and trust in acupuncture and acupuncturists.

### 3.1. Acupuncture compared with needling control

Five studies compared acupuncture with needle controls, all using superficial needles either on or off the 'correct' acupuncture points. They used between nine and 16 sessions of treatment to a variety of points, and study sample sizes were between 24 and 103. All showed significant reductions in the frequency and severity of hot flushes in both groups, but none showed a significant difference between groups, or even strong trends. So the present evidence suggests that there is little difference in the effectiveness (or ineffectiveness) of up to 16 sessions of real acupuncture and non-specific needling in the treatment of hot flushes. It would be interesting to see the effect of more prolonged courses of treatment.

If this information is put together with the results of the study reported in Section 2, then the evidence is in favour of acupuncture having a clinically useful effect on hot flushes but that this effect does not depend on the needle site, or on the depth of needle insertion.

### 3.2. Acupuncture compared with blunt needle control

One study compared TCM acupuncture with blunt, non-penetrating control needles which in this case were placed at non-acupuncture points [14]. All 29 participants received a formal TCM diagnosis. For the active treatment group, points were selected according to a standardized TCM diagnostic algorithm and a treatment manual. Non-points were selected for the control group from pre-defined locations in the arms, abdomen dorsum and legs. The participants received nine sessions over seven weeks. Acupuncture reduced hot flash severity index significantly compared with blunt needle control, though frequency only showed a trend and there was no difference in the quality of life subscale for vasomotor symptoms (Table 1).

This small study showed no more than a trend, but the results are interesting enough in themselves to justify further similar studies with larger sample sizes.

**Table 1**

	Active acupuncture		Blunt needle control	
	Baseline	Change	Baseline	Change
Severity index	2.4	0.6	2.3	0.1
Frequency	10.3	4.8	10.9	3.2
Vasomotor QoL	7.2	1.6	6.9	1.6

## 4. Acupuncture for hot flushes related to induced menopause

Treatment with hormone therapy is not an option for patients with oestrogen-dependent cancers, so these women frequently seek alternative interventions. In addition, menopause may be induced intentionally in these patients by the use of anti-oestrogens, and 80% of women receiving this therapy will experience hot flushes.

An extensive experience with acupuncture for induced menopause has been reported in detail by Filshie who found that 79% of patients achieved 50% reduction in hot flash frequency [15]. Frisk et al. found a greater than 50% reduction of hot flash frequency in 19 of 27 women who completed acupuncture treatment [16]. The effect was still seen at 12 months in 14 women although they received no further acupuncture. The control group receiving hormone therapy reported almost complete cessation of flushes by 12 weeks.

In an initial exploratory study in 38 women to determine the clinical effect, 12 weeks of either acupuncture or applied relaxation were associated with greater than 50% reduction in hot flush frequency after 12 weeks which was slightly greater still after 6 months [17]. These changes were supported by similar changes in the Kupperman Index. A further analysis showed that the women's psychological well-being also improved and mood improved with electroacupuncture [18].

Deng et al. included 72 women in an RCT comparing eight sessions of either standardised acupuncture or blunt needle control [19]. At six weeks, acupuncture was associated with 0.6 fewer hot flushes per day than blunt needle control, which was not a significant difference. The authors comment that the treatment duration may not have been sufficient, since the mean score in the genuine acupuncture group was still progressively deviating from the control group at the end of treatment.

An RCT compared acupuncture with control needling in 59 women who had completed surgery and radiotherapy and were experiencing hot flushes due to tamoxifen-induced menopause [20]. Women received 15 treatments over 10 weeks of either genuine, standardised acupuncture or control acupuncture with superficial insertion into non-acupuncture points. Mean daily flush frequency reduced from 9.5 to 4.7 in the acupuncture group, and from 12.3 to 11.7 in the control group. These differences were significant. Corresponding changes were seen in the frequency of nocturnal flushes, as well as the Kupperman index. The differences between the groups were still largely maintained at 12 weeks follow up.

This preliminary evidence of the role of acupuncture in hot flushes in induced menopause is promising.

## 5. Possible mechanisms of acupuncture

A stable core body temperature is important for optimal function and integrity of the body [21]. It has been hypothesized that the core body temperature is regulated within a thermoneutral zone, between an upper sweating threshold and a lower shivering threshold. Within this thermoneutral zone, sweating and shivering does not occur. These mechanisms maintain the core body temperature within the pre-set thresholds [22].

Temperature regulation is considered a complex, highly regulated, and integrated network of neuroendocrine, autonomic, and somatomotor responses [21]. The three major components involved in thermoregulatory function include afferent thermosensitive pathways providing information about core body temperature; central processing areas in the CNS; and peripheral vasculature, which receives efferent signals controlling vasodilatation and vasoconstriction.

The physiological mechanisms causing the vasomotor episodes are not known in detail, and different hypotheses have been studied. Facets of these theories may contribute, in part, to this thermoregulatory dysfunction [23].

One major theory, originally proposed by Tataryn in 1980 [24] and further studied by, among others, Freedman et al. [22,25–27], suggests that the physiological changes occurring during the menopausal transition include a narrowing of the thermoneutral zone. A normally insignificant increase in the core body temperature will then trigger a heat loss response, i.e. a hot flush. Neurochemical changes are caused by the alterations in sex-hormones during the menopausal transition [28]. It has been suggested that the concentration of endorphins in the hypothalamus decreases with decreasing oestrogen concentrations. The reduced endorphin levels increase the release of serotonin and norepinephrine, and this may in turn cause a drop in the set point in the thermoregulatory centre in the hypothalamus and elicit inappropriate heat loss [25,26,29]. The heat loss is achieved by vasodilatation and sweating, and these reactions may be mediated by the potent vasodilator calcitonin gene-related peptide (CGRP) [30]. Endogenous opioids modulate the release of CGRP at the spinal cord level [31], and postmenopausal women with vasomotor symptoms had increased urinary excretion of CGRP [30].

Acupuncture probably affects serotonin and beta-endorphin activity in the central nervous system [3,32], and may thus influence the thermoregulatory center and make it more stable. One study showed that CGRP decreased in 24-h urine after acupuncture therapy in women with hot flashes [30], though this was not confirmed [11].

## 6. Conclusion

Acupuncture is a complementary therapy used by women to reduce their hot flashes due to natural or artificial menopause. Acupuncture is clearly associated with an effect on hot flashes that is greater than natural remission alone, and the evidence suggests that this might be due to a general effect of needling, not restricted to acupuncture points. This effect of acupuncture, if confirmed, is likely to involve an influence on the thermoregulatory centre by release of serotonin and beta-endorphin.

## Competing interests

Adrian White is employed by the British Medical Acupuncture Society as editor for the journal *Acupuncture in Medicine*.

## Contributors

Einar Borud and Adrian White both contributed to the paper and agree the final text.

## Provenance and peer review

Commissioned and externally peer reviewed.

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