



Review

Menopausal problems and acupuncture

Borud E, Grimsgaard S, White A*

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

ARTICLE INFO

Article history:

Received 12 January 2010

Received in revised form 6 April 2010

Accepted 8 April 2010

Keywords:

Acupuncture

Menopause

Hot flushes

Systematic review

ABSTRACT

Hot flushes are common and distressing in postmenopausal women. Treatment with oestrogens carries significant health risks. The current hypothesis for their mechanism involves a narrowing of the thermoneutral zone, which may be counteracted by interventions that increase oestrogen, endorphin or serotonin levels, or decrease noradrenalin levels. Acupuncture has several mechanisms with the potential to reduce hot flush frequency and severity. This article reviews the current clinical trial literature.

Sixteen studies are included in the review. Three studies comparing acupuncture with no specific therapy show that acupuncture treatment leads to a reduction of around 50% in hot flush frequency. There were seven comparisons between acupuncture and other therapy: three showed acupuncture to have a significantly smaller effect on frequency than oestrogen therapy, two found a similar effect to relaxation, one found a significantly greater effect than the food supplement oryzanol, and one was unclear. Out of seven studies that compared acupuncture with some other form of needle penetration, whether superficial or deep and whether on or off acupuncture points, five showed no effect, one showed an effect on frequency, and another on severity but not frequency. These studies provide little support for a point specific effect of acupuncture in this condition. Two studies compared acupuncture with non-penetrating, blunt needles: one was significantly positive for flush severity but not frequency, and the other showed no effect.

In conclusion, the results from all studies are in agreement with the hypothesis that acupuncture needling relieves hot flushes. There are few data however supporting the hypothesis that the effect of acupuncture is point specific. Future research should investigate whether there is a biological effect of needling on hot flushes or not, whether tailored treatment is superior to standardised treatment, and ways of delivering treatment that causes least discomfort and least cost.

© 2010 Elsevier B.V. All rights reserved.

Contents

1.	Introduction	58
1.1.	Menopausal problems	58
1.2.	Acupuncture	58
2.	Results	58
2.1.	Studies of acupuncture for menopausal vasomotor symptoms	58
2.2.	Pragmatic trials	59
2.3.	Sham-controlled trials	60
2.4.	Systematic reviews	60
3.	Discussion	60
3.1.	Overall effect of acupuncture	60
3.2.	Needle effect	61
3.3.	Acupuncture mechanisms	61
3.4.	Future studies	61
4.	Conclusion	61
	References	61

* Corresponding author. Peninsula Medical School, University of Plymouth, UK.
E-mail address: Adrian.white@pms.ac.uk (A. White).

1. Introduction

1.1. Menopausal problems

The secretion of the ovarian hormones oestrogen and progesterone decreases when a woman is around 50 years old, and eventually menstruation stops. This period in life is called the menopause (Nelson, 2008). Vasomotor episodes with hot flushes and night sweating are the most prevalent complaints related to menopause. A hot flush is described as a feeling of intense heat in the face, neck and chest. It lasts on average of 4 min, ranging from a few seconds up to 10 min or more, and may be accompanied by sweating. Around two thirds of all women experience hot flushes, and 10–20% of these find the flushes very distressing (Stearns et al., 2002). Other symptoms related to the menopause are disturbed sleep, anxiety and depression, somatic symptoms, reduced memory and concentration, urinary incontinence and sexual problems. However, it may be difficult to distinguish between symptoms related specifically to the menopause, and symptoms related to ageing in general and other physical and psychosocial factors. The presence of a 'menopausal syndrome' including physical and psychological symptoms in addition to vasomotor symptoms has been questioned (Avis et al., 2005). The main focus in this paper will be on vasomotor symptoms.

Women from different parts of the world report different symptoms related to the menopause. While vasomotor episodes may dominate in the West, women in the Far East report muscle aches and joint pain as their main symptoms (Haines et al., 2005). Whether these differences are caused by biological or socio-cultural factors or both is not known (Nelson, 2008).

Reports on the duration of vasomotor symptoms vary considerably. Clinical guidelines report duration from half a year to two years for most women (Anonymous, 2004a, b). A recent longitudinal study from Australia found the duration of bothersome menopausal symptoms for women who completed 13 years of follow-up and who never used HT to be 5.2 ± 3.8 (mean \pm SD) years (Col et al., 2009).

The physiological mechanisms causing the vasomotor episodes are not known in detail, and different hypotheses have been studied. One major theory suggests that the physiological changes occurring during the menopausal transition include a narrowing of the thermoneutral zone within the thermoregulatory zone, which is identified with the pre-optic anterior nuclei of the hypothalamus and anatomically adjacent to nuclei that contain luteinising hormone releasing hormone (LHRH). A normally insignificant increase in the core body temperature will then trigger a heat loss response, i.e. a hot flush (Freedman, 2005; Sturdee, 2008).

The alterations in sex-hormones during the menopausal transition cause neurochemical changes (Shanafelt et al., 2002). It has been suggested that the concentration of endorphins and serotonin in the hypothalamus decreases with decreasing oestrogen concentrations (Sturdee, 2008). The reduced endorphin and (particularly) serotonin levels increase the release of noradrenaline, and this may in turn cause a drop in the set point in the thermoregulatory centre in the hypothalamus and elicit inappropriate heat loss (Casper and Yen, 1985; Freedman et al., 1995; Freedman and Krell, 1999; Sturdee, 2008). According to this hypothesis, any intervention that increases oestrogen, endorphin or serotonin levels, or decreases noradrenalin levels may be expected to reduce hot flushes. The heat loss is achieved by vasodilatation and sweating, and these reactions may be mediated by the potent vasodilator calcitonin gene-related peptide (CGRP) (Wyon et al., 1995). Endogenous opioids modulate the release of CGRP at the spinal cord level (Collin et al., 1993), and one study showed that postmenopausal women with vasomotor symptoms had increased urinary excretion of CGRP (Wyon et al., 1998).

1.2. Acupuncture

Acupuncture is part of traditional Chinese medicine (TCM), one of the oldest healing systems in the world. TCM is still a part of the Chinese health system today (Tang et al., 2008). Variants of TCM acupuncture, based on the old Taoist theories of Yin and Yang and Qi ("energy"), are practised throughout the West today (Tang et al., 2008).

Biomedical acupuncture is an adaptation of Chinese acupuncture that seeks to explain the effects of the needling with theories from established medical physiology, anatomy and pathology (White and Med, 2009). The traditional concepts of Yin and Yang and Qi are not involved, and biomedical acupuncture is considered a treatment that may plausibly be integrated with science-based health care (White and Med, 2009). 'Biomedical acupuncture' or 'Western medical acupuncture' is already in widespread use in the Western world. The term 'electro-acupuncture' is used when needles are inserted and stimulated with an electric current.

The physiological processes involved in acupuncture treatment are not fully known, but factors of importance may include changes in autonomic nerve functioning (Knardahl et al., 1998; Loaiza et al., 2002; Wang et al., 2002), hormones such as cortisol (Kotani et al., 2001; Sato et al., 1996) and oxytocin (Carlsson, 2002; Pak et al., 2000), neuropeptides such as β -endorphin (Andersson and Lundberg, 1995) and serotonin (Cheng and Pomeranz, 1981; Goodnick et al., 2000), cytokines (Bonta, 2002; Son et al., 2002; Xu et al., 2002), and alterations in collagen network communication (Langevin and Vaillancourt, 1999; Langevin et al., 2002). Acupuncture probably affects serotonin and noradrenaline activities in the central nervous system (Han, 2004; Yano et al., 2004), and thus has the potential to influence the thermoregulatory centre, making it more stable (Wyon et al., 1995). A change in the beta-endorphin concentration may also affect CGRP excretion. One study showed that CGRP decreased in 24-hour urine after acupuncture therapy in women with hot flushes (Wyon et al., 1995).

This article reviews the clinical trial evidence on the effectiveness of acupuncture for hot flushes due to natural and surgical menopause. We consider the evidence from RCTs of courses of needle acupuncture (excluding continuous acupuncture, acupressure and moxibustion) that were included in two recent systematic reviews (Cho and Whang, 2009; Lee et al., 2009), together with RCTs from our own files, and additional RCTs located by updated database searches for 'acupuncture' and 'menopaus*' in PubMed, Embase and Cochrane Central conducted in December 2009. We included trials with any control group, including no treatment, other treatment or sham acupuncture. Sham or placebo acupuncture can be defined as "interventions mimicking 'true' acupuncture/'true' treatment, but deviating in at least one aspect considered important by acupuncture theory, such as skin penetration or correct point location" (Linde et al., 2009). We prefer the term 'sham' since it is not clear whether any such intervention can be physiologically inert (Lundberg et al., 2009).

2. Results

2.1. Studies of acupuncture for menopausal vasomotor symptoms

We included 16 RCTs that met our criteria, and have summarised their essential data in Table 1. One study was reported in two sections, and was run in parallel with another study comparing oestrogen with placebo tablets (Wyon et al., 2004; Zaborowska et al., 2007). Nine reports defined the primary outcome measure(s). All studies except one (Cohen et al., 2003) reported between group statistical analysis, and *P* values given in the table are for between group comparisons. Five studies reported the Kupperman Index as well as frequency or severity data (Frisk et al., 2008; Hervik and Mjalund, 2009; Nedstrand et al., 2005; Wyon et al., 1995; Wyon et al., 2004); to simplify the table, we omitted the Kupperman Index on the basis

Table 1
RCTs of acupuncture for hot flashes: study characteristics and outcomes.

Author	Participants ^a	Acupuncture intervention	Control	Outcomes ^b , % reduction: intervention vs control groups
<i>vs usual care</i>				
Avis et al (2008) See also below	56 (3 arms)	Tailored TCM, 16 sessions in 8 weeks	a) Superficial, non-points b) Usual care	Frequency: 39% vs 48% vs 27%; no significant difference between acupuncture groups, acupuncture superior to usual care ($P<0.05$)
Borud et al. (2009a,b,c)	267	Tailored TCM, 10 sessions in 12 weeks, life style advice	Life style advice, OTC drugs allowed	Frequency: 48% vs 28 % ($P<0.001$).
Kim et al (2009)	175 peri and postmenopause, natural and surgical	Standardised, 12 sessions during 4 weeks	No treatment, OTC drugs allowed	Hot flash score: 66% vs 29% ($P<0.0001$)
<i>vs other therapy</i>				
Wyon et al (2004), and Zaborowska et al. (2007) See also below	45 (4 arms)	Electroacupuncture, 14 sessions over 12 weeks	a) Superficial, non-points b) Oral oestradiol c) Relaxation	Frequency: 52% vs 53% vs 90% vs 46% (no group effect, but oestrogen group \times time interaction $P=0.002$)
Nedstrand et al (2005)	38, surgical or tamoxifen induced	Electroacupuncture, 14 sessions in 12 weeks	Relaxation	Frequency: 51% vs 51%, no significant difference
[Zhou et al (2006)] ^c	90	Electroacupuncture, 36 sessions over 3 months	Nylestriol 2 mg twice/month	Kupperman Index: result unclear
[Zhang (2006)] ^c	65	Semi-standardised, 24 sessions over 4 weeks	Oryzanol 20 mg 3 times/day	Kupperman Index: significantly greater fall in acupuncture group ($P<0.01$)
Frisk et al (2008)	45, Tamoxifen or other (breast cancer patients)	Electroacupuncture, 14 sessions 12 weeks	Hormone replacement (various)	Frequency: 55% vs 100% at 12 weeks ($P<0.001$)
Zhou et al (2009)	46, surgical	Standardised, 24 sessions over 12 weeks plus acupressure	Hormone replacement, tibolone	Frequency: 27% vs 50% ($P<0.05$). Severity: no significant difference
<i>vs sham control</i>				
Wyon et al (1995)	24	Electroacupuncture, 10 sessions in 8 weeks	Superficial, same points	Frequency: >50%, no significant difference between groups
Cohen et al (2003)	18	Standardised, 6 sessions in 9 weeks	Acupuncture 'tonic' formula	Severity: greater reduction in TCM group, but no statistical analysis
Wyon et al (2004) see also above	45 (4 arms)	Electroacupuncture, 14 sessions over 12 weeks	a) Superficial, non-points b) Oral oestradiol c) Relaxation	Frequency: 52% vs 53% vs 90% vs 46%, no significant difference between acupuncture groups
Vincent et al (2007)	103	Standardised, 10 sessions in 5 weeks	Deep needling non-points	Flush score: 40% vs 38%, no significant difference
Nir et al (2007)	29	Tailored (manualised) TCM, 9 sessions over 7 weeks	Non-penetrating needles	Frequency: 42% vs 32%, no significant difference. Severity: 25% vs 4% ($P=0.042$)
Kim et al (2007)	52	Standardised, 16 sessions in 8 weeks	Superficial, same points	Severity: 60% vs 48%, no significant difference
Deng et al (2007)	72, 'treatment for breast cancer'	Standardised, 8 sessions in 4 weeks	Non-penetrating needle control	Frequency: 29% vs 24%, no significant difference (trend in favour of acupuncture)
Avis et al (2008), see also above	56 (3 arms)	Tailored TCM, 16 sessions in 8 weeks	a) Superficial, non-points b) Usual care	Frequency: 39% vs 48% vs 27%, no difference between acupuncture groups, acupuncture superior to usual care ($P<0.05$)
Hervik and Mjaland (2009)	59, tamoxifen induced	Standardised, 15 sessions in 10 weeks	Superficial, non-points	Frequency: 51% vs 5% ($P<0.01$)

^a Postmenopausal women with natural menopause unless otherwise stated.

^b Primary outcomes (stated or implied) at end of treatment. All comparisons are between groups.

^c Published in Chinese: data from Cho and Whang (2009).

that it is a compound measure that includes symptoms other than hot flashes.

2.2. Pragmatic trials

Pragmatic or practical clinical trials measure the benefits of the treatment in everyday clinical practice – the effectiveness (MacPherson, 2004). It is important to observe that the pragmatic study design does not allow the estimation of what proportion of the clinical benefit was due to the effects of the needling itself, and what was due to placebo effects, including expectations and the patient-provider interaction. We consider pragmatic trials in two groups according to whether the control intervention is usual care (i.e. no specific adjunctive therapy), or another treatment. The trials are summarised in Table 1.

Avis et al. (2008) carried out a randomized study ($N=56$) with three arms (TCM acupuncture, sham acupuncture and usual care) among women with natural menopause. The participants in the two acupuncture groups received a prolonged course of acupuncture. The TCM acupuncture consisted of standardised core points, with the

addition of points based on the acupuncturist's judgement of TCM diagnostic syndrome category. Sham acupuncture consisted of shallow needling in non-acupuncture points without eliciting De Qi. The results showed a significantly greater decrease in daily flush frequency (joint primary end point) between the two acupuncture groups and the usual care group (about 40% compared with 10%).

The ACUFLASH study ($N=267$) (Borud et al., 2009a; Borud et al., 2009b) was a pragmatic, randomized, controlled trial with two arms, testing acupuncture as a complete treatment package. Two 'real-life' treatment policies available to postmenopausal women with vasomotor symptoms were compared, namely acupuncture plus self-care and self-care alone. The primary endpoint was change in mean hot flush frequency from baseline to week 12, and the secondary endpoint was health-related quality of life, as measured with the Women's Health Questionnaire. The results suggested that use of TCM acupuncture plus self-care can lead to a quicker reduction of hot flush frequency and intensity and increase in hours of sleep per night, and a quicker increase in health-related quality of life regarding vasomotor symptoms, sleep problems and somatic symptoms than self-care alone. The difference in change between study

groups was not significant at 12 months (Borud et al., 2009b) (Fig. 1). Post hoc analysis showed that no group with any particular TCM syndrome diagnosis fared better than any other group. The same core points were used for many patients, and no particular needling locations were associated with enhanced effects (Borud et al., 2009c).

In a similar recent study, Kim et al. (2009) randomized perimenopausal and menopausal women ($N=175$) to receive either acupuncture, together with infrared irradiation over the abdomen, during four weeks, or usual care. The reduction in hot flush score (joint primary endpoint) at the end of treatment was 66% in the intervention group compared with 29% in the controls, a highly significant difference.

There were seven comparisons (in five studies) between acupuncture and other treatments for menopausal hot flushes. Three studies found acupuncture significantly less effective than conventional hormone therapy on hot flush frequency (Wyon et al., 2004; Frisk et al., 2008) and Kupperman Index (Zhou et al., 2009), and the result of one study comparing acupuncture with nylestriol on Kupperman Index is unclear (Zhou et al., 2006). Acupuncture had a similar effect to relaxation in two comparisons (Nedstrand et al., 2005; Zaborowska et al., 2007), and in one study was superior to oryzanol, (Zhang, 2006) a supplement derived from rice bran oil that lacks documentation but is promoted for treatment of menopausal symptoms.

2.3. Sham-controlled trials

The nine included studies used various different forms of sham control procedure. The first group of six studies compared acupuncture with superficial needling. Only one study used needles inserted superficially in the same points as the 'real' acupuncture, i.e. testing the effect of needle insertion: this study showed that the frequency of hot flushes decreased significantly by more than 50% among women who received standardised electro-acupuncture ("true" acupuncture with needles inserted in TCM acupuncture points) (Wyon et al., 1995). A similar reduction of hot flushes was observed in the control group, receiving sham acupuncture with superficial needle insertion.

Five studies compared acupuncture with superficial needling of non-acupuncture points. A second study by Wyon ($N=30$) reached a very similar conclusion as the first, i.e. no significant difference in change of hot flush frequency between study groups. (Wyon et al., 2004; Sandberg et al., 2002). In a study of 103 participants, Vincent et al. (2007) found no difference between groups at the end of treatment, but at the week 12 follow up, the hot flush score reduction was 27% in the treatment group, and 45% in the control group. Two other studies (Kim et al., 2007; Avis et al., 2008) found no difference between

acupuncture and superficial needling in non-acupuncture points. In a marked contrast, the study by Hervik and Mjaland (2009) in women with tamoxifen induced menopause showed a large, statistically significant and clinically meaningful superiority of acupuncture for hot flush frequency over superficial needling of non-acupuncture points.

The small RCT ($N=18$) by Cohen et al. (2003) compared standardised TCM acupuncture with an acupuncture formula for a 'tonic'. The report is difficult to interpret and no analysis was conducted, but the authors concluded that real acupuncture was more effective with a 76% reduction of hot flush severity. Finally, two studies compared acupuncture with a non-penetrating needle, a blunt device that is held in position on the skin. One study of 29 participants by Nir et al. (2007) found that TCM acupuncture reduced hot flush severity, though not frequency, compared with sham acupuncture. A study by Deng et al. (2007) in 72 women with induced menopause found no significant difference between the groups, though the authors commented that the acupuncture group was still improving at the end of the four week course of treatment, and a longer course may have revealed differences. At eight sessions, the acupuncture given in this study was the shortest course of all studies.

Most of the cited studies had few participants. All used some sort of standardised acupuncture treatment in the active treatment group, although two studies (Nir et al., 2007; Avis et al., 2008) used standardised algorithms and treatment manuals to take into account individual TCM diagnoses. All the studies used sham acupuncture as control. Two studies used non-penetrating needles at non-acupuncture points, the other studies used needling/superficial needling at non-acupuncture points. Seven studies failed to demonstrate any differences in the effect between 'true' acupuncture and 'sham' acupuncture, and two found some effect.

2.4. Systematic reviews

Recently, there have been two systematic reviews of acupuncture for hot flushes (Cho and Whang, 2009; Lee et al., 2009). Only sham-controlled RCTs were included in the second review. Lee et al. (2009) included six trials with 309 patients, and Cho and Whang (2009) add five more trials from the Chinese literature. Two of these five Chinese trials are included above, and the other three trials use forms of therapy rarely offered in the West – embedding of catgut in the acupuncture point, and auricular acupressure.

Both reviews conclude that there is no evidence that acupuncture is an effective treatment for hot flushes in comparison with sham acupuncture, both point to lack of rigour in the studies, and both recommend further research.

3. Discussion

3.1. Overall effect of acupuncture

Three studies that compared acupuncture with usual care (or only lifestyle advice) showed consistent results: in all three, acupuncture was significantly superior in reducing hot flush frequency over the course of treatment. The effect of acupuncture in these studies was a short-term reduction in hot flush frequency of between 40 and 66%, which is at the level of symptom relief generally regarded as clinically significant (Sloan et al., 2001). In these three studies, usual care was associated with a reduction of just less than 30% in hot flush frequency. This figure is commonly associated with response to placebo medication in clinical trials (Sloan et al., 2001) and probably represents the placebo response plus natural history of the condition. This suggests that there may be little 'nocebo' effect from women's disappointment in receiving only usual care after they had volunteered for an acupuncture study.

This evidence is consistent, has been generated by three different research centres, and involves about 500 participants mostly with

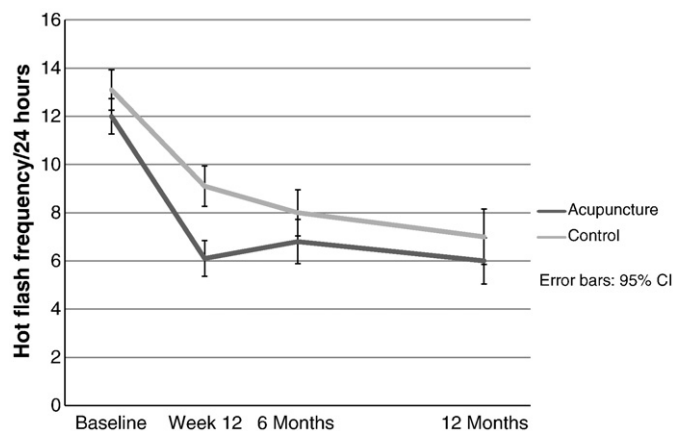


Fig. 1. Change in mean hot flash frequency from baseline to 12 months in the ACUFLASH study (Borud et al., 2009b).

natural menopause. Thus, the current evidence suggests that acupuncture treatment, when considered as a 'system' of treatment that combines the psychological effects of consultation, traditional diagnosis and treatment as well as any physical effects of needling, is an effective treatment for women who are disturbed by hot flushes from natural menopause.

Studies that compare acupuncture with conventional hormone treatment for hot flushes do not add important information, since it is already generally accepted that acupuncture is less effective than hormones. Acupuncture is probably chosen by women who want a safer alternative and are willing to accept smaller benefit (Borud et al., 2007). Acupuncture was superior to oryzanol, which is of unknown effect.

3.2. Needle effect

Turning now to the question whether the needles themselves have a 'biological' (or 'physiological') effect in addition to their placebo effect, we should carefully define two different possible hypotheses: 1) the TCM hypothesis, that acupuncture needling is effective when given at specific acupuncture points according to a TCM diagnosis; and 2) the western medical hypothesis, that acupuncture needling is effective as long as it stimulates nerve tissue.

The seven studies in which acupuncture needling at correct points according to TCM was compared with sham needling are limited by small sample sizes. The results of five are similar: whether the control group had correct points needled superficially, or had non-point locations needled either deeply or superficially, these results in general suggest that there is no point specific effect of acupuncture for hot flushes. Two studies were positive: one showed an effect on hot flush frequency both day and night in women taking tamoxifen (Hervik and Mjaland, 2009); the other study was small ($N=18$), is difficult to interpret and did not conduct statistical analysis (Cohen et al., 2003).

Other data supports the absence of point specificity of acupuncture for this condition: tailored acupuncture, which could be regarded as particularly point specific, was used in three studies (Avis et al., 2008; Borud et al., 2009a; Nir et al., 2007) but was not associated with larger effects (39%, 48%, and 42% respectively) than standardised acupuncture in the remaining studies (66%, 27%, 40%, 29% and 51%, see Table 1), though of course other factors contribute to differences between studies. A post hoc analysis showed no superiority of any particular TCM diagnosis (Borud et al., 2009c).

Two studies used non-penetrating needles in the control groups to test the hypothesis that needle penetration is the stimulus necessary for the effect. One of these studies, (Nir et al., 2007) was small ($N=29$), but is the one study in this group showing a significant difference in the severity of flushes though only a trend in frequency. The other study, (Deng et al., 2007) showed no difference. It was conducted among patients receiving active cancer treatment, and may have used insufficient treatment (as discussed above). The evidence therefore does not allow clear conclusions, but is consistent with the hypothesis that needling sufficient to stimulate nerves is effective for reducing menopausal symptoms. This is the main hypothesis that should be tested in future studies. It may require innovative methods to overcome the known problems of producing truly inactive control procedures for acupuncture (Lund and Lundeberg, 2006).

3.3. Acupuncture mechanisms

Given the current lack of knowledge about the mechanisms of postmenopausal hot flushes (Sturdee, 2008), it would be unwise to speculate in detail on the possible mode of action of acupuncture. We suggested in the Introduction, that the known mechanisms of acupuncture have considerable potential for effects on vasomotor symptoms.

3.4. Future studies

Finally, we consider whether the current evidence suggests any important design features for future studies. Acupuncture can be effective for women with induced menopause, who often experience more severe and frequent flushes than women with natural menopause. However, two such studies found the effect below 30% (Deng et al., 2007; Zhou et al., 2009), so initial research is recommended to explore possible response predictors and optimal treatments in these women. The data in Table 1 show that electroacupuncture appears to achieve consistently greater responses than manual acupuncture, which is an important hypothesis to test. Most of these studies used more than 10 needles, and it is important to test whether results can be achieved with fewer needles to reduce patient discomfort and to simplify treatment. The evidence suggests that a schedule offering treatment twice weekly will probably achieve more rapid relief of symptoms. At least 10 sessions should be given, since the two studies that used less obtained less than 30% reduction (Deng et al., 2007; Nir et al., 2007). However, the optimal number of sessions cannot be deduced from the present evidence. Acupuncture that is tailored to the patient is unlikely to be more effective than standardised acupuncture, though this should be formally tested both because it is an important claim for acupuncture and because tailored acupuncture increases treatment costs considerably.

4. Conclusion

In conclusion, the results from all studies are in agreement with the hypothesis that acupuncture needling, whether it is real or sham acupuncture, relieves hot flushes. Few data support the hypothesis that the effect of acupuncture on hot flushes is point specific. Future research should aim to provide further evidence on whether or not the insertion of acupuncture needles has a physiological effect on hot flushes in addition to their psychological (placebo) effect, whether tailored treatment is superior to standardised treatment, and should address ways of delivering treatment that causes least discomfort at least cost.

References

- Andersson, S., Lundeberg, T., 1995. Acupuncture—from empiricism to science: functional background to acupuncture effects in pain and disease. *Med. Hypotheses* 45, 271–281.
- Anonymous, 2004a. Executive summary. *Hormone therapy*. *Obstet. Gynecol.* 104, 15–45.
- Anonymous, 2004b. Treatment of menopause-associated vasomotor symptoms: position statement of The North American Menopause Society. *Menopause* 11, 11–33.
- Avis, N.E., Brockwell, S., Colvin, A., 2005. A universal menopausal syndrome? *Am. J. Med.* 118 (Suppl 12B), 37–46.
- Avis, N.E., Legault, C., Coeytaux, R.R., Pian-Smith, M., Shifren, J.L., Chen, W., et al., 2008. A randomized, controlled pilot study of acupuncture treatment for menopausal hot flushes. *Menopause* 15, 1070–1078.
- Bonta, I.L., 2002. Acupuncture beyond the endorphin concept? *Med. Hypotheses* 58, 221–224.
- Borud, E.K., Alraek, T., White, A., Fonnebo, V., Grimsgaard, S., 2007. The effect of TCM acupuncture on hot flushes among menopausal women (ACUFLASH) study: a study protocol of an ongoing multi-centre randomised controlled clinical trial. *BMC Complement. Altern. Med.* 7, 6.
- Borud, E.K., Alraek, T., White, A., Fonnebo, V., Eggen, A.E., Hammar, M., et al., 2009a. The acupuncture on hot flushes among menopausal women (ACUFLASH) study, a randomized controlled trial. *Menopause* 16, 484–493.
- Borud, E.K., Alraek, T., White, A., Grimsgaard, S., 2009b. The acupuncture on hot flushes among menopausal women study: observational follow-up results at 6 and 12 months. *Menopause*.
- Borud, E.K., Alraek, T., White, A., Grimsgaard, S., 2009c. The acupuncture treatment for postmenopausal hot flushes (Acufash) study: traditional Chinese medicine diagnoses and acupuncture points used, and their relation to the treatment response. *Acupunct. Med.* 27, 101–108.
- Carlsson, C., 2002. Acupuncture mechanisms for clinically relevant long-term effects—reconsideration and a hypothesis. *Acupunct. Med.* 20, 82–99.
- Casper, R.F., Yen, S.S., 1985. Neuroendocrinology of menopausal flushes: an hypothesis of flush mechanism. *Clin. Endocrinol.* 22, 293–312 (Oxf).
- Cheng, R.S., Pomeranz, B., 1981. Monoaminergic mechanism of electroacupuncture analgesia. *Brain Res.* 215, 77–92.

- Cho, S.H., Whang, W.W., 2009. Acupuncture for vasomotor menopausal symptoms: a systematic review. *Menopause* 16, 1065–1073.
- Cohen, S.M., Rousseau, M.E., Carey, B.L., 2003. Can acupuncture ease the symptoms of menopause? *Holist. Nurs. Pract.* 17, 295–299.
- Col, N.F., Guthrie, J.R., Politi, M., Dennerstein, L., 2009. Duration of vasomotor symptoms in middle-aged women: a longitudinal study. *Menopause*.
- Collin, E., Frechilla, D., Pohl, M., Bourgoin, S., Le, B.D., Hamon, M., et al., 1993. Opioid control of the release of calcitonin gene-related peptide-like material from the rat spinal cord in vivo. *Brain Res.* 609, 211–222.
- Deng, G., Vickers, A., Yeung, S., D'andrea, G.M., Xiao, H., Heerdt, A.S., et al., 2007. Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients. *J. Clin. Oncol.* 25, 5584–5590.
- Freedman, R.R., 2005. Hot flashes: behavioral treatments, mechanisms, and relation to sleep. *Am. J. Med.* 118 (Suppl 12B), 124–130.
- Freedman, R.R., Krell, W., 1999. Reduced thermoregulatory null zone in postmenopausal women with hot flashes. *Am. J. Obstet. Gynecol.* 181, 66–70.
- Freedman, R.R., Norton, D., Woodward, S., Cornelissen, G., 1995. Core body temperature and circadian rhythm of hot flashes in menopausal women. *J. Clin. Endocrinol. Metab.* 80, 2354–2358.
- Frisk, J., Carlhall, S., Kallstrom, A.C., Lindh-Astrand, L., Malmstrom, A., Hammar, M., 2008. Long-term follow-up of acupuncture and hormone therapy on hot flashes in women with breast cancer: a prospective, randomized, controlled multicenter trial. *Climacteric* 11, 166–174.
- Goodnick, P.J., Breakstone, K., Wen, X.L., Kumar, A., 2000. Acupuncture and neuropathy. *Am. J. Psychiatry* 157, 1342–1343.
- Haines, C.J., Xing, S.M., Park, K.H., Holinka, C.F., Ausmanas, M.K., 2005. Prevalence of menopausal symptoms in different ethnic groups of Asian women and responsiveness to therapy with three doses of conjugated estrogens/medroxyprogesterone acetate: the Pan-Asia Menopause (PAM) study. *Maturitas* 52, 264–276.
- Han, J.S., 2004. Acupuncture and endorphins. *Neurosci. Lett.* 361, 258–261.
- Hervik, J., Mjaland, O., 2009. Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial. *Breast Cancer Res. Treat.* 116, 311–316.
- Kim, D.I., Rho, J.J., Choi, M.S., Lee, S.D., Roh, J.W., Yoon, S.H., et al., 2007. A clinical trial to assess the efficacy of acupuncture on hot flashes in postmenopausal women. *Korean J. Orient. Med.* 28, 74–85.
- Kim, K.H., Kang, K.W., Kim, D.I., Kim, H.J., Yoon, H.M., Lee, J.M., et al., 2009. Effects of acupuncture on hot flashes in perimenopausal and postmenopausal women—a multicenter randomized clinical trial. *Menopause*.
- Knardahl, S., Elam, M., Olausson, B., Wallin, B.G., 1998. Sympathetic nerve activity after acupuncture in humans. *Pain* 75, 19–25.
- Kotani, N., Hashimoto, H., Sato, Y., Sessler, D.I., Yoshioka, H., Kitayama, M., et al., 2001. Preoperative intradermal acupuncture reduces postoperative pain, nausea and vomiting, analgesic requirement, and sympathoadrenal responses. *Anesthesiology* 95, 349–356.
- Langevin, H.M., Vaillancourt, P.D., 1999. Acupuncture: does it work and, if so, how? *Semin. Clin. Neuropsychiatry* 4, 167–175.
- Langevin, H.M., Churchill, D.L., Wu, J., Badger, G.J., Yandow, J.A., Fox, J.R., et al., 2002. Evidence of connective tissue involvement in acupuncture. *FASEB J.* 16, 872–874.
- Lee, M.S., Shin, B.C., Ernst, E., 2009. Acupuncture for treating menopausal hot flashes: a systematic review. *Climacteric* 12, 16–25.
- Linde, K., Allais, G., Brinkhaus, B., Manheimer, E., Vickers, A., White, A.R., 2009. Acupuncture for tension-type headache. *Cochrane Database Syst. Rev.* CD007587.
- Loaiza, L.A., Yamaguchi, S., Ito, M., Ohshima, N., 2002. Electro-acupuncture stimulation to muscle afferents in anesthetized rats modulates the blood flow to the knee joint through autonomic reflexes and nitric oxide. *Auton. Neurosci.* 97, 103–109.
- Lund, I., Lundeberg, T., 2006. Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls? *Acupunct. Med.* 24, 13–15.
- Lundeberg, T., Lund, I., N. Slund, J.M.T., 2009. The Emperor's sham – wrong assumption that sham needling is sham. *Acupunct. Med.* 26 (4), 239–242.
- Macpherson, H., 2004. Pragmatic clinical trials. *Complement. Ther. Med.* 12, 136–140.
- Nedstrand, E., Wijma, K., Wyon, Y., Hammar, M., 2005. Vasomotor symptoms decrease in women with breast cancer randomized to treatment with applied relaxation or electro-acupuncture: a preliminary study. *Climacteric* 8 (3), 243–250.
- Nelson, H.D., 2008. Menopause. *Lancet* 371, 760–770.
- Nir, Y., Huang, M.I., Schnyer, R., Chen, B., Manber, R., 2007. Acupuncture for postmenopausal hot flashes. *Maturitas* 56, 383–395.
- Pak, S.C., Na, C.S., Kim, J.S., Chae, W.S., Kamiya, S., Wakatsuki, D., et al., 2000. The effect of acupuncture on uterine contraction induced by oxytocin. *Am. J. Chin. Med.* 28, 35–40.
- Sandberg, M., Wijma, K., Wyon, Y., Nedstrand, E., Hammar, M., 2002. Effects of electroacupuncture on psychological distress in postmenopausal women. *Complement. Ther. Med.* 10, 161–169.
- Sato, A., Sato, Y., Suzuki, A., Uchida, S., 1996. Reflex modulation of catecholamine secretion and adrenal sympathetic nerve activity by acupuncture-like stimulation in anesthetized rat. *Jpn J. Physiol.* 46, 411–421.
- Shanafelt, T.D., Barton, D.L., Adjei, A.A., Loprinzi, C.L., 2002. Pathophysiology and treatment of hot flashes. *Mayo Clin. Proc.* 77, 1207–1218.
- Sloan, J.A., Loprinzi, C.L., Novotny, P.J., Barton, D.L., Lavasseur, B.I., Windschitl, H., 2001. Methodologic lessons learned from hot flash studies. *J. Clin. Oncol.* 19, 4280–4290.
- Son, Y.S., Park, H.J., Kwon, O.B., Jung, S.C., Shin, H.C., Lim, S., 2002. Antipyretic effects of acupuncture on the lipopolysaccharide-induced fever and expression of interleukin-6 and interleukin-1 beta mRNAs in the hypothalamus of rats. *Neurosci. Lett.* 319, 45–48.
- Stearns, V., Ullmer, L., Lopez, J.F., Smith, Y., Isaacs, C., Hayes, D., 2002. Hot flashes. *Lancet* 360, 1851–1861.
- Sturdee, D.W., 2008. The menopausal hot flush—anything new? *Maturitas* 60, 42–49.
- Tang, J.L., Liu, B.Y., Ma, K.W., 2008. Traditional Chinese medicine. *Lancet* 372, 1938–1940.
- Vincent, A., Barton, D.L., Mandrekar, J.N., Cha, S.S., Zais, T., Wahner-Roedler, D.L., et al., 2007. Acupuncture for hot flashes: a randomized, sham-controlled clinical study. *Menopause*. 14, 45–52.
- Wang, J.D., Kuo, T.B., Yang, C.C., 2002. An alternative method to enhance vagal activities and suppress sympathetic activities in humans. *Auton. Neurosci.* 100, 90–95.
- White, A.R., Med, E.B.A., 2009. Western medical acupuncture: a definition. *Acupunct. Med.* 27, 33–35.
- Wyon, Y., Lindgren, R., Lundeberg, T., Hammar, M., 1995. Effects of acupuncture on climacteric vasomotor symptoms, quality-of-life, and urinary-excretion of neuropeptides among postmenopausal women. *Menopause* 2, 3–12.
- Wyon, Y., Frisk, J., Lundeberg, T., Theodorsson, E., Hammar, M., 1998. Postmenopausal women with vasomotor symptoms have increased urinary excretion of calcitonin gene-related peptide. *Maturitas* 30, 289–294.
- Wyon, Y., Wijma, K., Nedstrand, E., Hammar, M., 2004. A comparison of acupuncture and oral estradiol treatment of vasomotor symptoms in postmenopausal women. *Climacteric* 7, 153–164.
- Xu, Z.F., Wu, G.C., Cao, X.D., 2002. Effect of electroacupuncture on the expression of interleukin-1beta mRNA after transient focal cerebral ischemia. *Acupunct. Electrother. Res.* 27, 29–35.
- Yano, T., Kato, B., Fukuda, F., Shinbara, H., Yoshimoto, K., Ozaki, A., et al., 2004. Alterations in the function of cerebral dopaminergic and serotonergic systems following electroacupuncture and moxibustion applications: possible correlates with their antistress and psychosomatic actions. *Neurochem. Res.* 29, 283–293.
- Zaborowska, E., Brynhildsen, J., Damberg, S., Fredriksson, M., Lindh-Astrand, L., Nedstrand, E., et al., 2007. Effects of acupuncture, applied relaxation, estrogens and placebo on hot flashes in postmenopausal women: an analysis of two prospective, parallel, randomized studies. *Climacteric* 10, 38–45.
- Zhang, H., 2006. Influence of acupuncture on the clinical manifestation and beta-endorphin level in female patients with menopausal symptoms with auricular acupressure. *Chin. J. Clin. Rehabil.* 10, 1–3.
- Zhou, J., Qin, Z., Li, W., 2006. Clinical observation on therapeutic effect of electroacupuncture at Sanyinjiao (SP6) on peri-menopausal syndrome. *Chin. Acupunct. Moxibustion* 26, 617–620.
- Zhou, J., Qu, F., Sang, X., Wang, X., Nan, R., 2009. Acupuncture and auricular acupressure in relieving menopausal hot flashes of bilaterally ovariectomized chinese women: a randomized controlled trial. *Evid. Based Complement. Alternat. Med.*