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REVIEW ARTICLE

How long do the effects of acupuncture on hot flashes persist in cancer patients?

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Abstract
Purpose Acupuncture has been suggested as therapy for hot flashes in women with breast cancer and men with prostate cancer. In this systematic review, we sought to evaluate the long-term effects on vasomotor symptoms after the end of a defined treatment period of acupuncture in women with breast cancer and men with prostate cancer.
Methods A literature search revealed 222 articles within the field. With defined exclusion criteria, we identified 17 studies. We also used the Jadad quality score and identified seven studies with a score of at least 3.
Results Six of seven identified studies qualified for inclusion in an analysis that measured frequency of hot flashes weighted in relation to number of patients (n=172). The average reduction from baseline to end of acupuncture (ranging between 5 and 12 weeks of treatment) showed 43.2 % reduction of hot flashes. At the last follow-up (mean 5.8 months, range 3–9 months) after the end of therapy, the weighted reduction from baseline was sustained at 45.6 % in the 153 of 172 patients (89 %) who were followed up.
Conclusions Data from six prospective analyzed studies indicate at least 3-month effects after the end of acupuncture treatment for flashes in women with breast cancer and men with prostate cancer. However, larger randomized trials with long-term follow-up will be needed to confirm these preliminary findings.

Keywords Acupuncture · Breast neoplasm · Prostatic cancer · Hot flashes

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Introduction

More than 50 % of perimenopausal and postmenopausal women suffer from vasomotor symptoms with hot flashes and sweating, which are perceived as being very uncomfortable and may interfere with daytime activities, sleep, and quality of life (QoL) [1]. Older men have also been reported to have hot flashes [2–4], especially men castrated due to prostate cancer [5, 6]. Breast cancer is the most common cancer in women, and prostate cancer is the most common in men. Hot flashes are more common, severe, and long-lasting in women with breast cancer than in healthy postmenopausal women [7–10], and adjuvant therapy such as with tamoxifen may increase both the frequency and intensity of the flashes [11–13]. Hormone therapy (HT) using estrogen alone or combined with progestagens is the gold standard treatment for hot flashes in climacteric women [14], but use of HT increases the risk of cardiovascular events [15, 16] and the incidence and recurrence of breast cancer [15, 17, 18].

Generalized prostate cancer is commonly treated with castration therapy. The prevalence of hot flashes in men with prostate cancer and surgical or medical castration is 58–80 % [19, 20], and more than one fourth report this as the most

troublesome adverse effect of their therapy [6], an effect that usually persists more than 5 years [21].

The rising number of breast and prostate cancer survivors, with high prevalence of vasomotor symptoms, has increased the demand for nonhormonal treatments of vasomotor symptoms. Several nonhormonal treatments have been suggested for women [22–27], but none appears as effective as HT, which reduces the frequency and severity of hot flashes by 75 % compared to placebo [14]. Furthermore, many of these nonhormonal treatments are not suitable because of potentially serious adverse events in women with breast cancer [28, 29]. Similar or identical therapies have also been tried in castrated men but usually with weak effects on hot flashes and adverse effects [30–36].

Acupuncture, a treatment option that does not cause any serious adverse side effects, has been tried for hot flashes. The rationale is the notion that acupuncture increases central β-endorphin activity [37], which probably affects and stabilizes thermoregulation in the hypothalamus and, in turn, decreases vasomotor symptoms [38–40]. Acupuncture therapy has been associated with a decreased number and intensity of hot flashes in menopausal women, both with and without breast cancer [38, 41–45], and in men with castration-treated prostate cancer [46–48]. The decrease of hot flashes in women with breast cancer was not as pronounced with acupuncture as with HT, but greater than reported for placebo [14, 24, 49]. However, acupuncture has yet not been sufficiently compared with placebo. Although placebo needles have been used in research [50–52], they may not completely lack effect, and their use as a sham treatment has therefore been criticized [53, 54].

Acupuncture treatments are usually administered for between 4 and 12 weeks, but the effects have been reported to persist as long as several months [41, 45–48].

The aim of the present study was to review the literature and our own data [41, 45–47] and to assess the long-term effects of a defined treatment period of acupuncture on vasomotor symptoms in women with breast cancer and men with prostate cancer.

Methods

A first literature search was performed during November 2011 and another in October 2012. By using the databases PubMed, ISI Web of Science, SCOPUS, Cochrane library, and the MeSH terms Acupuncture Therapy AND Breast Neoplasm*/Breast Tumor*/Breast cancer/Mammary Carcinoma* AND Prostatic Neoplasms/Prostate Neoplasm*/Prostate Cancer*/Prostatic Cancer*/Prostatic Tumor*/Prostate Tumor* AND Hot Flash (for PubMed), we identified all studies published in English and reported the use of acupuncture for the treatment of hot flashes. Abstracts or, in the absence of abstracts or sufficient facts in the abstract, the complete texts were read in order to select the articles for inclusion in the review. Reviews, case studies, notes, letters to the editor, correspondence, as well as abstracts from congresses were excluded but, due to the small number of studies identified, we included uncontrolled trials.

Thereafter, we gave points to each article according to the Jadad quality score [55]. Points were given to each study, from 0 to 5 points, depending on whether certain criteria were fulfilled. These criteria (having 1 point each) were the following: randomization, appropriate method of randomization described, withdrawals and drop outs clearly described, double-blinding, and appropriate double-blinding described. Since acupuncture by nature cannot be double-blinded, the maximum Jadad quality score that could be given in the present review of acupuncture studies was 3 points, which we considered to indicate acceptable quality. We identified the type of acupuncture, the duration of the treatment, the follow-up time after the end of treatment, and the possible reduction of hot flash frequency or severity by the end of acupuncture therapy and at the last follow-up.

Results

In total, we identified 263 articles from the databases, and after removal of duplicates, 222 studies remained to be screened (Fig. 1). If the abstract described the study with sufficient clarity, articles were excluded using only the abstract, but when necessary, the full text of articles was read and assessed (n=24). Of the 222 papers we identified, 17 studies [40, 45–48, 56–67] fulfilled the criteria as not being reviews, case studies, notes, letters to the editor, correspondence, or conference abstracts. Seven of these 17 studies [41, 45, 47, 56–58,

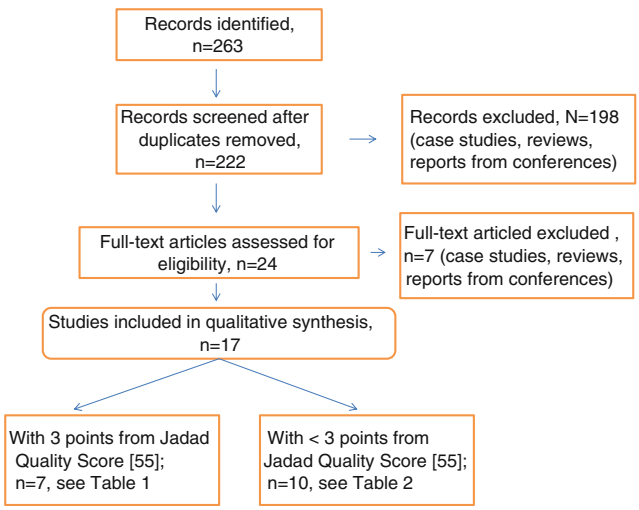

Fig. 1 Flowchart showing the results of database search on effects of acupuncture on hot flashes in patients with breast and prostate cancer, using PubMed, Scopus, and CinAhl (modified from the PRISMA statement; www.prisma-statement.org)

67] reached a Jadad quality score of 3 and were used for further analysis of duration and/or frequency of acupuncture treatment and follow-up time after the end of therapy (Table 1). Ten of the 17 studies [46, 48, 59–66] did not reach a Jadad quality score of 3 (Table 2); 1 was a randomized controlled trial (RCT) with insufficient description of randomization, 7 were open noncontrolled studies, 1 was a retrospective record study, and 1 was a qualitative study.

Randomized controlled studies reaching 3 points from the Jadad quality score

Seven controlled studies [41, 45, 47, 56–58, 67] reached 3 points according to the Jadad quality score, and these are summarized in Table 1. Follow-up time after the end of the acupuncture treatment ranged between 3 [57, 67] and 21 months [45]. All studies showed persisting effects at the time of the last follow-up after the end of the acupuncture treatment. Because the study of Bokmand and Flyger [67] only reported complaints from hot flashes and not frequency of flashes, it is regarded as not comparable with the six other studies reporting the frequency of flashes. It was therefore excluded from further analysis, although the authors found a significant reduction in the complaints in women with breast cancer.

Deng et al. found a 30 % reduction of hot flashes in 39 women with breast cancer, from 8.7 to 6.2/24 h after 6 weeks of acupuncture. The effect remained at 6.1 flashes/24 h at follow-up 5 months after the end of therapy (n=33) [56].

Hervik and Mjaland also reported a reduction of hot flashes in 30 women with breast cancer, from 9.5 flashes daytime to 4.7 after 10 weeks of acupuncture. Twelve weeks after the end of acupuncture, the frequency further decreased to 3.2 flashes daytime [57].

Nedstrand and coworkers reported that flashes decreased from 8.4 at baseline to 4.1/24 h after 3 months of therapy and further to 3.5/24 h 6 months after the end of therapy in 17 women with breast cancer who completed 12 weeks of acupuncture [41]. Frisk and coworkers reported that in 19 women with breast cancer who had 12 weeks of electroacupuncture, the number of flashes decreased from 9.6 to 4.3/24 h during therapy. In 14 women who were followed for 9 months after the end of therapy, the number of flashes remained at 4.9/24 h, and 7 women who were followed for 24 months during which they had no other therapy had 2.1 flashes/24 h [45]. In a study by Liljegren et al., a 30 % reduction of flashes was seen in 38 breast cancer patients who completed acupuncture, from 8.4 to 5.7 flashes/24 h at the end of treatment. The reduction was still observable in 36 women 3 months after the end of acupuncture, i.e., 5.6 flashes/24 h [58].

The only study in men with prostate cancer that reached 3 points according to the Jadad quality score was reported by Frisk et al. [47]. They randomized 31 men with prostate cancer between traditional acupuncture (TA) and electroacupuncture (EA), and 29 men completed the treatment. In the EA group, hot flashes diminished from 7.4 at baseline to 4.1/24 h at the end of therapy and 4.7 flashes/24 h 6 months after the end of therapy. At 9 months after the end of therapy, the number of hot flashes had slightly increased to 6.2 flashes/24 h, however, still a 17 % reduction compared to baseline. In the TA group, hot flashes decreased even more, from 6.4 at baseline to 3.4/24 h at the end of therapy, and 9 months after the end of therapy, there was still a 34 % reduction of hot flashes compared to baseline, i.e., 4.1/24 h.

Table 1 The seven included studies reaching Jadad quality score of 3 points concerning acupuncture treatment of breast cancer and/or prostate cancer patients for hot flashes occurring in breast cancer and/or prostate cancer patients

Source	Cancer disease/material	Design	Acupuncture	Follow-up time after the end of therapy
Nedstrand et al. 2005 [41]	Breast cancer/38 women	RCT	N=17 EA, N=14 AR; EA vs AR twice weekly for 2 weeks and once weekly for 10 weeks	6 months
Deng et al. 2007 [56]	Breast cancer/72 women	RCT	N=40 TA, N=30 CA; TA vs CA twice weekly for 4 weeks	5 months
Frisk et al. 2008 [45]	Breast cancer/45 women	RCT	N=19 EA, N=18 HT; EA vs HT twice weekly for 2 weeks and once weekly for 10 weeks	21 months
Frisk et al. 2009 [47]	Prostate cancer/31 men	RCT	N=14 EA, N=15 TA; EA vs TA twice weekly for 2 weeks and once weekly for 10 weeks	9 months
Hervik and Mjåland 2009 [57]	Breast cancer/59 women	RCT	N=30 TA, N=29 CA; TA vs CA twice a week for 5 weeks and once a week for 5 weeks	3 months
Liljegren et al. 2010 [58]	Breast cancer/84 women	RCT	N=38 TA, N=36 CA; TA vs CA twice a week for 5 weeks	3 months
Bokmand and Flyger 2012 [67]	Breast cancer/94 women	RCT	N=31 TA, N=29 CA, N=43 NT; TA vs CA vs NT once a week for 5 weeks	3 months

Here, we give the results for acupuncture treatment and summarize the type, duration and/or frequency of acupuncture treatment, and the follow-up time after the end of therapy

RCT randomized controlled study, *EA* electroacupuncture, *AR* applied relaxation, *TA* traditional acupuncture, *CA* control acupuncture/sham acupuncture, *NT* no treatment, *HT* hormone therapy

Table 2 The ten included studies reaching Jadad quality score of less than 3 points concerning acupuncture treatment for hot flashes occurring in breast cancer and/or prostate cancer patients

Source	Cancer disease/material	Design	Acupuncture	Follow-up time after the end of therapy
Hammar et al. 1999 [46]	Prostate cancer/7 men	Open pilot study	*N*=6 TA, twice weekly for 2 weeks and once weekly for 10 weeks	3 months
Tukmachi 2000 [59]	Breast cancer/22 women	Open single armed; TA combined with detoxifying healthy diet program, two sessions/week	*N*=22; 3–7 weeks, two sessions/week, 4–14 sessions in total	1 month
Filshie et al. 2005 [60]	Breast cancer/166 women/ 1 man; high risk for breast cancer/11 women; prostate cancer/11 men; other diseases/5 women	Retrospective	*N*=194 TA, 6 weeks plus self acupuncture or semipermanent studs, up to 6 years	Not applicable
Walker et al. 2007 [61]	Breast cancer/16 women	Quality study, retrospective	*N*=16 AA, duration not given	6 months
Harding et al. 2008 [62]	Prostate cancer/60 men	Open pilot study	*N*=60 AA, weekly for 10 weeks	None
Beer et al. 2010 [63]	Prostate cancer/25 men	Open single armed	*N*=22 EA, twice a week for 4 weeks and once a week for 6 weeks	None
de Valois 2010 [64]	Breast cancer/54 women	Open single armed	*N*=50 TA, once a week for 8 weeks	4.5 months
Walker et al. 2010 [65]	Breast cancer/50 women	RCT	*N*=25 TA; TA vs venlafaxine twice a week for 4 weeks and once a week for 8 weeks	12 months
Ashamalla et al. 2011 [48]	Prostate cancer/17 men	Intention to treat	*N*=14 EA, twice a week for 4 weeks	7 months
Otte et al. 2011 [66]	Breast cancer/10 women	Open single armed	*N*=8; three treatments within 2 weeks	1 month

Here, we give the results for acupuncture treatment and summarize the type, duration and/or frequency of acupuncture treatment, and the follow-up time after the end of therapy

RCT randomized controlled study, *TA* traditional acupuncture, *AA* auricular acupuncture, EA electroacupuncture

Nine months after the end of treatment, 11 men in the EA group and 13 men in the TA group were evaluated [47].

All the six studies reporting frequency of hot flashes and fulfilling the Jadad quality criteria found at least a 30 % reduction in frequency of hot flashes from baseline to the last follow-up, on average 5.4 months (range 3–9 months) after the end of acupuncture. This follow-up includes 91 % (*n*= 184) of the 203 women who completed acupuncture and the men reported by Frisk et al. [45].

The average reduction from baseline to the end of therapy (ranging between 5 and 12 weeks of treatment) in the six studies [41, 45, 47, 56–58] that measured frequency of hot flashes weighed in relation to the number of patients in the respective study showed a 43.2 % reduction of hot flashes. At the last follow-up (mean 5.8 months, range 3–9 months after the end of therapy), the weighted reduction from baseline in the 153 of 172 patients (89 %) who were followed up was sustained (45.6 %).

Randomized controlled studies reaching below 3 points from the Jadad quality score

Ten studies reached less than 3 points in the Jadad quality score, and these are summarized in Table 2 [46, 48, 59–66]. The follow-up time after the end of acupuncture treatment ranged between "no follow-up" [60, 62, 63] and 12 months [65]. All studies but one showed persisting effects in a number of patients at the time of the last follow-up after the end of the acupuncture treatment. One study showed no reduction 4 weeks after the end of acupuncture treatment, but in this study, there were only three acupuncture treatments over 2 weeks in ten women [66].

Discussion

After reviewing published studies on acupuncture as treatment of hot flashes in men with prostate cancer and women with breast cancer, we identified seven studies that met our predefined inclusion criteria. These studies described the randomization process and gave the reasons for drop outs sufficiently well. Six [41, 45, 47, 56–58] of the seven studies had measured the frequency of hot flashes. In these six studies with data from 153 patients, weighted in relation to the number of patients in the respective studies, we found a 43.2 % reduction of hot flashes at the end of therapy compared to baseline, a result that was sustained at the last follow-up, a mean of 6 months (range 3–9) after the end of therapy.

Out of the other ten studies [46, 48, 59–66] that did not reach 3 points according to the Jadad quality score [55], seven

studies reported results during a follow-up [46, 48, 59, 61, 64–66]. All results, except for one study [66], were in agreement with the results from the six studies that met our criteria; i.e., they showed a reduced frequency of hot flashes up to 12 months after the end of therapy.

It could only be speculated on why acupuncture treatment causes persistent decreases of hot flashes long after the end of therapy. In women as well as men with hot flashes, the flashes are usually long-standing, but the number and intensity gradually decrease. The reason for this decrease may be an adaptation of the thermoregulation to lower sex steroid concentrations. Acupuncture may be speculated to stimulate this adaptation in the thermoregulatory center by means of mechanisms such as the production of β-endorphins in the hypothalamus [37–40]. A systematic review of 34 original papers has shown with the use of functional magnetic resonance imaging that acupuncture activates and deactivates different areas in the brain. However, the results from the different studies were heterogeneous, and there was a broad network of regions of processing, not only somatosensory but also cognitive and affective processing that may have effects on different symptoms [68]. We can speculate that acupuncture affects the activity and responses of nerve stimulation in the thermoregulation center, and thereby, the patient may have better control of the vasomotor symptoms that can also persist after the end of therapy. This issue should be scientifically explored.

Our results are based on the few studies that fulfilled our criteria, which of course is a limitation. It is also true that the variables used differed between the studies, between number of flashes/day and number/24 h. Similarly, the acupuncture therapies given differed regarding to the number of needles, the choice of acupuncture points, the number of therapy sessions, etc. All these factors of course affect the conclusions, but the similarity in reduction of number of flashes/day among the included studies is a strength of the study.

Another weakness is the subjectively reported frequency of flashes, but previous studies have found a high correlation between subjectively reported and objectively measured (skin conductance) number of hot flashes [69].

It could be argued that the flashes may have been spontaneously relieved; however, hot flashes in women with breast cancer [7–10] and in men with prostate cancer [21] seem to be long-lasting by nature. According to Carpenter et al. [7], more than 50 % of women with breast cancer still report hot flashes 10 years after menopause, and 70 % of men with hot flashes still reported them 5 years after the start of castration treatment [21]. Furthermore, in a study of 876 women [70], neither placebo nor raloxifene decreased hot flashes over 30 months in the women who reported flashes. In men with prostate cancer and flashes, no patient out of 452 with androgen ablation was relieved from hot flashes during a median follow-up time of 18.5 months [20]. Based on these data, we do not believe that the decrease in flashes during and after acupuncture therapy is solely a spontaneous part of a physiological process.

In conclusion, we found a small number of published, randomized, prospective controlled trials with a follow-up period that dealt with the effects of acupuncture on the frequency of hot flashes in cancer patients. The reduction of hot flashes after acupuncture from our analyses indicated an almost 50 % reduction of the number of hot flashes per 24 h and sustained at the last follow-up after the end of acupuncture. Thus, the effects of acupuncture are at least similar to other nonhormonal therapies [22–27] but with very few side effects. Acupuncture can be considered as a treatment option for troublesome hot flashes in patients with breast or prostate cancer. According to a study based on semistructured interviews with breast cancer survivors, patients emphasized that acupuncture should be viewed as a natural alternative to medications (71). However, more rigorous studies of larger-sample size and longer follow-up are needed to confirm these results. We cannot yet explain the mechanisms of why the effects of acupuncture on hot flashes persist several months after the end of therapy.

Conflict of interest We declare no conflicts of interest. We have control of primary data regarding our own publications of original articles, but not primary data from other authors whose publications are included in this systematic review. We agree to allow the journal to review primary data regarding our own publications if requested.

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