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Using Traditional Acupuncture for Breast Cancer-Related Hot Flashes and Night Sweats

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Abstract

Objectives: Women taking tamoxifen experience hot flashes and night sweats (HF&NS); acupuncture may offer a nonpharmaceutical method of management. This study explored whether traditional acupuncture (TA) could reduce HF&NS frequency, improve physical and emotional well-being, and improve perceptions of HF&NS.
Design/settings/location: This was a single-arm observational study using before and after measurements, located in a National Health Service cancer treatment center in southern England.
Subjects: Fifty (50) participants with early breast cancer completed eight TA treatments. Eligible women were $\geq$35 years old, $\geq$6 months post active cancer treatment, taking tamoxifen $\geq$6 months, and self-reporting $\geq$4 HF&NS incidents/24 hours for $\geq$3 months.
Interventions: Participants received weekly individualized TA treatment using a core standardized protocol for treating HF&NS in natural menopause.
Outcome measures: Hot Flash Diaries recorded HF&NS frequency over 14-day periods; the Women's Health Questionnaire (WHQ) assessed physical and emotional well-being; the Hot Flashes and Night Sweats Questionnaire (HFNSQ) assessed HF&NS as a problem. Measurements taken at five points over 30 weeks included baseline, midtreatment, end of treatment (EOT), and 4 and 18 weeks after EOT.
Results for the primary outcome: Mean frequency reduced by 49.8% (95% confidence interval 40.5–56.5, $p < 0.0001$, $n = 48$) at EOT over baseline. Trends indicated longer-term effects at 4 and 18 weeks after EOT. At EOT, seven WHQ domains showed significant statistical and clinical improvements, including Anxiety/Fears, Memory/Concentration, Menstrual Problems, Sexual Behavior, Sleep Problems, Somatic Symptoms, and Vasomotor Symptoms. Perceptions of HF&NS as a problem reduced by 2.2 points (standard deviation = 2.15, $n = 48$, $t = 7.16$, $p < 0.0001$).
Conclusions: These results compare favorably with other studies using acupuncture to manage HF&NS, as well as research on nonhormonal pharmaceutical treatments. In addition to reduced HF&NS frequency, women enjoyed improved physical and emotional well-being, and few side-effects were reported. Further research is warranted into this approach, which offers breast cancer survivors choice in managing a chronic condition.

Introduction

Adjuvant hormonal treatments such as tamoxifen are an essential part of the treatment regimen for early breast cancer, used to prevent recurrence.[1] Hot flashes and night sweats (HF&NS) are the most frequently occurring side-effects,[2,3] with up to 80% of women taking tamoxifen reporting them as troublesome.[4] With nearly 46,000 new diagnoses of breast cancer annually in the United Kingdom and over 1 million worldwide,[5] the problem of HF&NS is widespread, with estimates of over 100,000 women in the UK experiencing these symptoms at any given time.

Hot flashes are experienced as subjective sensations of heat, whose intensity, duration, and associated symptoms vary according to the individual. A feature of natural menopause, the mechanism of HF&NS is not fully understood. Estrogen withdrawal or reduction, changes in gonadotrophin levels, and the action of catecholamines are implicated

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but no clear mechanisms have been identified.[6–8] Biological and psychologic factors such as cultural factors, environment, and stress may also act as triggers, adding layers of complexity to the pathophysiology.[6,9,10] Wide variations in the manifestation of HF&NS associated with natural menopause make it difficult to identify general population patterns: Prevalence ranges from 24% to 93% in the United States and northern Europe have been reported.[7] Frequency and severity vary from woman to woman, and may fluctuate within individuals as they progress through the menopause transition. The challenges of managing and measuring these variable and subjective symptoms are well documented.[6,11]

Breast cancer survivors experience HF&NS more frequently than women in natural menopause, and these cancer-related flashes may be more severe, distressing, and of greater duration.[12,13] Occurrences may be accompanied by a range of physical sensations, including sweating, flashing or redness, palpitations, dizziness, feelings of suffocation, nausea, tingling sensations in the hands, and chills before or after the flash. Accompanying emotional symptoms may include anxiety, feelings of panic, irritation, annoyance, frustration, and even suicidal feelings. Night sweats disturb sleep patterns, leading to fatigue and irritability.[6,11] HF&NS are disabling and socially embarrassing; their effect on quality of life is serious and often under-rated.[8]

In patients with breast cancer, HF&NS may occur regardless of the woman's natural menopause status: Young women may experience menopausal symptoms prematurely; women whose cancer diagnosis coincides with their menopause may have exacerbated symptoms; and postmenopausal women may experience an unwelcome return of symptoms. Tamoxifen users are often advised that their symptoms will diminish over time.[14,15] However, studies show that women suffer uncomfortable levels of HF&NS at an average of 3 years into the typical 5-year period of tamoxifen therapy,[4] and these symptoms may continue after completion of the therapy.[16] While not life-threatening, HF&NS may cause nonadherence to adjuvant hormonal therapy, potentially compromising long-term survival.[17]

Although hormone replacement therapy (HRT) is considered the most effective treatment for managing menopausal symptoms,[18] its long-term use is controversial, with fears that it may lead to increased risk of breast cancer, thromboembolism, and endometrial cancer[19,20] and to increased risk of recurrence in patients with breast cancer.[21] Women diagnosed with breast cancer are usually advised to stop taking HRT,[19] and many women stop voluntarily when they receive a breast cancer diagnosis.[22] In light of this, women and their medical professionals are eager to seek alternative means of addressing HF&NS.[19,23] A range of pharmacological preparations have been investigated, including antidepressants (especially the selective serotonin reuptake inhibitors (SSRIs) such as venlafaxine and paroxetine), antihypertensives such as clonidine, and the anticonvulsant gabapentin.[8,23]

Many women do not wish to experience further side-effects of pharmacological preparations, or they simply do not wish to take medication additional to their adjuvant hormonal therapy.[4] For these women, complementary and alternative medicine approaches may offer choices and may include vitamin E, plant-derived remedies such as soy and clover isoflavones, alfalfa, relaxation, cognitive behavioral treatment, exercise, and lifestyle changes.[4,8,24]

The treatment of menopausal symptoms is discussed in the literature of Chinese medicine,[24–28] and the results of a number of controlled studies suggest that acupuncture may be beneficial for managing HF&NS in natural menopause.[29–34] Therefore, acupuncture might also offer the possibility of managing HF&NS related to adjuvant hormonal treatment, and the aim of this study was to investigate this.

At the time of the design of this study, the literature on using acupuncture to manage HF&NS in women with breast cancer comprised mainly uncontrolled studies, including Tukmachi's[35,36] case series of 22 women treated with acupuncture, diet, and lifestyle; Cumins and Brunt's[37] trial of 26 patients (abstract only); and Towlerton's[38] study of 12 women treated with semipermanent indwelling studs. More recently, a number of studies using a range of methods have contributed to the literature in this area[39,40] including Porzio's[41] pilot study using acupuncture to treat 15 women taking tamoxifen and Filshie's[42] audit of long-term management of vasomotor symptoms using acupuncture and self-acupuncture. Randomized controlled trials include Nedstrand's[43] comparison of electro-acupuncture with relaxation ($n = 31$); Deng's[44] comparison of "true" and "sham" acupuncture ($n = 72$); Frisk's[45] long-term follow-up of a comparison of electro-acupuncture with HRT ($n = 45$), and Hervik's[46] comparison of traditional Chinese and sham acupuncture ($n = 59$). While there are many methodological problems with these studies, including their small size and the challenge of finding appropriate placebo controls, there is consensus that the use of acupuncture in this area warrants further research.[39,40]

This research investigates whether the traditional acupuncture (TA) protocols used to treat the symptoms of natural menopause could be applied to management of tamoxifen-related HF&NS. At the time of this study, tamoxifen was the criterion standard for preventing recurrence (although it has been augmented by the aromatase inhibitors [AIs] for postmenopausal women, and it remains the drug of choice for the premenopausal). The main research questions were as follows:

1. Can TA be used to manage HF&NS that are a side-effect of tamoxifen as an adjuvant treatment for early breast cancer?
2. Does TA affect the overall physical and emotional well-being of the recipient?

The purpose of the study was to systematically measure the effects in both the short and longer-terms, to obtain a first measure of this approach, and to test the suitability of the outcome measures. It was hypothesized that using TA could reduce the frequency of hot flashes by 50% at the end of eight treatments in one third of the study participants, and that participants would show overall improvements in physical and emotional well-being.

Materials and Methods

Study design

This study is a prospective single-arm observational study using before and after measurements. It accords with stages 0–2 of the Medical Research Council's guidelines for developing and evaluating complex interventions.[47,48] Participants attending for eight sessions of TA, delivered on a once-

weekly basis, were monitored for 30 weeks during which there were five measurement points: 2 weeks before treatment commenced (Baseline), after the fourth acupuncture treatment (Mid-tx), at the end of treatment (EOT), 4 weeks after EOT (Post tx 4), and 18 weeks after EOT (Post tx 18) (Fig. 1). This permitted measurement of any short and longer-term effects; however, our primary outcome measurement point was EOT.

The West Hertfordshire Hospitals NHS Trust Local Research Ethics Committee granted ethical approval, and the study was carried out in the cancer drop-in center associated with Mount Vernon Cancer Centre (MVCC) in Northwood, Middlesex, England. Participants were recruited over a 19-month period from March 2001 through September 2002.

Study outcomes

HF&NS frequency was the primary outcome measure, collected using paper-based hot flash diaries. Designed in-house, the diary took the form of a small booklet that

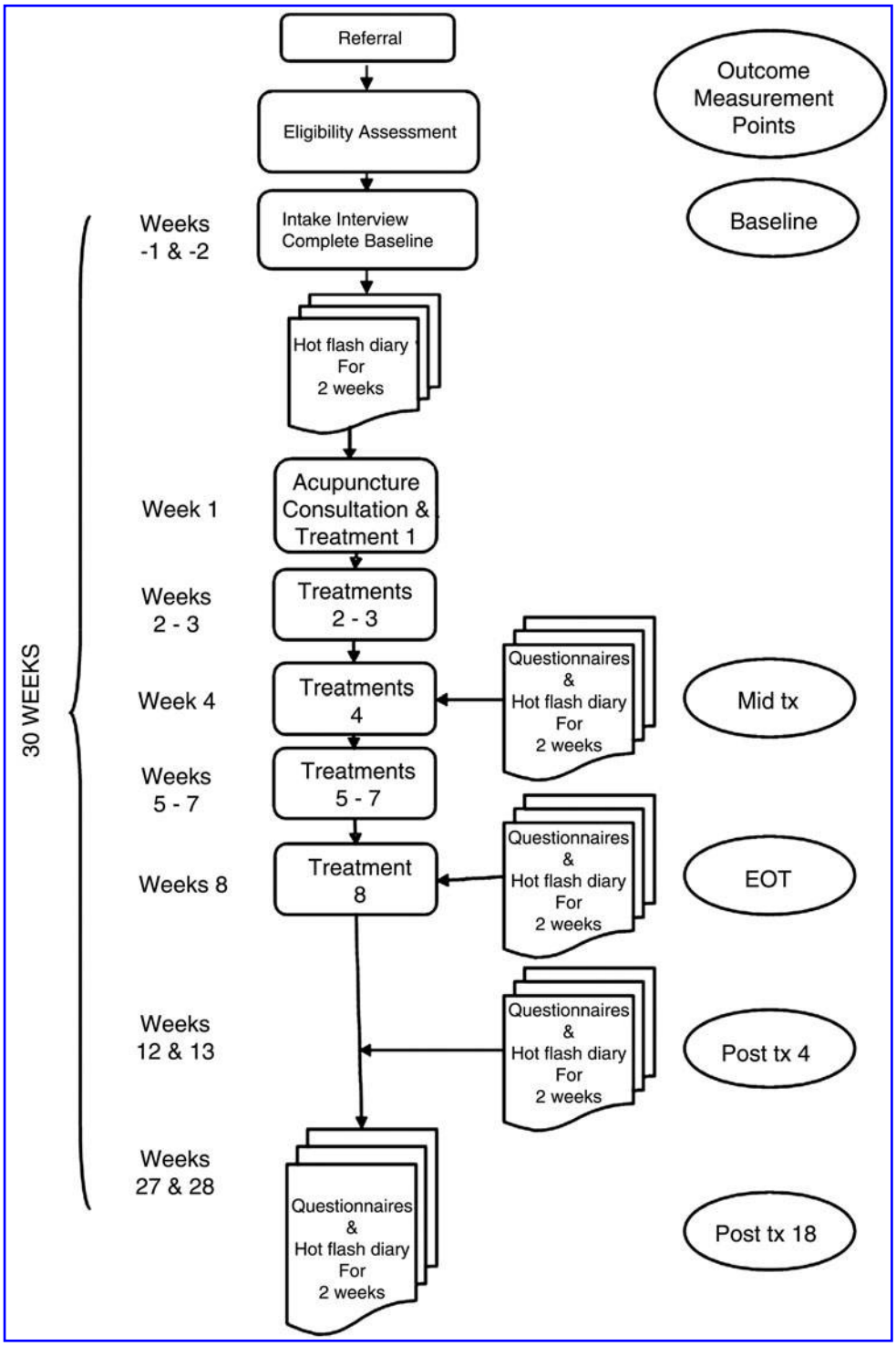

FIG. 1. Flow diagram showing measurement points. EOT, end of treatment.

allowed for 24-hour-a-day recording, for a period of 14 days per diary. Participants were instructed to record every HF&NS incident, ideally as it happened.

There is debate about whether objective measures provide more accurate data about HF&NS than subjective self-reports.[49] Objective measures that register changes in skin temperature, core body temperature, and sweat rates require use in a controlled, laboratory environment, usually for short periods of time.[50] This restricted monitoring time does not give information about "real-life" circumstances, or patterns of flashing over time. Self-reported measures are perceived by some to be inaccurate, with problems of incomplete self-reports at night as well as during waking hours,[49,51] and evidence of false-positive rates compared with objective measures.[12] However, researchers at the Mayo Clinic, after conducting several clinical studies into HF&NS, argue that daily diaries exhibit consistency and reliability, with few missing data.[52]

Physical and emotional well-being were measured using two validated questionnaires: the Women's Health Questionnaire (WHQ) and the Hot Flashes and Night Sweats Questionnaire (HFNSQ).[9,53]

The WHQ is a self-administered health-related quality-of-life measure, designed to assess physical and emotional well-being in women from the ages of 45–65 undergoing the natural menopausal transition.[54] Its 36 statements are divided into the nine domains or subscales shown in Table 1. Respondents indicate their agreement with the statements using a 4-point Likert scale. Responses are calculated as described in the *WHQ Women's Health Questionnaire User Guide*.[55] The result is a 10-point scale from 0.00 to 1.00, with lower scores indicating better quality of life, and higher scores signifying more serious symptoms. Test–retest is reliable across a 2-week time interval. The WHQ is sensitive to change, and a meaningful clinically significant change on the subscales is a difference of 0.10 to 0.20.[54]

The HFNSQ is designed to measure the subjective responses of women to their HF&NS.[4,9] From it, the Problem Rating Score (PRS) is derived, using the mean of the sum of three 10-point scales (problem factors) on which women rate how much they regard their HF&NS as a problem, how much distress they cause, and how much they interfere with daily life. The PRS is a more reliable indicator than hot flash frequency of how bothersome women find their HF&NS, and a change of 2 points is clinically significant (M. Hunter, personal communication, January 8, 2010). Test–retest reliability is high across a 2–3-week interval.[9]

The frequency of measurements is illustrated in Figure 1. Three (3) other semistructured questionnaires, designed to elicit written feedback from participants about their experience of having acupuncture and participating in the study, were administered at EOT, Post tx 4, and Post tx 18.

Study population/patient eligibility

The study was open to women taking tamoxifen as adjuvant treatment for early breast cancer treated at MVCC. Eligibility criteria included patients aged 35 years or older with breast cancer; 6 or more months post active cancer treatment (surgery, chemotherapy, radiotherapy); without relapse or metastatic disease; taking tamoxifen for 6 or more months; experiencing HF&NS for 3 or more months and self-reporting an average of 4 or more HF&NS per 24-hour period; and able to speak, read, and understand English. Concomitant preparations for relieving HF&NS, whether prescription or over-the-counter, were allowed provided the participant had taken them for at least 3 months before joining the study and intended to continue taking them for the duration of their involvement. Women with advanced disease were excluded.

Referrals were through the oncology consultant, breast care nurse, or self-referral via the drop-in center. The research acupuncturist (BdV) screened referrals by telephone, and sent eligible women a participant information sheet explaining the study. Prospective participants attended an intake interview and signed a consent form after the intervention and the study were clarified for them. The research acupuncturist administered the baseline questionnaires (including baseline medical and sociodemographic details), set up future appointments, and gave the participant a Hot Flash Diary to keep until the first treatment 2 weeks later.

Table 1. Women's Health Questionnaire (WHQ) Results for the Primary Measure, End of Treatment (EOT) Over Baseline

	Baseline			*EOT*			*Paired differences (baseline—EOT)*					*Paired samples* t*-tests*		
										95% CI				
WHQ scale	*Mean*	*SD*	N =	*Mean*	*SD*	N =	*Mean*	*SD*	N =	*LL*	*UL*	t =	df	p = *
ANX	0.26	(0.27)	53	0.09	(0.13)	47	0.17	(0.25)	47	0.09	0.24	4.50	46	**.0001**
ATT	0.57	(0.31)	52	0.48	(0.33)	48	0.09	(0.37)	47	-0.02	0.19	1.59	46	.12
DEP	0.21	(0.25)	53	0.16	(0.23)	47	0.06	(0.20)	47	0.00	0.12	2.07	46	**.044**
MEM	0.59	(0.35)	52	0.31	(0.33)	48	0.24	(0.35)	47	0.14	0.35	4.69	46	**.0001**
MEN	0.33	(0.24)	53	0.17	(0.20)	48	0.15	(0.18)	48	0.09	0.21	5.69	47	**.0001**
SEX	0.46	(0.32)	44	0.34	(0.33)	41	0.14	(0.31)	38	0.04	0.24	2.82	37	**.008**
SLE	0.65	(0.32)	53	0.40	(0.31)	47	0.25	(0.34)	47	0.15	0.35	5.05	46	**.0001**
SOM	0.49	(0.21)	53	0.34	(0.21)	48	0.15	(0.22)	48	0.09	0.21	4.88	47	**.0001**
VAS	0.99	(0.07)	53	0.83	(0.26)	48	0.17	(0.26)	48	0.09	0.24	4.45	47	**.0001**

*Significance (2-tailed).

SD, standard deviation; CI, confidence interval; LL, lower limit; UL, upper limit; ANX, Anxiety/fears; ATT, Attractiveness; DEP, Depressed Mood; MEM, Memory/Concentration; MEN, Menstrual Symptoms; SEX, Sexual Behavior; SLE, Sleep Problems; SOM, Somatic Symptoms; VAS, Vasomotor Symptoms.

Acupuncture treatment

The acupuncturist practiced "integrated" acupuncture, a style used extensively in the UK, which draws on both Eight-principles and Five Elements theoretical frameworks of TA.[56] She developed a protocol based primarily on Eight-principles theories for treating natural menopause symptoms because there was scant information concerning tamoxifen-related HF&NS in the literature. The protocol assumed Kidney *Yin* Deficiency as the root of the hot flashing,[25,26,57] and it included strategies for managing night sweats,[26,28,58] and to clear Heat and resolve Damp, which contemporary colleagues observed to be associated with tamoxifen (G. Maciocia, personal communication 26 October 26, 1999 and T. Alræk, personal communication, January 22, 2001). Drawing on the Five Elements theoretical framework, the first treatment was an Aggressive Energy (AE) Drain. In some schools of Five Elements practice, this is the first treatment administered, and is especially indicated for patients who have had serious or life-threatening disease, intensive drug therapies, or intense emotions over a period of time, all of which may apply to women who have been diagnosed with and treated for breast cancer.[57,59]

There is often an expectation in research that acupuncture protocols will use a fixed or limited set of points; however, we felt it was important to capture the flexibility of practice that is characteristic of TA in a usual clinical setting. Thus, although there was a core protocol at the heart of this approach, there was also the option to use points for the individual participant. The core protocol comprised two steps:

- Treatment 1: AE Drain
- Treatments 2 - 8: Treat HF&NS

Treatments 2–8 were supplemented with acupuncture points selected for the individual according to traditional diagnosis.

Table 2 shows the treatment principles, points and procedures used in the core protocol.

The first treatment, lasting 2 hours, comprised taking a full case history including pulse and tongue diagnosis, after which the AE Drain was administered. The acupuncturist analyzed the case history to determine the individualized points for the patient, and administered these at subsequent treatments in addition to the core protocol. Individualized points could be changed as the participant progressed through treatment. In addition, and according to usual TA practice, guidance for improving health through practices for daily living was provided. Advice was given as appropriate for the individual participant, and addressed a range of aspects including eating habits, rest, exercise, and managing stress.[58,59] Succeeding treatments lasted 1 hour, and there was no attempt to limit the therapeutic relationship (establishing good rapport with the patient is considered an essential part of Five Elements acupuncture).[59]

Statistical analysis

Quantitative data were entered into SPSS version 13. Using data recorded over 14 days in the Hot Flash Diary, the mean and the median number of HF&NS per day was calculated for each participant at each measurement point. Missing data were imputed where at least 50% of the data had been collected and the data appeared to be missing at random (de Valois B 2006, unpublished PhD thesis).[60] The individual participant means were not normally distributed,

Table 2. Treatment Principles, Points, and Procedures for Core Protocol

Treatment 1: Aggressive energy drain

Point reference	*Methods*
Bl 13 *Feishu* Bl 14 *Jueyinshu* Bl 15 *Xinshu* Bl 18 *Ganshu* Bl 20 *Pishu* Bl 23 *Shenshu* Plus 3 check needles	Insert needles bilaterally using superficial insertion. Do not obtain *de qi.* Insert 3 check needles into the muscle nearby, one for each "group" of needles. Observe for signs of erythema around the needles. Leave all needles for 20 minutes, or until erythema disappears.

Treatments 2–8: Treat hot flashes and night sweats

Treatment principle	*Points*	*Methods*
Nourish Kidney *Yin*	Lu 7 *Lieque* Kid 6 *Zhaohai* Ren 4 *Guanyuan* Sp 6 *Sanyinjiao*	Insert all needles using even technique, and obtain *de qi*. All points are used unilaterally. Open the *Ren Mai* (Directing Vessel): Insert needle into Lu 7 first, on the side not affected by breast cancer, then Kid 6 on the opposite side. Retain for a total of 20 minutes.
Stop night sweats	He 6 *Yanglao* Kid 7 *Fuliu*	Once Lu 7 and Kid 6 are inserted, needle the remaining points.
Clear Heat	LI 11 *Quchi*	Do not manipulate the needles.
Resolve Damp	Sp 6 *Sanyinjiao* Lu 7 *Lieque* LI 11 *Quchi*	After the 20 minutes, remove all needles. Kid 6 is penultimate needle removed, and Lu 7 the last.

showing a positive skew. Thus, for descriptive purposes the median data were used, and the mean and median were then calculated for all participants. Log transformation of the means for each participant produced a normal distribution, allowing parametric *t* tests to be used for comparison with baseline scores.[61,62] Data from the WHQ and HFNSQ were analyzed using Student's *t*-tests.

Results

The primary measure was the change in HF&NS frequency at EOT over baseline. We were also interested in short- and long-term effects, and in this article we present HF&NS data from all measurement points. WHQ and HFNSQ data at EOT are also presented, and the data from the remaining measurement points are detailed elsewhere (de Valois B 2006, unpublished PhD thesis).

Study participant characteristics

Of the 54 women recruited, 50 completed the course of eight TA treatments. Two (2) did not proceed beyond the intake interview (1 stopped taking tamoxifen, the other chose not to continue beyond the interview); 1 withdrew after three treatments, citing transportation problems, and 1 after six treatments, giving no reason. Fifty-two (52) participants completed baseline questionnaires, 48 completed Mid-tx and EOT measurements, and 47 completed Post tx 4 and Post tx 18 follow-up questionnaires. The mean age at baseline was 54.3 years (standard deviation [SD] = 7.9, range 37–68). The mean time since breast cancer diagnosis was 1.9 years (SD = 0.9, range 1.0 – 4.7), and since starting tamoxifen the mean time was 1.7 years (SD = 0.9, range 0.5 – 4.6). Table 3 displays the demographic and clinical data for the 52 women at baseline.

Table 3. Demographic and Clinical Characteristics at Baseline

	n = *52 (%)*
Demographic characteristics	
Marital status	
Married (first marriage)	34 (65)
Remarried	5 (10)
Living with partner	5 (10)
Divorced	5 (10)
Widowed	3 (6)
Educational qualifications	
Less than compulsory school education	5 (10)
Compulsory school education (e.g., school certificate, GCSEs)	25 (48)
Post compulsory school education below university level	16 (30)
University level	4 (8)
Postgraduate level	2 (4)
Current employment status	
Retired	17 (33)
Not working at present	5 (10)
Working part time	22 (42)
Working full time	8 (15)
Ethnic background	
White British	48 (92)
White other	2 (4)
Missing data	2 (4)
Clinical characteristics	
Cancer treatment history	
Breast surgery	51 (98)
Radiotherapy	46 (89)
Chemotherapy	26 (50)
Time taking tamoxifen	
6–12 months	10 (19)
1–2 years	28 (54)
3–4 years	13 (25)
>4 years	1 (2)
Menopause status[a]	
Perimenopause (last period within previous year)	6 (12)
Menopause (no period within previous 1–5 years)	19 (36)
Postmenopause (no period in over 5 years)	24 (46)
Missing data	3 (6)
Participants using preparations to manage HF&NS	
Pharmaceutical (including clonidine, SSRIs)	6 (12)
Over the counter (including evening primrose oil, black cohosh, red clover, Menosan)	25 (48)
Participants with a history of:	
Taking hormone replacement therapy	34 (65)
Hysterectomy	13 (25)

[a]Based on the stages of reproductive aging workshop (STRAW) staging system (Soules et al., 2001).

GCSEs, general certificate of secondary education; HF&NS, hot flashes and night sweats; SSRIs, selective serotonin reuptake inhibitors; HRT, hormone replacement therapy.

Safety. Acupuncture was well tolerated, with few adverse effects reported or observed. Mild discomfort on needling, occasional bleeding or mild bruising at needle sites, and tiredness after treatment especially in the early stages were reported (de Valois B 2006, unpublished PhD thesis).[63] These effects are consistent with the findings of a large acupuncture safety study.[64]

Hot flash and night sweat frequency. Table 4 shows the mean, medians, and ranges of HF&NS per day over the 14 days at baseline and EOT for the 48 participants returning diaries at EOT.

As discussed above, using log transformations to normalize the data enabled the percentage change in HF&NS frequency to be calculated. Table 5 shows the results for all four measurement periods compared with baseline frequencies. Data for the primary endpoint, the change at EOT over baseline, are highlighted.

The hypothesis for this study was a reduction in HF&NS frequency of 50% in 33.3% of participants at EOT. To test this, we ranked the log transformed data per participant in order of percentage change. This showed that 45.8% (22) participants reported a reduction of $\geq$50%, 39.6% (20) reported a reduction of <50%, and 12.5% (6) showed no improvement.

WHQ measurements at EOT. Table 1 shows the results for the nine domains of the WHQ at baseline and EOT, and the paired differences show the changes at EOT over baseline. Paired samples *t* tests indicate that at EOT there was a significant change for all WHQ domains except Attractiveness.

Table 4. Hot Flashes and Night Sweats Frequency Per Day Over the 14-Day Measurement Periods

	Baseline (n = *48*)	*EOT* (n = *48*)
Mean (standard deviation)	10.7 (6.5)	6.5 (5.3)
95% Confidence interval	8.9–12.6	4.9–8.0
Median (interquartile range)	9.0 (7.3)	4.8 (5.4)
Minimum mean score	3.5	1.0
Maximum mean score	35.0	21.0
Range	31.5	20.0

EOT, end of treatment.

Problem rating score (PRS). Figure 2 shows the change in the PRS. The mean difference in the score at EOT over baseline was 2.22 (SD = 2.15, $n = 48$, $t = 7.16$, $p < 0.0001$).

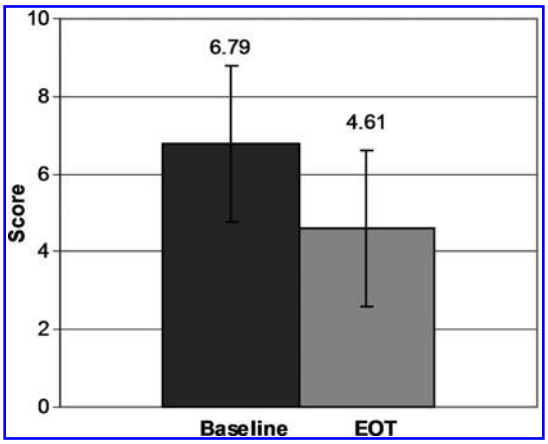

FIG. 2. Changes in the Problem Rating Score at end of treatment (EOT) over baseline.

Discussion

The aims of this single-arm observational study were to explore whether TA could be used to manage tamoxifen-related HF&NS in women with early breast cancer, and to identify whether TA treatment could affect physical and emotional well-being. The data provide promising results, with a mean reduction in frequency of HF&NS of nearly half at the end of eight treatments and with 85.4% of participants experiencing some degree of reduction. Data also indicate a longer-term benefit, with HF&NS frequency maintaining a reduction of over 41% at 4 and 18 weeks after EOT. Short-term data recorded in the 2-week period after the fourth treatment show that there is already a reduction of just over 40%, while the data at EOT demonstrated that continued treatment brings a further 10% improvement.

The WHQ data indicate that participants experienced improvements in a range of aspects of emotional and physical well-being. Statistically, all of the WHQ subscales except Attractiveness showed significant improvements at EOT. Clinically meaningful improvements were observed with Sleep Problems, Memory/Concentration, Vasomotor Symptoms and Anxiety/Fears, Somatic Symptoms and Menstrual Symptoms, and Sexual Behavior. The 2.2-point reduction in the Problem Rating Score indicates that participants found their HF&NS less bothersome, with a change of 2 points on the scale being clinically significant.

Table 5. Reductions in Hot Flashes and Night Sweats Frequency, Using Log Transformed Data

Measurement point	n =	*Mean % reduction*	*95% CI Lower*	*95% CI Upper*	t =	p < *
lnBaseline - lnMid tx	48	40.8%	31.0%	50.0%	6.9	0.0001
lnBaseline – lnEOT	**48**	**49.8%**	**40.5%**	**56.5%**	**8.7**	**0.0001**
lnBaseline – lnPost tx 4	47	41.2%	31.0%	49.5%	6.8	0.0001
lnBaseline – lnPost tx 18	47	41.8%	29.1%	49.5%	6.0	0.0001

*Significance (two-tailed).
"ln" as a prefix indicates the log transformed value. CI, confidence interval; Mid-tx, fourth acupuncture treatment; Post tx 4, 4 weeks after end of treatment (EOT); Post tx 18, 18 weeks after EOT.
Bolded data indicate the primary endpoint, the change at EOT over baseline.

This study has a number of strengths. It is the first study to our knowledge to systematically measure the application of a TA protocol based on the Chinese medicine theories of natural menopause to pharmaceutically induced menopausal symptoms. Although a core standardized protocol was used, treatments were tailored to the individual participants' presenting symptoms and constitution. Allowing this individualization, which accords with usual clinical practice,[65] was useful to address the variety of syndromes presented by the participants. As discussed previously, the core protocol was designed to address Kidney *Yin* Deficiency, widely regarded as the predominant syndrome underlying menopausal hot flashes.[66] Clinically, a range of syndromes were encountered, with *Yang* Deficiency (Kidney and/or Spleen) presenting frequently, along with forms of *Qi* Deficiency, *Qi* Stagnation, Blood Deficiency, and *Shen* Disturbance. This clinical experience suggests that in designing future trials, a wide range of syndromes should be accommodated in the study design. The incidence of *Yang* Deficiency also indicates that applying moxibustion (the use of heat generated by the herb *Artemesia vulgaris* to stimulate acupuncture points), often contraindicated in the treatment of hot flashes, is an appropriate treatment strategy for some individuals.[67]

In this study, the wider effects of acupuncture treatment on physical and emotional well-being were measured, extending its focus beyond changes in the main complaint only. This is important, because acupuncturists and their patients often report improvements in other symptoms and overall well-being.[68–70] Additionally, trends suggest long-term improvement.

This study also shows that it is possible to recruit women who have had invasive treatments for breast cancer to acupuncture studies.[63] Compliance with acupuncture treatment suggests they found this intervention acceptable, and most completed the course of treatments (de Valois B 2006, unpublished PhD thesis).[63] Keeping repeated daily diaries of HF&NS occurrence, as well as completing other questionnaires, is possible and allows for good data collection.[71] The diaries were also useful tools for self-management: Some participants found that diary-keeping gave them a feeling of control, enabling

them to identify hot flash patterns and triggers, and to develop their own strategies for dealing with them.

The data also contribute to what is known about HF&NS experienced by women taking tamoxifen. Medical advice is that symptoms will diminish over time; however, over half of the participants had been taking tamoxifen for 1–2 years, and a quarter of the participants on this study were still experiencing uncomfortable levels of HF&NS during the last 3 years of the 5-year period of their adjuvant hormonal treatment (Table 3). This confirms that for these women, HF&NS are a chronic problem, requiring long-term management. Data collected in the diaries provides further insight into the nature of tamoxifen-related HF&NS. As Table 4 shows, hot flash frequency varied widely across this sample, ranging from an average of 3.5 to 35 incidents per day in the 2-week baseline measurement. This also suggests that women with relatively low numbers of flashes find them sufficiently troublesome to seek remedies.

This was an early-stage observational study to evaluate acupuncture as a complex intervention, to assess the feasibility of this approach for a future randomized controlled trial.[47] It has a number of limitations. Its single-arm design does not control for placebo effects. The challenges of designing appropriate placebo controls for acupuncture studies are well documented: blinding of acupuncturists and participants is problematic, as is finding an inert intervention with which to compare the acupuncture. It is becoming widely recognized that the variety of "sham" acupuncture designs typically used in acupuncture research (from specially designed nonpenetrating needles to using non-acupuncture points) generate physiologic effects, and are therefore not truly inert.[72–75] Rigid adherence to double-blinding and sham controls risks distorting acupuncture into an artificial construct that no longer resembles "real-world" acupuncture, thereby providing research results that have little clinical relevance.[76,77] Complementary medicine researchers advocate pragmatic randomized controlled trials (RCTs), which compare acupuncture treatment with the best usual treatment for a condition, as an effective way of retaining the authenticity of practice and the complexity of the therapeutic intervention, as well as maintaining scientific rigor.[78–80] While pragmatic studies may be a way forward for acupuncture studies, it remains a tendency for funding organizations, ethics committees, and other evaluators of research to insist on blinding and/or sham controls in acupuncture research design.[81] Influencing these views remains a major challenge to acupuncture researchers.

Similarly, in this study there was no attempt to limit the therapeutic relationship, also classically regarded part of the placebo effect. The powerful effect of a strong practitioner–patient relationship on symptom improvement has been demonstrated with patients with irritable bowel syndrome,[82] and is likely to be a component in the improvements in this study. However, establishing rapport is an integral part of many acupuncture styles practiced in the West. This study aimed to assess normal acupuncture practice as a complex intervention,[76,78] and it was not the intention to investigate individual components of acupuncture treatment.

This study was conducted in a single acupuncture clinic, which served a mainly white British patient group. They were treated by a single acupuncturist (BdV) who was also the investigator. Thus, generalizability of the study results to the wider population of women with early breast cancer may be limited.

Furthermore, a number of study participants did not adhere to the study protocol of weekly acupuncture, sometimes leaving gaps between treatments and extending beyond the 8-week period. Ensuring regular weekly treatment may have improved the response; however, although future studies should be designed so participants clearly understand the need for regular treatment to optimize the effects, some flexibility should be factored in to allow for life events that prevent such regular treatment, such as bereavements, illness, surgery, and holidays—occurrences that interrupted many participants' progress through treatment.

Establishing the optimum dose is also an outstanding issue. The literature does not indicate optimum treatment frequency or duration, and future research could usefully investigate increased frequency, as well as extending the duration of treatment to determine whether the HF&NS could be further reduced.[83] At the time of this study, tamoxifen was the criterion standard treatment for preventing recurrence of breast cancer; research into using acupuncture to manage the HF&NS associated with the AIs that are increasingly prescribed for postmenopausal women could also be conducted.

Despite these limitations, the results of this exploratory study showing a mean reduction of 49.8% in HF&NS frequency compares favorably with other acupuncture studies. A review of the available evidence for using acupuncture to manage menopausal symptoms concludes that the majority of women in the studies had a reduction of >50% with continued effects of up to 6 months.[39] Although there are problems with the design and size of these studies, all contribute to the growing body of exploratory evidence for this approach to manage HF&NS.

The results of this study compare well with research conducted into nonhormonal treatment options for HF&NS in women with breast cancer. Of the SSRIs, a RCT of venlafaxine over placebo reduced flashes by a median of 61% compared with 27% with placebo;[84] a RCT of paroxetine reduced flashes by 65% compared with a 38% reduction with placebo,[85] and fluoxetine reduced flashes by 50% compared with a 36% reduction in the placebo group.[86] However, side-effects of these drugs included mouth dryness, decreased appetite, nausea and constipation, and many women are reluctant to take antidepressants to manage the side-effects of adjuvant hormonal treatments.[4] There are also concerns that SSRIs may lower the effectiveness of tamoxifen.[87] A RCT of oral clonidine showed a 38% reduction in hot flashes compared with 24% placebo after 8 weeks of treatment,[88] while a study of transdermal clonidine showed only moderate (20%) reduction.[89] In both studies, participants reported side-effects including difficulty sleeping, mouth dryness, constipation, and drowsiness. In our study, 12% of participants were using pharmaceutical products to manage tamoxifen side-effects, and were still experiencing sufficient discomfort to seek out additional means to manage their HF&NS.

Conclusions

The data from this exploratory single-arm observational study suggest that TA may offer an option for managing the HF&NS associated with adjuvant hormonal treatment in

women with early breast cancer. TA has few side-effects, and appears to improve physical and emotional well-being. Confirmation of these results, using a RCT, could have important implications for breast cancer survivors to manage their menopausal side-effects with means that are not pharmaceutical, thus offering them greater choice and control in managing their long-term quality of life. Further research is warranted, both in determining optimum dose, and with larger-scale studies designed with randomization and controls appropriate to evaluating a complex intervention.

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