Acupuncture and self acupuncture for long term treatment of vasomotor symptoms in cancer patients – audit and treatment algorithm

Jacqueline Filshie, Tara Bolton, Doreen Browne, Sue Ashley

Abstract

Introduction  Since hormone replacement therapy given for long periods is now recognised to produce serious side effects, patients with troublesome vasomotor symptoms are increasingly using non-hormonal treatment including acupuncture. Several randomised controlled trials have shown that acupuncture reduces menopausal symptoms in patients experiencing the normal climacteric. It may have this effect by raising serotonin levels which alter the temperature set point in the hypothalamus. Vasomotor symptoms can be extreme in breast cancer patients and patients with prostate cancer who are undergoing anticancer therapy. The safety of some herbal medicines and phytoestrogens has been questioned, as they could potentially interfere adversely with the bioavailability of tumouricidal drugs. A previous study reports short term benefit from acupuncture, and the aim of this report is to describe our approach to long term treatment.

Acupuncture approach  After piloting several approaches, six weekly treatments were given initially at LI4, TE5, LR3 and SP6 and two upper sternal points, but avoiding any limb with existing lymphoedema or prone to developing it. If there were no contraindications, patients were given clear instructions on how to perform self acupuncture using either semi-permanent needles or conventional needling at SP6, weekly for up to six years, for long term maintenance.

Audit methods and results  A retrospective audit of electronic records was carried out by a doctor not involved in treatment. A total of 194 patients were treated, predominantly with breast and prostate cancer. One hundred and eighty two patients were female. The number of pre-treatment hot flushes per day was estimated by the patient: in the 159 cases providing adequate records, the mean was 16 flushes per day. Following treatment, 114 (79%) gained a 50% or greater reduction in hot flushes and 30 (21%) a less than 50% reduction. Treatment was abandoned in those who responded poorly or not at all. The duration of treatment varied from one month to over six years with a mean duration of nine months. Seventeen patients (9%) experienced minor side effects over the six year period, mostly minor rashes; one patient described leg swelling but this was likely to be due to a concurrent fracture.

Conclusion  Acupuncture including self acupuncture is associated with long term relief of vasomotor symptoms in cancer patients. Treatment is safe and costs appear to be low. An algorithm is presented to guide clinical use. We recommend the use of self acupuncture with needles at SP6 in preference to semi-permanent needles in the first instance, but poor responders use indwelling studs if they fail to respond adequately to self acupuncture with regular needles. Point location may be of less importance than the overall ‘dose’, and an appropriate minimum dose may be required to initiate the effect.

Keywords

Self acupuncture, menopausal vasomotor symptoms, breast cancer, prostate cancer, audit.
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and ischaemic heart disease. However, recent studies found an increased risk of breast cancer, heart attacks and strokes in patients on HRT. In view of this, patients increasingly access alternative, non-hormonal treatment for menopausal symptoms. A number of reviews of the effectiveness of complementary therapies for hot flushes have been published.

While these symptoms may occur in natural menopause, they also commonly occur in patients with breast cancer, when chemotherapy or hormone manipulation cause premature menopause. The symptoms can be noticeably worse than hot flushes due to the normal menopause and can cause considerable distress, disrupting sleep and adversely affecting the quality of life. In these patients, HRT is potentially dangerous due to the administration of endogenous oestrogen. The treatments which cause the most symptoms include anti-oestrogens such as tamoxifen, aromatase inhibitors such as anastrozole and drugs which act on the pituitary to inhibit the hormonal axis – the gonadotrophin releasing hormone (GnRH) analogues such as goserelin (see Table 1). Men with prostate cancer undergoing androgen ablation treatment such as treatment with GnRH analogues may also experience severe hot flushes, which have been reported to be the most distressing symptom of GnRH analogue treatment.

Though tamoxifen has proven benefit in reducing the recurrence rates and mortality from breast cancer, it causes vasomotor symptoms in up to 62% of patients, which are disabling in 22% and can even result in 10% of patients stopping treatment.

### Table 1 Commonly used anti-oestrogen and anti-androgen drugs

<table>
<thead>
<tr>
<th>Aromatase inhibitors</th>
<th>Anti-oestrogen</th>
<th>Tamoxifen</th>
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<tbody>
<tr>
<td>Anastrozole</td>
<td>Letrozole</td>
<td>Exemestane</td>
</tr>
<tr>
<td>Leuprolin</td>
<td>Goserelin</td>
<td>Bicalutamide</td>
</tr>
<tr>
<td>Cyproterone</td>
<td>Flutamide</td>
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</table>

Much psychological distress is caused by a life changing diagnosis like breast cancer; patients often need mutilating surgery that may result in a poor body image, decreased libido etc; and in addition they may have side effects of medication. The symptoms in both men and women can lead to sleep disturbances, fatigue, and irritability and can persist for longer than five years.

Other conventional approaches to treatment of natural climacteric symptoms include medroxyprogesterone, megestrol acetate, clomidine, paroxetine, venlafaxine, and gabapentin. The safety of progestogens in cancer patients has been put into question. In addition, numerous herbal products, including phytoestrogens and soy, have been tested with varying results. The safety of phytoestrogens remains unclear to date, and the use of black cohosh is potentially unsafe: in a recent animal study, black cohosh was given to transgenic mice which had developed breast tumours and was associated with deterioration of metastatic disease.

Herbal medicines also carry the potential risk of herb-drug interactions, and for example they may interfere with the bioavailability of some cytotoxic drugs. Red clover contains isoflavones, which should be avoided in patients with hormone sensitive tumours, and also inhibits cytochrome P450 thus potentially increasing the bioavailability of cytotoxic drugs and other drugs metabolised by this pathway. Conversely St John's wort, which induces cytochrome P450, may reduce the bioavailability of some cytotoxic drugs, as has been shown in the case of imatinib, and irinotecan. The current advice to breast cancer patients at the Royal Marsden Hospital is to avoid the following products: anise, black cohosh, blue cohosh, dong quai, fennel (oil), flax or flax seed, ginseng (American, Panax, Siberian), isoflavones or phytoestrogens, liquorice, milk thistle, raspberry leaf, red clover, soy or soya (in quantities greater than a normal diet contains), wild thyme, and wild yam.

An alternative safe, non-drug and non-herbal, treatment for menopausal symptoms is needed for patients whose symptoms are severe, particularly if severe enough for them to consider giving up anticancer treatment. Acupuncture has been used for the natural climacteric, for patients having tamoxifen treatment for breast cancer, and for patients with prostate cancer. One of three RCTs for hot flushes in the natural menopause by Wyon and colleagues compared two forms of acupuncture – deep needling with needling sensation (de qi) and electroacupuncture (EA) to four points, compared

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www.medical-acupuncture.co.uk/aimintro.htm
with superficial acupuncture. Both doses, deep and superficial, reduced the number of flushes by 50% or more and improved the quality of life; relief was sustained for three months. At three month follow up assessment, the superficial treatment tended to experience more flushes than the EA group. Interestingly the urinary excretion of calcitonin gene related peptide (CGRP), a powerful vasodilator that is released during a hot flush, also decreased over the treatment period.

A second RCT by Sandberg et al 2002 in patients experiencing symptoms from the natural climacteric also compared EA with superficial treatment. Again, both arms demonstrated statistically significant improvement in symptoms, with improved mood at six months in the EA group. More recently, EA was compared with superficial acupuncture and oral estradiol for vasomotor symptoms in postmenopausal women: all treatments were associated with a statistically significantly reduction of hot flushes until the 24 week follow up. There was no difference between acupuncture groups and the authors suggested that acupuncture was a viable alternative for treatment of postmenopausal women.

Hot flushes due to tamoxifen therapy have also been improved by the use of acupuncture. Most studies so far have shown that acupuncture has only short-term benefits, yet the symptoms are likely to persist for five years or more. We report here our own clinical experience in developing new forms of treatment to extend the effect of acupuncture for up to six years, and an audit of our results.

**Acupuncture approach for hot flushes**

Acupuncture for flushes was given by JF and DB in a cancer pain clinic setting where acupuncture was already in use for pain. As time went by, referring physicians noted our success in treatment of hot flushes and referred more patients specifically for acupuncture. Interestingly the urinary excretion of calcitonin gene related peptide (CGRP), a powerful vasodilator that is released during a hot flush, also decreased over the treatment period.

In an attempt to increase the duration of action of acupuncture in these patients, we started to use semi-permanent indwelling studs (0.22mm press needle, double plaster, Acumedic, London). We also used studs in patients who failed to respond quickly to body acupuncture alone. In a previous report we described 12 patients with disabling flushes secondary to tamoxifen who were treated with weekly acupuncture using SP6 and LR3 and then semi-permanent indwelling needles at SP6 which maintained symptom relief for up to 36 months.

Contraindications to the use of semi-permanent needles in cancer patients have been described, and include valvular heart disease or valve replacement because of the risk of subacute bacterial endocarditis, an indwelling pacemaker, current chemotherapy and radiotherapy likely to produce intermittent severe immunosuppression with neutropenia. Patients who have had a splenectomy are relatively immunocompromised and more susceptible to infections, so should be included in the group in whom indwelling studs are contraindicated. In addition, standard contraindications to the use of studs in all patients include: 'strong reactors' to acupuncture, in case they become too sleepy with treatment; patients with known hepatitis B or C, to avoid the risk of blood borne infection to others if the stud falls out and is mislaid; and local factors that increase risk eg oedema.
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Subsequently, we taught patients how to use self acupuncture with studs at SP6. They were given clear instructions on how to cleanse the skin with a spirit swab first, how to insert the semi-permanent needle without dextersilising the site and how to secure it with a clear plastic dressing. Patients were instructed to massage the semi-permanent needles several times a day and to change the studs weekly using sterile precautions and preferably while someone else was present. They were taught to change the insertion site slightly each week to avoid damage to skin. Patients were given clear instructions to remove the studs if the skin became red and inflamed or sore, and they were given a pot for safe storage of the used needles and told to return this to their next clinic appointment for safe disposal in a sharps box.

Later, we found that bio-occlusive dressings did not last as long in patients who, for example, did a great deal of sport and were thus likely to perspire much of the time, or take showers or baths more frequently than average. We taught these patients to use self acupuncture with conventional needles at SP6 for sessions of 10 minutes. We also used this approach with patients in whom studs were contraindicated. They were recommended to do this weekly.

Sometimes we found that, in the course of time, the effect of the self acupuncture needling with weekly needles or studs alone would diminish. In these cases, extra top-up treatments were given using the initial regimen, ie SP6, LR3, L14, TE5 and ASAD points. Patients then resumed self acupuncture with standard needling or indwelling studs on a weekly basis for as long as symptomatic control was necessary. Then, in addition to the weekly self acupuncture, the interval between top-up treatments was increased as soon as possible for as long as the patient could cope. For example, the intervals between hospital visits could range from a two weekly top-up initially to one, three or four monthly visits in most patients, and up to annual visits in occasional patients. This approach was found to be the best for prolonged success.

Audit methods

A retrospective survey was carried out of the medical records of all patients treated with acupuncture for hot flushes from November 1990 to April 2003. Names of all patients were identified by one of the authors (SA) from the hospital’s comprehensive electronic records. One hundred and ninety-four patients were identified and their case notes examined longitudinally for up to six years. The data were analysed by one of us (TB) who had not treated any of the patients, to reduce measurement bias.

Frequency of flushes as reported by the patient was extracted from the records, where available. Since treatment of flushes started as an addition to the main function of the clinic – namely, treatment of pain – we did not introduce formal diaries to record flushes accurately. Patients estimated and reported the average numbers of hot flushes per day and night before treatment and this was entered in the record. The two practitioners used different methods of reporting the response, either as the percentage decrease or as number of flushes per day. Data were extracted for before treatment and throughout the time they used the treatment for up to six years.

Results

Of the 194 patients treated, 182 were female aged between 35 and 83 years (mean 54 years). Twelve patients were male aged between 47 and 79 years (mean 66 years). The majority of patients had breast cancer (167, including one male). Eleven were at high risk for developing breast cancer and were included in the 'Tamoplac' study, ie randomised to have tamoxifen or placebo for eight years. Eleven patients had prostate cancer and the remaining patients included: one each with ovarian cancer, Hodgkin’s disease, non-Hodgkin’s lymphoma, and acute myeloid leukaemia; and one patient who was referred by the occupational health department with complex medical problems. One hundred and forty-six (75%) patients were directly referred for acupuncture treatment of hot flushes and 48 for both hot flushes and pain.

The number of hot flushes before treatment was recorded in 159 cases, but missing in 27 records. The number ranged from two per day to constant flushing throughout the day in eight patients. The mean number of flushes for those recorded was 16 per day, but this figure is an underestimate since it does not include the eight patients who had flushes all day.

The nature of the flushes ranged from short to long duration, from mild to drenching sweats requiring changes of bed clothes and bed sheets, and from intermittent episodes to constant feelings of
flushing and hot sweats throughout the day and night. The patients often complained of severe insomnia and reduced quality of life as a result.

Most patients included in the audit were referred as a "last resort" having failed to respond to various drug and non-drug treatments such as evening primrose oil, clonidine, venlafaxine and homeopathy. Many also had complex psychological problems that may have contributed to the distress caused by the symptoms. Formal psychological testing and pain scoring, which are performed routinely on the majority of patients referred for pain control, were not performed for patients referred for hot flushes because of time and resource limitations. The documented cause of the flushes varied, with tamoxifen and withdrawal of HRT being the most common (see Table 2) and there was frequently more than one cause.

The majority of patients, 144 (74%), were given self acupuncture with semi-permanent acupuncture needles at the point SP6 after an average of 4.7 treatments. Fourteen patients (7%) were taught self acupuncture with standard needles when semi-permanent needles were deemed clinically inappropriate or unsafe (see below). Nine patients (5%) used both at different times, eg mainly using studs but switching to one off needling when going on holiday for example, to avoid the need for dressings. The duration of the treatment with studs varied from one month to over six years, with a mean of nine months.

The results are presented in Table 3 in a way that accommodates both clinicians’ approaches to assessing the response. We considered a reduction of 50% or more in flush frequency to be a clinically useful effect. One hundred and fourteen (79%) patients using self acupuncture studs had greater than 50% reduction, and 30 (21%) had less than 50% reduction, see Table 3. Treatment was usually abandoned after six treatments if the response was less than 50%. Occasionally, patients were keen to continue with acupuncture even if they only had a 30%-50% reduction in flushes because they felt that the improvement significantly enhanced their quality of life.

From the electronic records, one author (TB) coincidentally found that the chance of a sustained effect was greatest in patients who had a reduction in symptoms of at least 50% after the first treatment.

The complications that were reported or identified on examination are listed in Table 5. The patient in whom leg swelling was noticed after treatment had a concurrent fracture to the same tibia which may well have contributed to the swelling. Overall, complications were low (9%) and mostly minor.

<table>
<thead>
<tr>
<th>Table 2 Causes of flushes reported by 194 patients</th>
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<tbody>
<tr>
<td>Tamoxifen</td>
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<tr>
<td>HRT withdrawal</td>
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<tr>
<td>GnRH analogues</td>
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<tr>
<td>Chemotherapy</td>
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<tr>
<td>Cancer-related</td>
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<tr>
<td>Menopausal symptoms with no other identifiable causes</td>
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<tr>
<td>Aromatase inhibitors</td>
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<tr>
<td>Oophorectomy or hysterectomy</td>
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<tr>
<td>Semi-mature had multiple causes recorded</td>
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<thead>
<tr>
<th>Table 3 Reduction of hot flushes reported with use of semi-permanent studs</th>
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<tr>
<td>Reduction</td>
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<tr>
<td>--------------------------------</td>
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<tr>
<td>&lt;50%</td>
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<tr>
<td>50%</td>
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<tr>
<td>&gt;50%</td>
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<tr>
<td>100%</td>
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<tr>
<td>Total</td>
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<table>
<thead>
<tr>
<th>Table 4 Incidence of contraindications to use of semi-permanent studs in 144 patients</th>
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<tbody>
<tr>
<td>Valvular heart disease</td>
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<tr>
<td>Pacemaker</td>
</tr>
<tr>
<td>Current chemotherapy</td>
</tr>
<tr>
<td>Oedema of leg</td>
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<tr>
<td>Anticoagulant treatment with warfarin</td>
</tr>
<tr>
<td>Poor compliance</td>
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<tr>
<td>Sensory abnormality (likely not to respond)</td>
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<tr>
<td>Strong reactor</td>
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<tr>
<td>Eczema</td>
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<tr>
<td>Nerveous syins</td>
</tr>
<tr>
<td>Local infection</td>
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<tr>
<td>Poor circulation</td>
</tr>
<tr>
<td>Obese – difficult landmarks</td>
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<tr>
<td>Arthritis – poor skin</td>
</tr>
<tr>
<td>Total</td>
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<table>
<thead>
<tr>
<th>Table 5 Side effects of studs reported in 144 patients</th>
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<tbody>
<tr>
<td>Red mark where stud had been</td>
</tr>
<tr>
<td>Allergy to dressing</td>
</tr>
<tr>
<td>Rash or red or inflammation</td>
</tr>
<tr>
<td>Skin infection from stud</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Made leg cramps worse</td>
</tr>
<tr>
<td>Leg swelling after insertion (concurrent fracture same leg)</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Total</td>
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</tbody>
</table>
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The contraindications to using studs in the audited group are shown in Table 4 and any side effects reported in Table 5.

How audit changed practice

As a result of this audit, we changed our practice to try to reduce the complication rate, even though complications were already low in number (9%) and minor. We used self acupuncture with standard needles at SP6 bilaterally with 36 gauge Seirin needles in preference to semi-permanent studs, as first line treatment. So far, this appears to have achieved a lower complication rate (data not presented). Semi-permanent studs are now reserved for use only where there is no response or a poor response to self acupuncture with standard needles.

We have also developed an algorithm for treatment (Figure 1) and find this approach especially useful in busy clinical practice.

Discussion

There is an increasing interest in complementary therapies for pain and symptom control in cancer patients, many of whom wish to avoid conventional medication largely because of the side effects. The safety of progestogens, a number of SSRIs, and phytoestrogens is still not known for certain, and herbal treatments may interfere with the efficacy of a range of current anti-cancer treatment and hormone-modifying drugs, particularly as anti-cancer hormone manipulation is often necessary for up to five years (eg tamoxifen).

Figure 1. This is an algorithm for long term treatment with acupuncture and self-acupuncture.
Self acupuncture with semi-permanent or standard needles represents a form of treatment which can be used over long periods by cancer patients who have troublesome hot flushes and night sweats.

Previous studies of acupuncture show that the reduction in hot flushes is of short duration. For example, in one study the rate of hot flushes reduced at the end of treatment in patients with prostate cancer,17 yet 14 weeks later it had returned to baseline. Hot flushes and night sweats in cancer patients are likely to be long term. We have already shown that the results of a course of four to six sessions of body acupuncture can be maintained over long periods using self acupuncture with either semi-permanent or standard needles,16 or, as in this communication, using standard needles.

At the time of this audit, several other studies were underway at the Royal Marsden Hospital to investigate the effects of relaxation and SSRIs on hot flushes, recruiting patients directly from the breast clinics. Therefore acupuncture was used very much as a last resort in difficult, unresponsive cases. If treatment was offered to consecutive patients, whatever their severity of symptoms, we would anticipate that a higher proportion would have a sustained response to an initial course of treatment, reducing the need for self acupuncture.

The details of the pathophysiology of hot flushes remain unknown, although several hypotheses exist. Figures 2 and 3 illustrate some of the ways in which acupuncture might relieve symptoms. Calcitonin gene related peptide (CGRP) is released into the circulation during a hot flush.15 Acupuncture causes the release of β-endorphin which has an inhibitory effect on CGRP. Wyon and colleagues showed that the urinary excretion of CGRP was reduced with acupuncture (Figure 2).16

Increasing β-endorphin levels also have a negative effect on luteinizing hormone surges and may reduce symptoms in this way. Additionally, low oestrogen concentrations, low serotonin concentrations and stress can lead to an increase in 5-HT2A receptors in the hypothalamus and thus alter the temperature set point, which leads to symptoms of hot flushes and sweating (Figure 3).16 Acupuncture is known to increase 5-HT and may thus reverse these effects.16 This may be the non-drug equivalent of treatment with SSRIs.

Since the mechanism of acupuncture for this indication is probably largely central, point location may be of less importance than the overall dose. The initial course of treatment might have induced genetic up-regulation which was then maintained by less frequent top-up treatment. Therefore if, for example, a patient had bilateral axillary dissections and so the use of acupuncture points on the arm was contraindicated, other strong acupuncture points such as ST36 may have been appropriate. It was important that a significant loading dose was given when commencing treatment ie six weekly treatments initially, with top-up treatments at increasing intervals. A lower dose of say two needles only at weekly intervals may have been insufficient to give relief.

Acupuncture has a good safety profile, with a low incidence of side effects recorded in two large prospective studies.62 63 This audit did reveal an incidence of 9% of minor side effects associated with self acupuncture with semi-permanent studs. Putting this in context, 66.3% of patients in a recent study of pregabalin for neuropathic pain had more than one side effect and a significant proportion of these discontinued therapy.64 As a result of the 9% incidence, we changed our practice quite successfully to use sessions of self acupuncture with
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needles instead of studs as a routine. Studies are now only used in a small minority of patients at the Royal Marsden Hospital who have inadequate relief with needling alone. From clinical observations over two years since completing the audit, use of the algorithm in Figure 1 has undoubtedly helped reduce the side effect rate even further.

Evaluating the cost effectiveness of acupuncture treatment is complex and needs to take account of costs of premises, practitioner, equipment etc in achieving improved quality of life, as shown for acupuncture for headache. The potential benefit of enabling patients to remain on treatment that they might otherwise abandon could be very large. The cost of acupuncture needles is minimal, approximately £5 total for the initial six week treatment course and about 20 pence each week for self acupuncture with needles. The cost of using semi-permanent studs would be slightly higher to include the dressing and spirit swabs.

Conclusion
Hot flushes and night sweats can be disabling in cancer patients and often need long term therapy. Acupuncture treatment delivered as an initial course in clinic and maintained by self acupuncture with either needling sessions or semi-permanent indwelling studs can provide symptom control for up to six years. This treatment has a low incidence of side effects and may currently be the safest form of treatment course and about 20 pence each week for self acupuncture with needles. The cost of using semi-permanent studs would be slightly higher to include the dressing and spirit swabs.

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Reference list


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