



Acupuncture and cancer

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ABSTRACT

Acupuncture has become a popular complementary treatment in oncology, particularly as patients seek non-pharmacological alternatives to provide symptom control. A considerable body of evidence suggests that acupuncture modulates neurological processes to bring about its effects. This basic research is supported by an increasing number of positive clinical studies of varying quality. Lower quality studies have hampered the widespread acceptability of acupuncture, with some deeming the inter-personal skills of the practitioner to be more powerful than the needle or its equivalent. More recent randomised control trials (RCTs) have sought to settle this controversy, with mixed results. The literature was searched to identify, where possible, RCTs involving acupuncture and various common cancer symptoms. A potential role for acupuncture was found in the following cancer symptoms: pain, nausea and vomiting, xerostomia, hot flushes, fatigue, anxiety, depression and insomnia. Acupuncture is safe with minimal side-effects, and is clinically effective for the management of these symptoms. Continuing research using validated methodology is essential. In the interim, health professionals should be open to explore the use of acupuncture with their cancer patients.

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1. Introduction

The demand for complementary therapies amongst oncology patients has gained significant momentum over recent years. One Europe-wide survey highlighted the fact that over a third of cancer patients are utilising complementary therapies as they seek *additional* means of treating their cancer symptoms and/or the side-effects of their treatment (Molassiotis et al., 2005). To a certain extent, this indicates an unmet need within conventional medicine, which in some cases, drives patients to seek risky and unproven alternative therapies (Filshie and Rubens, 2006). Most complementary therapies are not specific to a particular cancer diagnosis, as symptoms do not always depend on the primary diagnosis itself but rather on the toxicities associated with treatment and the site of disease. Hence, patients with different cancer diagnoses often share similar symptoms.

Acupuncture has its origins in Traditional Chinese Medicine. It is based on the theory that one can regulate the flow of “Qi”, or vital energy, by the stimulation of certain points on the body with needles, or with pressure in the case of acupressure. Current scientific evidence points to the nervous system as the mediator of acupuncture's effects (Han, 2003; Wu et al., 1999; Zhao, 2008). Release of myriad neurotransmitters and changes in brain functional MRI signals are observed during treatment. Moreover, acupuncture can alter gene expression, upregulating opioid production (Guo et al., 1996; Lee and

Beitz, 1993). It is the strength of current scientific evidence that has made acupuncture more acceptable to Western-trained doctors and given birth to Western Medical Acupuncture (White et al., 2008).

Nonetheless, many Western-trained doctors retain a skeptical view of acupuncture, attributing its effects to one of placebo, including the inter-personal skills of the practitioner. Such skepticism has made a sham acupuncture control arm a requirement for RCTs of acupuncture (Sagar, 2008). The eternal controversy over the use of penetrating and non-penetrating sham controls means that many ‘control treatments’ are far from inactive (White et al., 2008). Some sham needles are akin to stage daggers, in that they withdraw a blunt needle back into the handle sheath during skin application. In functional MRI studies, true acupuncture induced brain activation in the hypothalamus and nucleus accumbens, and deactivated areas of the anterior cingulate cortex, amygdala, and hippocampus. Such changes were not observed in sham stimulation, which affected the sensory cortex only. In terms of analgesia, these data suggest that acupuncture modulated the affective–cognitive aspect of pain perception (Wu et al., 1999). Furthermore, correlations between signal intensities and analgesic effects have been reported (Zhang et al., 2003).

Further work on PET scanning showed that acupuncture induced extra effects in the ipsilateral insula beyond the sham needle, which also had greater effects in activation patterns than a control (Pariente et al., 2005).

Acupuncture for oncology should be administered by a suitably qualified practitioner who can maintain a constant dialogue with the oncology team treating the patient. It is a safe method of treatment, with a low side-effect profile, which in part adds to its popularity

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amongst patients (Sagar, 2008; Witt et al., 2009). Significant adverse effects are rare in acupuncture, <0.55 per 10,000 patients (White, 2004).

In an oncology setting, the contraindications and cautions advised on practising acupuncture are outlined in Table 1, and guidelines for safe practice within this field have previously been published (Filshie and Hester, 2006).

A wide variety of acupuncture techniques are both available and effective. RCTs reviewed here also include patient-administered acupuncture, electroacupuncture, acupressure and auricular acupuncture. The 'dose' of acupuncture used varies widely amongst practitioners with a common treatment schedule comprising weekly treatments for six weeks or twice a week for three weeks. In advanced cancer, the treatment schedule needs appropriate adjustment to the time available. Cancer patients can appear to be more sensitive than others to acupuncture, and these 'strong reactors' often require shorter gentler treatments (Mann, 2000). Needle point selection also varies enormously, and Western medical practitioners use segmental, trigger and traditional points appropriate to the symptom experienced (White et al., 2008). In part, a lack of consensus on optimal dosage, point selection and treatment length makes the interpretation of meta-analyses of acupuncture trials difficult.

Recent advances in acupuncture clinical research suggest that acupuncture may provide clinical benefit for oncology patients in symptom control and supportive care. Symptoms that seem to respond to acupuncture treatment include pain, gastrointestinal side-effects, hot flushes, shortness of breath, fatigue, anxiety, depression and insomnia. An estimated 45% of patients are living five years or more post cancer treatment worldwide (Coleman et al., 2008). These patients welcome a supportive therapy, which can reduce symptoms without the need for long-term medication. Finally, acupuncture also has potential as adjunctive care in the palliative and end-of-life setting (Standish et al., 2008).

Table 1

Contraindications and cautions for use of acupuncture in oncology. Adapted from Table: 10.1.12.2. from p.776 from Ch.10.1.12: Acupuncture by Jacqueline Filshie & John W. Thompson from "Oxford Textbook of Palliative Medicine, 4e". Edited by Hanks, Geoffrey et al. (2009). By permission of Oxford University Press.

Acupuncture is contraindicated
❖ In patients who refuse e.g. in cases of extreme needle phobia
❖ In patients with severe clotting dysfunction, or who bruise spontaneously
Semi-permanent needles are contraindicated
❖ In patients with valvular heart disease – risk of sub-acute bacterial endocarditis
❖ In patients with neutropenia – risk of infection
❖ In patients post-splenectomy – risk of infection
Electroacupuncture is contraindicated
❖ In patients with an intracardiac defibrillator
Needling should be avoided
❖ Directly onto a tumour nodule or into an area of ulceration
❖ In lymphoedematous limbs or limbs prone to lymphoedema
❖ In the ipsilateral arm in patients who have undergone axillary dissection – risk of lymphoedema
❖ In areas of spinal instability – risk of cord compression secondary to acupuncture's muscle relaxing properties
❖ Into a prosthesis – risk of leakage of saline/silicone
❖ Over intracranial deficits following neurosurgery
Cautions
❖ Cancer patients may be very sensitive to acupuncture, so close supervision is advised especially during the first treatment.
❖ Take extra care with patients who are 'strong reactors' to acupuncture
❖ Care should be taken not to needle too deeply over the chest wall in cachectic patients
❖ Disease progression should be always considered in those who become suddenly tolerant to acupuncture having previously responded well
❖ Patients prone to keloid scar formation
❖ Pregnancy
❖ Epilepsy – patients need to be accompanied
❖ Confused patients
❖ Electroacupuncture in patients with a cardiac pacemaker

2. Pain

The World Health Organization analgesic ladder is still widely used for pain control (Stjernsward et al., 1996). Yet over half of cancer patients still suffer significant pain and this adversely impacts on their quality of life (van den Beuken-van Everdingen et al., 2007). Pain may arise from the cancer itself, the treatments employed to eradicate the cancer, or may be completely unrelated to the cancer. The pharmacological failure to control pain alone has led to the use of non-drug treatments including acupuncture. The analgesic effects of acupuncture may permit a decrease in the requirement and side-effects of pharmaceuticals. It can also help those who are sensitive to normal doses of analgesics and conversely with those who have pain despite analgesic dose titration (Filshie and Thompson, 2009).

Several systematic reviews tend to support the use of acupuncture for a range of non-cancer specific pain conditions, to which an oncology patient, of course, is equally susceptible. These include back pain (Furlan et al., 2005), chronic knee pain (White et al., 2007), osteoarthritis (Manheimer et al., 2010), shoulder pain (Green et al., 2005), neck pain (Trinh et al., 2006), and acute dental pain (Ernst and Pittler, 1998).

In cancer-specific pain management, a placebo controlled RCT found that auricular acupuncture was effective compared with two controls for cancer patients with various forms of neuropathic pain (Alimi et al., 2003). However, a systematic review by Lee et al. in 2005 showed insufficient evidence for acupuncture for cancer pain (Lee et al., 2005), which was perhaps mainly due to the lack of sufficient trials. Several other RCTs have shown a role for acupuncture in the management of pain in patients after various cancer-related surgeries (Mehling et al., 2007), including post-thoractomy pain (Wong et al., 2006), and post gastrointestinal surgery (Kotani et al., 2001). Finally, there is emerging evidence to demonstrate the analgesic effectiveness of both acupuncture and electroacupuncture in breast cancer patients experiencing joint pain as a result of adjuvant aromatase inhibitor treatment (Crew et al., 2007; Mao et al., 2009).

3. Nausea and vomiting

Acupuncture stimulation at the point PC6 has repeatedly been shown to be a clinically useful anti-emetic treatment for post-operative nausea and vomiting and chemotherapy-induced emesis (Ezzo et al., 2006a, b; Lee and Fan, 2009; Streitberger et al., 2006). By 1998, the National Institute for Health in the US stated that, "acupuncture is a proven effective treatment modality for nausea and vomiting" (NIH, 1998). A three-arm RCT comparing conventional anti-emetics alone, with either electroacupuncture or minimal acupuncture plus anti-emetics, demonstrated that the electroacupuncture arm plus anti-emetics was the most effective for preventing nausea and vomiting associated with high dose chemotherapy (Shen et al., 2000). A review of acupuncture-point stimulation, including eleven RCTs, for chemotherapy-induced nausea or vomiting showed a benefit over drug therapy particularly for early nausea and vomiting (Ezzo et al., 2005). Moreover, acupressure, which patients can conveniently self-administer without needle involvement, was shown in the same publication to reduce the severity of acute nausea. Since then, two multi-centre longitudinal RCTs have shown that the beneficial effect of acupressure can significantly reduce the severity of both acute and delayed vomiting (Dibble et al., 2007; Molassiotis et al., 2007a). A cohort study showed that acupressure motion sickness bands improved nausea and vomiting in hospice patients (Wright, 2005).

Despite modern pharmacological therapies, many patients continue to suffer from post-operative and chemotherapy-related nausea and vomiting. Acupuncture or acupressure is simple to administer and merits wider consideration.

4. Xerostomia

Xerostomia is widely experienced by cancer patients for a variety of reasons (Davies et al., 2001, 2002) and is one of the more distressing late side-effects of radiation therapy used to treat head and neck cancers. Loss of taste and difficulty in speaking and swallowing are hallmarks of the condition. Recently, acupuncture treatment has been found to increase blood flow to the parotid glands, increase salivation, and to stimulate tissue regeneration in radiotherapy-damaged glands. Increased salivation and quality of life scores were clearly demonstrated in two studies (Garcia et al., 2009; Wong et al., 2003). In one of the studies, these benefits were still present at 6 months after the initial treatment (Wong et al., 2003). An additional study showed a benefit of acupuncture for pilocarpine-resistant xerostomia after radiotherapy treatment for head and neck cancers (Johnstone et al., 2001). Mechanisms by which acupuncture is effective include stimulation of both the parasympathetic (volume effect) and sympathetic (viscosity effect) nervous systems and release of the vasodilator calcitonin gene-related peptide (C-GRP), which also increases salivary secretion (Lundberg, 1999). Stimulation of various growth factors has also been implicated, which perhaps explains why the benefits of acupuncture can be seen months after treatment. A multi-centre RCT is currently underway through the Radiotherapy Oncology Group (RTOG) to further delineate the clinical benefits of acupuncture in this common and unpleasant symptom.

5. Cancer-related hot flushes

A course of acupuncture treatment has been found to reduce hot flushes associated with the normal menopause (see Borud, Grims-gaard and White in this volume) and also from hormonal treatments for cancer. Two RCTs found that acupuncture reduced hot flushes by up to 60% in women treated with Tamoxifen for breast cancer (Deng et al., 2007; Hervik and Mjaland, 2009). Comparing venlafaxine, a widely used pharmacological treatment for hot flushes, to acupuncture, revealed that venlafaxine was not superior in reducing vasomotor symptoms at 1 year after treatment (Walker et al., 2009). Those in the acupuncture group additionally reported improved libido, increased energy, improved clarity of thought and sense of well-being. Furthermore, the acupuncture group reported *no* adverse side-effects. This was in stark contrast to over 70% of the venlafaxine group who reported distressing side-effects such as nausea, dry-mouth and dizziness. An algorithm has been developed for the long-term treatment of hot flushes, with the observed effects of the initial course of treatment maintained for up to 6 years by weekly self-needling at SP6 or by using semi-permanent needles (Filshie et al., 2005). For self-needling, patients require clear demonstration of cleansing, insertion and safe disposal (Filshie and Hester, 2006). A prospective RCT has also confirmed the benefits of electroacupuncture and traditional acupuncture at controlling vasomotor symptoms, and associated distress, in men treated for prostate cancer (Frisk et al., 2009).

6. Dyspnoea

Clinical evidence for acupuncture in treating cancer-related dyspnoea is emerging. One pilot study showed significant improvement in the subjective scores of breathlessness, relaxation and anxiety at 90 min in patients with advanced cancer-related dyspnoea (Filshie et al., 1996). In these patients, steroids, opioids, nebulizers and oxygen therapies had failed. Furthermore, a reduction in the respiratory rate was sustained during the treatment period. These effects could be prolonged by insertion of 2 semi-permanent studs at the top of the sternum, which could be massaged as necessary to give rapid relief of dyspnoea. A subsequent RCT however, failed to show a difference between acupuncture and acupressure (Vickers et al., 2005). In this

study, the placebo treatment included one real needle, which may have been a confounding factor. Positive RCTs for other respiratory conditions show beneficial effects of acupuncture and acupressure in patients with chronic obstructive asthma, bronchiectasis and chronic obstructive pulmonary disease (Maa et al., 2003, 2007; Wu et al., 2004). A further RCT is in progress at the Royal Marsden Hospital London comparing acupuncture with morphine for advanced cancer-related breathlessness in patients with lung cancer.

7. Fatigue

Fatigue is an extremely common symptom in cancer patients (Minton et al., 2008). It is particularly prevalent in advanced cancer. Fatigue is also an adverse side-effect of chemotherapy and radiotherapy, which can persist long after the cessation of treatment. In a prospective phase II study on patients with persistent fatigue who previously had completed chemotherapy, acupuncture resulted in a significant reduction in baseline fatigue scores (Vickers et al., 2004). Results from this trial were endorsed by a 3-arm RCT comparing acupuncture, acupressure and sham acupuncture in patients with a variety of cancer diagnoses, who were one year post-chemotherapy (Molassiotis et al., 2007b). Acupuncture was associated with a 36% improvement in baseline fatigue scores, which accords well with the prospective trial and was significantly superior to acupressure and sham acupuncture. A further multi-centre trial is underway to test whether the effect can be prolonged by self-administered treatment in the UK.

8. Anxiety, depression and insomnia

The two upper sternal 'ASAD' points – anxiety, sickness and dyspnoea points are used extensively in the UK to control dyspnoea and also anxiety if found to be helpful following an initial treatment. Patients can massage acupuncture studs for 1–2 min on demand to provide anxiolysis (Filshie and Thompson, 2009). This has the added benefit of empowering the patient to control these distressing symptoms in the event of a panic attack.

Leo and Ligot's systematic review of RCTs of acupuncture in the treatment of depression concluded that despite the odds ratios of existing literature suggesting a role for acupuncture, the evidence thus far was inconclusive (Leo and Ligot, 2007). More recent evidence suggests that acupuncture when combined with antidepressant therapy has a faster therapeutic onset rate than pharmacotherapy alone, coupled with a reduction in the side-effect profile of the antidepressant medication (Duan et al., 2009). An additional RCT examining the treatment of hot flushes, revealed that compared to women taking venlafaxine, those receiving acupuncture felt they had more energy, improved clarity of thought, increased libido and a greater sense of well-being (Walker et al., 2009). In Mehling's study, massage and acupuncture in post-operative cancer patients who were also receiving usual care showed a significant improvement in their depressed mood with a short-lived significant improvement in tension and anxiety when compared to those receiving usual care alone (Mehling et al., 2007).

Acupuncture's role in insomnia has yielded mixed results. A small, non-cancer study found acupuncture reduced insomnia and anxiety significantly, with clear objective improvements in nocturnal melatonin secretion and in polysomnographic measures (Spence et al., 2004). A subsequent meta-analysis revealed that the improvement rate of insomnia produced by auricular acupuncture was significantly higher than that from Diazepam (Chen et al., 2007). However, a Cochrane systematic review of acupuncture for insomnia concluded that acupuncture or its variants were not more effective than control (Cheuk et al., 2007). As with the studies in anxiety and depression, larger high-quality clinical trials employing appropriate randomization and

blinding with longer follow-up, are warranted before any firm conclusions can be drawn.

9. Leucopaenia

The main body of evidence comes from China where a systematic review of RCTs was positive for increasing WBC in patients undergoing chemotherapy (Lu et al., 2007), however, the quality of trials was considered poor, and the authors suggest that the positive meta-analysis should be considered as exploratory. The patients in this review received acupuncture once a day, with a median of 16 sessions.

10. Conclusion

A review of recent RCTs of acupuncture in oncology suggests that it has a promising role in controlling a wide variety of cancer and treatment related symptoms. The evidence currently available suggests that acupuncture is a safe, low cost and effective therapy, which further permits cancer patients to actively participate in their own care plan. We still have much to learn about acupuncture, and further research incorporating well-designed clinical trials are needed. Elucidation of the most effective needle protocols and type of acupuncture for each symptom is also warranted. As encouraging evidence continues to emerge, acupuncture should be considered as a complement to first line treatment of symptoms in patients with cancer rather than one of last resort.

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