OICC
OTTAWA INTEGRATIVE CANCER CENTRE

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CENTRE DE CANCÉROLOGIE INTÉGRATIVE D'OTTAWA

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Professional Resource: Acupuncture

Proper (and Common) Name

Acupuncture; Japanese acupuncture; acupuncture therapy.

Common Uses in Cancer Care

Acupuncture is commonly used in cancer care to manage symptoms associated with cancer and cancer treatment, for example pain (1-8), chemotherapy induced nausea and vomiting (1-3, 5, 9-13), sleep disturbances (3, 10), fatigue (1, 4, 14, 15), anxiety and depression(3), and peripheral neuropathy (16). For breast and prostate cancer patients, acupuncture is also commonly used to manage hot flashes (3, 6, 9, 17-20); and, for patients with head and neck cancer it is commonly used to manage radiation-induced xerostomia (dry mouth) (1, 2, 4, 5, 9, 10, 14, 21, 22).

Route of Administration

Acupuncture treatments generally involve the insertion of fine needles into specific acupuncture points over the body. Moxibustion and cupping might also be used. Moxibustion is the application of heat via the herb *Artemesia vulgaris* (Mugwort), or Moxa. In Cupping, a partial vacuum is created in cups placed on the skin either by means of heat or suction. For patients who are too sensitive to needling, diodes, magnets and acupressure provide other treatment options. Japanese acupuncture treatment involves thinner or smaller needles with shallower insertions than Chinese acupuncture.

Mechanism of Action

From an Eastern perspective, acupuncture is based on the premise that there are patterns of Qi, or 'life energy' that flow through the body along meridians. Meridians can be conceptualized as energy channels that connect body organs and systems. Blockage or stagnation of the flow of Qi on these meridians can lead to pain and illness, and acupuncture attempts to relieve Qi blockages and restore health (6, 23).

Many Western scientists have tried to understand meridian Qi in relation to the body's connective tissue and related biochemical and bioelectrical signalling processes. They propose a number of mechanisms to be responsible for the observed effects of acupuncture. In the Western perspective no one mechanism seems sufficient to explain its effects. The most important mechanisms described from a

Western biomedical approach are related to pain inhibition primarily via endorphin release, as well as the potential anti-inflammatory and immunomodulatory effects of acupuncture.

Some acupuncture points coincide with 'trigger points', or anatomic sites of enriched innervation and muscular tension (6). Acupuncture stimulates nerve fibers within the interstitial network of 'loose' connective tissue (including subcutaneous tissue) (6, 14, 23-26), which activates both the peripheral and central nervous systems and results in the release of various neurotransmitters, including endorphins, monoamines, serotonin and encephalin, thereby blocking pain messages or altering the perception of pain (3, 23, 25-30). Pain may also be alleviated by suppressing the expression of interleukin-1 beta, a tumour derived factor that sensitizes primary afferent neurons to elicit cancer-related pain (29). An opioid-like mechanism also appears likely for example through the increased secretion of endogenous opioids, catecholamines, and serotonin in plasma and brain tissue (1, 25), which can contribute to decreased perception of pain, decreased reaction to pain as well as increased pain tolerance.

Acupuncture also appears to initiate an immune response. Human and animal studies document the effect of acupuncture on a range of immune markers, including: a decrease in levels of CD4+ and CD8+ cells, which are known to suppress overactive immune response (26, 27), an increase in natural killer (NK) cell activity (16, 26, 27), an increase in IgG, IgA, IgM (28), an increase in interleukin-2 and a decrease in cytokines interleukin-4 and interleukin-6 (26, 27), modulation of B and T cell populations that would favour antibody production (16, 26, 27) and enhanced cortisol production (27). Each of these immune markers represent possible surrogates for pain control, enhanced formation of blood cellular components and immunity (16, 27).

Specific mechanisms have been studied in relation to acupunctures effects on specific cancer- and cancer treatment-related symptoms. For example, management of neuropathy appears related to a release of adenosine, which is a neuromodulator that reduces sensitivity to painful stimuli (26). Related to xerostomia, functional magnetic resonance imaging studies have documented a relationship between stimulating acupuncture point LI-2 and the activation of the brain function area responsible for salivary production (1). Acupuncture's positive effect on anxiety might be explained through a modulating effect on neuropeptide Y and corticotrophin-releasing factor, which are both involved in the stress response (26).

Clinical Evidence related to Effectiveness

Several reviews, including systematic reviews of randomized controlled trials, have been conducted related to the clinical effectiveness of acupuncture for many cancer and cancer treatment related symptoms. In particular, strong evidence exists to support the use of acupuncture to manage uncontrolled pain and chemotherapy-induced nausea and vomiting. Accordingly the Society for Integrative Oncology recommends acupuncture for these indications in their Clinical Practice Guidelines (9).

Most reviews identify a problem with design flaws within many primary acupuncture studies (7, 19, 20, 29), including non-experimental designs (20), variability in acupuncture interventions and needling

techniques (7, 29, 31) and differing control and sham acupuncture interventions (12, 29, 31). Despite shortcomings in some studies, overall there is strong evidence to support a role for acupuncture in managing many symptoms associated with cancer and cancer treatment.

Pain

Several randomized controlled trials have demonstrated the effectiveness of acupuncture to help manage pain in cancer patients, including malignant pain, post-operative pain, radiation-induced chronic ulcers, and chemotherapy-induced neuropathic pain. These studies have assessed the use of acupuncture both as a complementary and alternative method to usual care (i.e. primarily pharmaceutical analgesics). Most studies demonstrate additional pain reduction with the addition of acupuncture treatment, or a comparable effect for acupuncture and usual care. Further, some studies have documented a reduced need for pharmaceutical analgesics to maintain patient comfort when acupuncture is used as a complementary intervention, which can also decrease the incidence and degree of drug induced side effects (1, 14).

A meta-analysis of results of 8 randomized controlled trials comparing acupuncture with conventional drug therapies, documented no difference between acupuncture and conventional drug therapies for pain reduction (n= 886; RR, 1.12; 95% CI 0.98 to 1.28; P=0.09). A separate meta-analysis of 7 randomized controlled trials compared the effects of acupuncture plus conventional drug therapies to conventional therapy alone on cancer pain and demonstrates favourable effects for acupuncture combined with conventional drug therapy for pain reduction (n=437; RR, 1.36; 95% CI 1.13 to 1.64; P=0.003). Finally, a Cochrane review of acupuncture for cancer-related pain in adults included 3 randomized controlled trials, including one of high methodological quality/low risk of bias. In this randomized controlled trial, 90 people with pain arising after cancer treatment despite stable medication were randomized to one of three groups—needles placed at correct acupuncture points (treatment group), needles placed at non-acupuncture points, or application of pressure at non-acupuncture points (control group). Pain intensity decreased by 36% at 2 months from baseline in the treatment group ($p<<0.001$), a significant difference compared with the two control groups, where little pain reduction was seen. (8) These results are especially important because most of the patients had neuropathic pain, which rarely responds to conventional treatment (9). Further, in this trial no adverse outcomes were reported (8).

Nausea and vomiting

Some of the strongest evidence exists to support the use of acupuncture for chemotherapy induced nausea and vomiting, including several positive randomized controlled trials (5), but the evidence is lacking regarding radiation-induced nausea (31). For example, a 2011 Cochrane review of acupuncture-point stimulation (including needles, electrical stimulation, magnets, or acupressure) for chemotherapy-induced nausea or vomiting, included 11 randomized trials and found overall that acupuncture-point stimulation, as compared to a control, reduced the incidence of acute vomiting (relative risk [RR], 0.82; 95% confidence interval [CI], 0.69Y0.99; P = .04) but not acute or delayed nausea severity. An earlier systematic review of acupuncture point stimulation for nausea and vomiting related to chemotherapy, pregnancy, or anesthetics reported that 11 out 12 placebo-controlled, randomized, double-blinded studies favoured acupuncture, particularly when involving the P6 acupuncture point on the volar surface of the wrist (11).

Acupuncture might offer the greatest effects when combined with standard antiemetic therapy. In one three-arm randomized controlled trial, 104 women with high-risk breast cancer who were receiving the

same antiemetic pharmacotherapy and high-dose chemotherapy and were randomly assigned to low-frequency electroacupuncture at P6 and ST36 points, minimal needling at P6 and ST36 with mock electrostimulation or no acupuncture and antiemetic drugs only. The results indicated that the group receiving electroacupuncture had significantly fewer episodes of nausea ($p < .001$) compared to the other groups. Those receiving minimal needling had fewer episodes of emesis than did the control group ($p = .01$) (32).

Fatigue

A few pilot trials have been published to document outcomes associated with acupuncture and post-chemotherapy fatigue and radiation-induced fatigue. In one pilot study, 37 people with post-chemotherapy fatigue were randomized to once-weekly therapy for 6 weeks or twice-weekly therapy for 4 weeks. Both groups demonstrated a mean improvement of 31% (95% confidence interval, 20.6%-40.5%) 2 weeks after completion of treatment (15). In another pilot, double blind trial 23 people undergoing radiation were randomized to either true or sham acupuncture once or twice per week for the duration of their 6-week radiation treatment. Again, both groups demonstrated improved fatigue and fatigue distress from baseline to 10 weeks (33).

Peripheral Neuropathy

There is limited research with regards to peripheral neuropathy. In one pilot study, 17 people with a diagnosis of chemotherapy induced peripheral neuropathy received 6 weeks of acupuncture, and 85 % of those patients reported improved neuropathy symptoms. Only 18 % reported no change. Forty-seven percent, or nearly half of the sample reported additional benefits, including increased sleep and relaxation (34). In a separate case series (16), five consecutive patients with advanced gynecologic cancers were given acupuncture treatment once a week for six weeks followed by four weeks of rest and then a second course of acupuncture for six additional weeks. Following acupuncture treatment, the five patients experienced improvement in sensation, gait, and balance and had decreased analgesic dosages. Some control of symptoms (pain, numbness, and tingling of fingers and toes) was obtained after the first treatment. No adverse side effects occurred, and the benefits of acupuncture were maintained for six months for four of the five patients involved.

Hot flashes

Several randomized controlled trials document decreased severity and frequency of hot flashes that could persist for up to 6 months post-acupuncture treatment (18, 31, 35). Results are consistent for both males and females (19, 20). Interestingly several studies also demonstrate consistent effects for both sham and true acupuncture (9, 31). For example, in one well-controlled randomized trial 72 breast cancer patients received either sham or true acupuncture twice-weekly for 4 weeks. Participants in the acupuncture group observed 0.8 fewer hot flashes per day than sham acupuncture at 6 weeks, but the difference did not reach statistical significance (35). However, one meta-analysis of results of 3 randomized controlled trials comparing true and sham acupuncture suggests favourable effects of acupuncture on reducing the frequency of hot flashes after treatment and during the treatment period compared with sham acupuncture (19).

One randomized trial explored the effects of acupuncture as compared to venlafaxine among women with breast cancer experiencing hot flashes caused by tamoxifen. In this study, acupuncture was shown to be as effective as venlafaxine in controlling hot flashes and not associated with the common side effects of venlafaxine. Further, the acupuncture group exhibited a sustained improvement at 2 weeks post-treatment, whereas the venlafaxine group developed more hot flashes post-treatment (17).

Xerostomia

Some evidence exists to suggest acupuncture can help relieve radiation-induced xerostomia. Several literature reviews, including one systematic review of 3 randomized controlled trials (21), consistently report improvements in salivary flow rate, a reduction in mouth dryness and hoarseness, and improved taste following acupuncture treatment and as compared to controls (4, 9, 14, 21, 22, 31). Review data are consistent with data from uncontrolled trials that similarly demonstrate improvements in salivary flow rates up to 6 months following acupuncture treatment, with continuous improvements in flow rate up to 3 years with ongoing treatment (36, 37).

Adverse Events and Side Effects

The consensus among reviewers of acupuncture in cancer care is that acupuncture is safe, with minimal side effects, when practiced by trained and licensed practitioners (4, 5, 9, 14, 29, 38-40). Mild adverse events include distress, fatigue, hematoma, bleeding or bruising at the insertion site, needling pain and a short-term (a few second) transient increase of vasomotor symptoms (13, 20, 41-44).

Significant adverse events are rare, with an estimated incidence of less than 0.55 per 10,000 individuals, or even less since the introduction of mandatory use of sterile and disposable needles (2, 7, 14, 27, 31, 43). Reported serious adverse events include pneumothorax, retroperitoneal hematoma, pericardial tamponade, bacterial meningitis, septicemia, spine and nerve injuries, asthma attack, hypertensive crisis, exacerbation of depression, and subarachnoid hemorrhage (5, 27, 43, 45, 46). Most adverse events can be prevented by taking universal precautions, using proper clinical techniques and having a proper understanding of internal and surface anatomy (27).

Interactions with other Therapies, including Drugs and Natural Health Products

Caution should be exercised in patients who are taking the anti-coagulant warfarin (47).

Cautions and Contraindications

Sterile needles are required for the safety of patients and to reduce the risk of infection (45, 48). Further, the insertion site should be cleaned to prevent the rare complications of abscess formation or septicemia.

Acupuncture should not be given at the site of tumor or metastasis, at the site of superficial tumour nodules or skin ulcerations, on broken skin, at a site of active infection or radiation burn, over an intracranial deficit or any open surgical wound, in limbs with lymphedema, in areas with considerable anatomic distortion from surgery, in the local area of an unstable spine (especially in patients with multiple myeloma), or in a prosthesis. Caution should be exercised in patients with a tendency to bruise

or bleed spontaneously (9, 47). Acupuncture is also contraindicated in patients with severe thrombocytopenia, coagulopathy, or neutropenia, in patients who are at risk of endocarditis due to heart valve abnormality, and in patients with a severe clotting disorder or who have needle phobia (2, 4, 6, 9, 27, 35, 47).

Semi-permanent needles should not be used in patients with valvular heart disease or in vulnerable neutropenic patients (47). Electroacupuncture should be avoided in patients with a demand pacemaker (47). Care should be taken with needling depth in cachectic patients, especially over the chest wall, and when the platelet count is depressed (14, 47). Needles should not be inserted in a limb with lymphoedematous swelling, instead it is recommended that the contralateral limb be needled to avoid risk of precipitating lymphedema or infection (2, 47, 48).

When patients who have been previously responsive to acupuncture suddenly stop responding, this might be a sign that there is disease progression; treatment should be stopped until this is investigated by their oncologist (2, 47).

When the proper precautions are followed, acupuncture is safe for pregnant women and children, when practiced by a qualified practitioner.

Frequency and length of treatment

The frequency and length of acupuncture treatments vary by individual, depending on symptom severity and desired outcomes. Typically, patients will attend 30-60 minute appointments once or twice per week for up to 6 weeks, or when symptoms begin to resolve. Fewer and less frequent treatments are required during a maintenance phase.

Disclaimer

The OICC has prepared this monograph, as part of a series of monograph development, to share results of a review of the scientific research evidence related to common therapies and products used within patient care at our centre. This and other monographs reflect therapies and products used within the defined scope of practice for our practitioners in Ontario, Canada. The information in this monograph should not be interpreted as medical advice nor should it replace the advice of a qualified healthcare provider.

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Monograph Development Methods

SEARCHING

Databases: AMED, CancerLit, the Cochrane Library, Medline, EMBASE, CINAHL, Natural Standard, AcuBriefs.

Search terms: Following a discussion with Bruce Cawdron, Ac the search strategy represents the form of acupuncture he practices at the OICC. This includes a focus on Japanese acupuncture, which includes shiatsu as the traditional form of Japanese massage. Two individuals who he identifies as fundamental influences to his practice style are Kiiko Matsumoto and Shudo Denmei. This context provides the basis for developing a search strategy within each electronic database that includes the combination of the following controlled vocabulary and keywords:

Controlled vocabulary: Acupuncture, Acupuncture Therapy, Neoplasms
Keywords: acupuncture, Japanese acupuncture , needling, cancer*, neoplasm*, carcino*, malignan*, lymphom*, tumor*, tumour*, oncolog*, Kiiko Matsumoto, Shudo Denmei {note: these are confirmed with Bruce}

Timeline: From inception to the most recent publication date of the database in question.

Language: Only English language studies will be included.

Reference list scan: Not unless a small amount of relevant studies are retrieved.

Contact experts: Not unless a small amount of relevant studies are retrieved.

SCREENING

All search results (titles and abstracts) will be screened by one reviewer and decisions for inclusion (yes/no/maybe) will be made based on the predefined PICOD-based inclusion/exclusion criteria outlined below. The full-text of articles passing through the title and abstract screening phase will be obtained and a final decision regarding their inclusion will be made based on the same inclusion/exclusion criteria by one reviewer. As needed, another reviewer will help resolve inclusion status for questionable items.

Inclusion Criteria:
Formal diagnosis with any type or stage of cancer; Any type of acupuncture therapy as long as some form of stimulation was applied to points along acupuncture meridians; Any comparison group will be included, including sham acupuncture, usual care, or pharmaceutical preparations; Outcomes including cancer symptoms and treatment side effects, emotional and psychological health, facilitating and maintaining a lifestyle shift; intervention study with a comparison group or systematic reviews

Exclusion Criteria:
Pre-clinical and any research that does not involve humans.

DATA EXTRACTION

Data will be extracted using a standardized and piloted form that includes fields within each monograph section. Data will be extracted independently by one reviewer.

DATA ANALYSIS

Data analysis will differ by monograph section, but will primarily be descriptive.

QUALITY ASSESSMENT

No quality assessment will be conducted.