Chapter 5
Acupuncture and Moxibustion for Cancer-Related Symptoms

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Abstract Acupuncture and moxibustion is increasingly utilized in cancer management. Recent research has continued to provide new evidence to support the use of these complementary treatment modalities for the supportive care of cancer patients during and after conventional therapies. Apart from nausea and vomiting, for which the strongest evidence exists to support acupuncture treatment, there are multiple other symptoms that have been shown to benefit from acupuncture and moxibustion. These symptoms are commonly encountered by patients in their cancer journey and include the very debilitating cancer pain syndrome to the least apparent symptoms like anxiety, depression and cancer-related fatigue. The alleviation of these symptoms is essential to ensure better patients' quality of life. Adoption of these acupuncture-related treatment modalities into clinical practice should be based on best evidence that ideally derived from well designed randomized controlled clinical trials. Non-invasive form of acupuncture point stimulation using transcutaneous electrical stimulation is also being investigated and the results of recent studies are promising. This chapter reviewed the current evidence from published laboratory and clinical trials to inform proper recommendation, utilization and further research of acupuncture and moxibustion management for cancer-related symptoms.

5.1 Introduction

Recent advances in cancer treatment have improved treatment outcomes of cancer patients. However, cancer patients continue to experience a wide variety of symptoms related to the cancers and its treatments. More aggressive treatments lead to more severe acute toxicities and their effective managements becomes an important factor to ensure patients' treatment compliance that may indirectly affect treatment outcomes. Improved survival of cancer patients also increases the prevalence of patients with chronic toxicities. Effective managements of these chronic toxicities are thus also important to improve patients' quality of life. Conventional managements

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of cancer-related symptoms may not be effective and research for effective treatment modalities continues. Acupuncture and its related techniques are one of the most common forms of complementary and alternative medicine that are widely accepted by the general public. Recent studies have shown that these interventions can provide effective relief for some cancer-related symptoms. This chapter reviews the current published evidence of the effectiveness of acupuncture and moxibustion in managing cancer-related symptoms.

5.2 Cancer Pain

Pain is common in patients with all types and all stages of cancer but particularly in advanced and terminal stages. In a recent systematic review, 33% of patient experienced pain after their curative treatments and 64% of patients with advanced stage disease have suffered from pain. In more than one third of patients who reported pain, the intensity of pain was noted to be moderate to severe (van den Beuken-van Everdingen et al. 2007).

Cancer pain can be broadly categorized into nociceptive, neuropathic or mixed according to mechanisms. Cancer itself and cancer treatments can damage organs and activate nociceptive receptors resulting in pain that is often localized (except from visceral origin where pain is often not well localized), constant and with an arching and throbbing quality. Direct nerve damages, however, typically result in burning and electric shock like quality pain that may radiate along the nerve innervation areas.

In conventional managements of cancer pain, clinical recognition of the pain mechanisms involved is important to direct management. For example, pain with a neuropathic component often needs medications such as anti-depressants and anti-convulsants to be effectively managed (Vorobeychik et al. 2011). In contrast, treatment of pain with acupuncture approaches requires the recognition of symptoms patterns. These patterns include the location and propagation pathway of pain in relationship to acupuncture meridian distributions or to the correspondence areas of established acupuncture "microsystems". In a "microsystem", the whole body is reflected in part of the body, such as the ear, the hand or the foot. Acupuncture points in a "microsystem" resemble the acupuncture points found in the whole body and can also be used to achieve treatment effects. Symptom patterns recognition also include the overall assessment of the body energetic status: an overall reduction of body energy often worsen pain experience and only by correcting this deficient status then pain can be effectively controlled.

5.2.1 Acupuncture for Cancer Pain

5.2.1.1 Mechanisms Exist to Suggest Acupuncture Can Be Effective for Pain

The mechanisms by which acupuncture treatments can relieve pain have been suggested in many laboratory and clinical studies. Opioid peptides have been shown to

be released at various regions of the central nervous systems upon acupuncture stimulation (Ji-Sheng 2003). Levels of other neurotransmitters, such as substance P that is related to inflammation and pain, have been shown to be reduced by electroacupuncture compared to that of controls in animal studies (Lee et al. 2009a). Modulation of the threshold of neuronal discharge of spinal dorsal horn neurons by electroacupuncture was also demonstrated in animal studies (Rong et al. 2005). Functional MRI studies offered further insight into the yet unclear complexity of acupuncture effects on pain perception. In human studies, activities of various regions of the brain known to be involved in pain perception, including the sensory cortical areas and the limbic system, were shown to be modulated in acupuncture analgesia (Wu et al. 1999; Hui et al. 2000). The frequencies of stimulation utilized in electroacupuncture were also shown to exert different modulation effects on the dynamic nociceptive neural network: high frequency stimulation induced analgesic effect on broader areas of the body while low frequency stimulation was more effective for adjacent painful areas.

5.2.1.2 Clinical Evidence Supporting Acupuncture Effectiveness

Acupuncture has been used for non-cancer and cancer-related pain, in fact, for many non-pain clinical conditions in China. In the west, acupuncture has also been widely utilized for pain management. A recent study showed that over 80% of chronic pain clinics offer acupuncture as an option for pain control (Woollam and Jackson 1998). Although there is plenty of anecdotal evidence to suggest acupuncture is effective in managing cancer-related pain, the acceptable gold standard remains in evidence provided through randomized controlled trials. There were, however, only few randomized trials examining acupuncture for cancer-related pain conducted to date and all showed positive results.

In one of these trials, Alimi et al. (2003) randomized 90 patients who attained a pain clinic for cancer-related pain with neuropathic nature into three groups. One group received true auricular acupuncture, another group received placebo auricular acupuncture and the last group had placebo auricular seeds. Eleven patients were excluded from the study analysis because of refusal to continue and violation of protocol for change in analgesics. Intensities of pain, measured using a visual analogue scale were assessed at baseline, 1 and 2 months from randomization. Patients in the true acupuncture group reported lower pain scores at 2 months compared to baseline than the other two placebo groups ($p < 0.001$). While the result of this trial was conclusive, the trial also highlighted common issues in conducting placebo trials with acupuncture. Acupuncturists who performed the assigned treatments were not blinded since it would have been difficult to be 'blinded' to putting needles and seeds. Unlike most randomized trial designs, acupuncture points formulas were not used since it is considered inappropriate in acupuncture practice that advocates individualized treatment approach that is believed to be more clinically effective. This trial also demonstrated the usefulness and convenience of using a 'microsystem' acupuncture technique alone for cancer-related pain.

In a prospective, open label, randomized controlled trial, Pfister et al. (2010) demonstrated that acupuncture may effectively reduce the moderate or severe pain in patients after neck dissection and radiotherapy. Seventy patients were randomized into acupuncture plus usual care and usual care alone. Hegu (LI4), Sanyinjiao (SP6), Baihui (GV20), Luozhen and auricular Shenman were used in all patients and were chosen based on classical functions. Local Ashi points and distal 'zone' points were also used on an individual basis. At 6 weeks after acupuncture, Constant-Murley Scores that measure pain, pain free range of motion and level of daily activities were significantly higher by 11.3 points in the acupuncture group compared to control ($p = 0.008$).

Crew et al. (2010) reported on a randomized controlled trial that compared acupuncture *vs* sham acupuncture in breast cancer patients with arthralgia and joint stiffness due to aromatase inhibitors. A total of 43 patients were recruited into the trial. The acupuncture treatments were delivered according to standard protocols. Individualized points for specific painful joint areas were allowed. Mean pain scores were decreased significantly in the acupuncture group compared to that of control (3.0 *vs* 5.5; $p < 0.001$).

Another randomized and again unblinded trial conducted by Dang and Yang (1998) focused on patients with stomach cancer who presented with cancer-related pain. Forty-eight patients were randomized into three groups: acupuncture with filiform needles alone, acupuncture with filiform needles plus point injections and control. Compared to the control group, the authors concluded that acupuncture treatments decreased pain significantly in the short-term after treatments. However, there was no significant difference in pain control in the long-term. There was also significant difference in the enkephalin plasma level before and after acupuncture treatments between the treatment group and the control group, supporting the observed effectiveness of these acupuncture treatment approaches.

In another randomized unblinded study (Xia et al. 1986), 76 patients with either lung, esophageal or stomach cancer-related chest pain were randomized equally into acupuncture treatment or control group. An energetic point, Zusanli (ST36) and a parasympathetic point, Neiguan (PC6) were used in all patients in combination with body points selected according to symptom patterns. The chest pain in all patients in the treatment group but not in the control group was alleviated or disappeared.

Given the lower methodological qualities of randomized controlled trials conducted, several research groups have utilized systematic review to explore the efficacy of acupuncture treatments in reducing cancer-related pain (Lee et al. 2005; Peng et al. 2010; Paley et al. 2011). The Cochrane review conducted by Paley et al. (2011) was the most recent updated attempt to review this efficacy issue. This review concluded that there was a lack of high quality studies to provide strong evidence to support the positive efficacy of acupuncture in cancer-related pain reduction. More appropriate designed randomized studies are needed to clarify this efficacy question. However it is likely that a long period will be needed for these randomized studies to be designed, conducted and analyzed. Given that there are so many different acupuncture approaches that can be effective to manage cancer-related pain, the complexity and the practicality in examining all available approaches can be a major barrier in

generating scientifically sound evidence to support acupuncture as an evidence-based option of cancer pain control.

In the meantime, well conducted prospective cohort and case controlled studies involving smaller number of patients such as those performed by Wong and Sagar (2006), Filshie and Redman (1985), as well as Paley and Johnson (2011) in examining acupuncture approaches for cancer pain will continue to offer insight and guidance in using acupuncture for cancer-related pain.

Continuous research in the efficacy of various acupuncture approaches for controlling cancer-related pain should be advocated. Acupuncture practitioners should keep themselves aware of the evidence that is based on well designed research results and continue to offer acupuncture as an option for cancer pain management. Convenience in treatment delivery, proven efficacy and practitioners training should be the basis in considering the types of acupuncture approach to be used for patients with cancer pain. When particular symptom pattern is recognized, selection of appropriate acupuncture points such as Qihai (CV6), ST36 can be used first, to improve deficient energy status. Points, preferably distal rather than close to the area of pain, selected from the involved meridian(s) can then be utilized to improve the 'energy flow' of the affected meridian(s). The addition of stimulating points, for example, LI4, sympathetic point and PC6, parasympathetic point, that are known to have analgesic effects can enhance the overall treatment results. A review of the recent Chinese publications regarding the usage of acupuncture and moxibustion in cancer pain provides an overview of the current pattern of practice (Huang 2011a).

5.2.2 Moxibustion for Cancer Pain

Moxibustion is a traditional Chinese medicine treatment modality that uses the heat produced by the burning of herbal preparations containing *Artemisia vulgaris*, instead of using needles, to stimulate acupuncture points (WHO Regional Office for the Western Pacific 2007). The herbal preparation is either formed into a small cone called moxa cone or into a cylinder shape called moxa stick. Moxibustion treatment is carried out either by directly burning moxa cone on the skin, or indirectly by burning moxa cone on a skin barrier made of various materials (for example, ginger and salt), or by burning a moxa stick to apply heat to acupuncture points without direct skin contact. Moxibustion is viewed to be important in traditional Chinese medicine practice in managing conditions that are diagnosed to have 'cold' or 'dampness' symptom pattern components or when sluggish or blockage of energy is perceived in a meridian. It is also utilized frequently for tonification of energy for weak patients. Since, the presence of pain represents a blockage of energy in the painful area, moxibustion has been advocated to treat cancer-related pain. Heat generated by moxa combustion helps to improve circulation of blood and energy in the body and *Artemisia vulgaris* that makes up the moxa cone itself has energy and blood motivating properties. Energetic points such as ST36, CV6 and Shenque (CV8) are common points for moxa treatment (Cheng 1987).

5.2.2.1 Mechanisms Also Exist to Support Moxibustion for Pain

Moxibustion, performed in various forms, has been shown to affect physiological functions. Microcirculatory changes with increase in local and whole body capillary blood flow were observed with moxibustion (Huang et al. 2011b). This increase in blood flow may help to alleviate inflammation that commonly occurs in cancer bearing areas (Laird et al. 2011). Autonomic nervous system activities were also influenced by moxibustion treatment with relative increase in parasympathetic activities (Litscher et al. 2009). Moxibustion may work through a correction of the autonomic nervous system activities by reducing the influence of the sympathetic nervous system, the chronic activation of which has been suggested to perpetuate pain and worsening pain experiences (Cho et al. 2011). Like acupuncture, moxibustion alone was shown to induce an increase secretion of endogenous morphine-like substances: endomorphin and dynorphin (Liu et al. 2010; Ma et al. 2010).

5.2.2.2 Some Clinical Evidence Suggests Moxibustion Is Effective

It is not surprising to find that there was no randomized placebo controlled trial conducted to provide good evidence that moxibustion can improve pain compared to placebo since it is not possible to generate acceptable placebo for a treatment involving heat sensation of a certain temperature range. In the few trials examining moxibustion in managing benign painful conditions reported in the literature, all adopted a comparison of moxibustion *vs* other interventions instead of a placebo (Chen et al. 2008; Su et al. 2009; Sun et al. 2009; Xu et al. 2009; Ma et al. 2010). Results of all these trials have suggested that moxibustion is effective in managing pain, but because of the poor study design of most trials, a recent systematic review still failed to provide concrete evidence of this treatment approach in managing benign painful conditions (Lee et al. 2010a).

In regards to the use of moxibustion in cancer-related pain, there was no clinical trial using moxibustion as a single treatment modality reported in the English literature. In the three published trials identified, all utilized moxibustion in combination with another active intervention in the treatment arms, Bian et al. (2004) examined the effectiveness of moxibustion and acupuncture and morphine injections compared to conventional morphine injections alone for cancer-related pain in 44 patients using a randomized trial design. The moxibustion combination group was shown to have better quality of life and better pain control. In another randomized study (Zhang (2007), 72 patients suffering from herpes zoster, a not uncommon condition experienced by cancer patients, were divided into two groups. The treatment group received acupuncture plus moxibustion and a control group received no active interventions. The herpes lesions were resolved within 3 days after treatments in 97% of patients and related symptoms including pain were demonstrated to be significantly better in the treatment group.

In a recent reported multicenter trial, 120 patients with herpes zoster infection were randomized equally into two groups. The treatment group was treated with

plum blossom needles to the lesions and selected acupuncture points followed by cotton sheet moxibustion, while the controlled group was treated with antiviral treatment using acyclovir cream on the affected areas and oral valaciclovir hydrochloride and vitamin B1. At 7 days post treatment, 80% of patients in the treatment group was reported cured of their herpes lesions compared to 45% in the controlled group. Pain, duration of blister and scarring and the overall duration for healing were all significantly shorter in the treatment group. However, the technique of cotton sheet moxibustion that aims to apply heat directly to the herpes lesions instead of acupuncture points may suggest the positive results of this trial attritbuted to some form of hyperthermia treatment and not traditional moxibustion (Yang et al. 2012).

To date there was no good evidence to show moxibustion alone improves cancer-related pain management. The use of moxibustion should be used as an adjunct treatment to other interventions with proven efficacy. Moxibustion should also be used according to the traditional guidelines within the scope of Chinese medicine practice. Again prospective cohort data should be systematically obtained for continuous analysis and to further provide evidence and guidance in utilizing this treatment modality for cancer-related painful conditions.

5.2.3 Acupuncture-Like Transcutaneous Nerve Stimulation May Be an Option for Some Patients

Non-invasive approach using transcutaneous nerve stimulator (TENS) has the advantage of easy treatment delivery by staffs or by patients themselves after minimal training. Using low frequencies (< 10 Hz) and high intensity stimulation over acupuncture points, acupuncture-like TENS (ALTENS), was found to mimic acupuncture treatment in that the Deqi sensation in real needle acupuncture can be elicited at the acupuncture points. It is known that ALTENS mainly stimulates α-delta and C fibres and is believed to achieve pain control by activating the descending pain suppression system and by the release of endorphins. In chronic pain conditions, ALTENS has been suggested to provide more effective pain control than placebo, and improves function more than standard TENS, though a meta-analysis failed to show conclusive evidence (Gadsby and Flowerdew 2000; Carroll et al. 2001). In a recent Cochrane review that only include three small randomized studies with two using conventional TENS and not ALTENS (Hurlow et al. 2012). The other study compared ALTENS and sham ALTENS for cancer pain or nausea and vomiting. There were only 15 patients included. The conclusion of this review indicated that there is insufficient evidence to support, (or refute) the effectiveness of TENS in cancer pain management.

At the Juravinski Cancer Centre (Hamilton, Canada), ALTENS (with a random electrode stimulation set up for minimizing brain habituation) is being offered as one of the options for patients with cancer-related pain that is not controlled by optimal analgesics or radiation therapy. Unpublished data suggested positive benefit for ALTENS as an adjunctive treatment for cancer pain control.

5.3 Nausea and Vomiting

One of the commonest symptoms cancer patients often experience is nausea and vomiting. The presence of this symptom not only affects patient's quality of life but also can be a limiting factor for cancer treatments. Multiple causes have been shown to contribute to the occurrence of nausea and vomiting in cancer patients. These include pharmacological, visceral, intestinal, central nervous system and vestibular causes (Fessele 1996). Although, pharmacological causes, mainly related to chemotherapies and narcotics, account for most incidence of nausea and vomiting, a throughout assessment to exclude possible causes, other than pharmacological ones, is important to ensure appropriate management is initiated. It is obvious that nausea and vomiting that is caused by mechanical intestinal obstruction or intracranial space occupying lesion is not expected to be relieved by pharmacological or acupuncture techniques. Delay in initiating appropriate treatments can lead to undesirable consequences.

5.3.1 Acupuncture

5.3.1.1 Mechanisms Exist Showing Acupuncture May Work for Nausea and Vomiting

Vomiting centre situated in an area in the medulla, integrates afferent stimuli from various sources, creates nausea sensation and initiates the vomiting reflex. These afferent stimuli include nervous signals from a special chemoreceptor trigger area, situated on the floor of the fourth ventricle, which responds to chemicals like chemotherapy agents or opioid-like substances, serotonin and histamine. Stimuli from cerebral cortex, cerebellar and vestibular nuclei also influence this centre (Streitberger et al. 2006).

Mechanisms by which acupuncture can lessen nausea and vomiting have been suggested by several clinical studies. In a study using acupuncture on PC6, a common acupuncture treatment point for nausea and vomiting, has shown that vagal activities that may suppress the vomiting centre, are significantly enhanced in the treatment group when compared to a sham acupuncture group (Huang et al. 2005). Modulation of serotonin and endogenous opiod systems through acupuncture activation of the serotonergic and noradrenergic fibers has also been observed (Mao et al. 1980; Han and Terenius 1982). Direct and indirect influence of stomach and gut smooth muscle activities with facilitated gastric emptying, gastric relaxation and suppression of retrograde peristalsis have also been suggested (Shiotani et al. 2004; Tatewaki et al. 2005). Functional magnetic resonance study showed that the cerebellar vestibular system activities are influenced by PC6 acupuncture but not by sham acupuncture (Yoo et al. 2004) (Fig. 5.1).

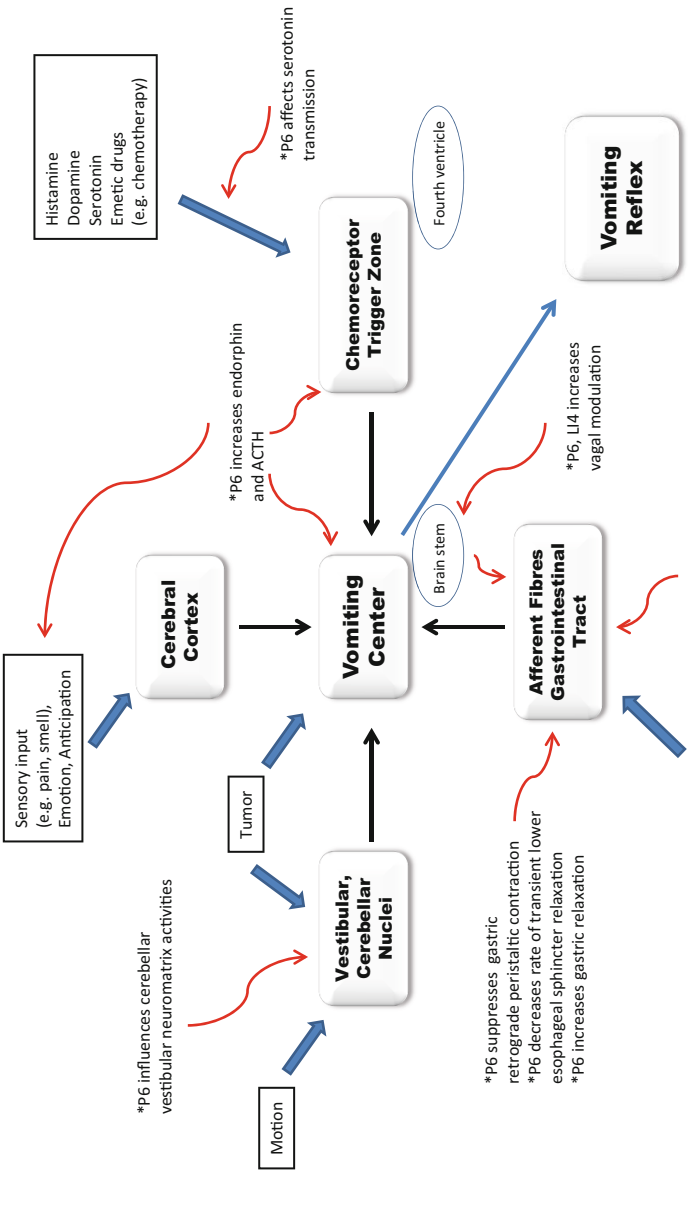

Fig. 5.1 Proposed mechanisms of action of acupuncture for nausea and vomiting. *ACTH* adrenocorticotropic hormone

5.3.1.2 Extensive Evidence Supports Acupuncture for Nausea and Vomiting

Extensive studies have been conducted and most reported positive effects of acupuncture for nausea and vomiting due to various causes. Over the last two decades, several meta-analysis and systematic reviews of randomized controlled trials were reported and continue to show acupuncture given alone or in combination with anti-emetic medications can provide better nausea control compared to control or anti-emetic medications (Vickers 1996; Lee and Done 2004; Ezzo et al. 2006; Lee and Fan 2009). These results have also led to the 1998 NIH (US) consensus statement that, "acupuncture is a proven effective treatment modality for nausea and vomiting".

The effect of PC6 acupuncture in managing nausea and vomiting has been mostly studied. Dundee et al. was the first group to show the use of PC6 alone increases the anti-emetic effect of drugs for peri-operative and chemotherapy-induced nausea and vomiting (Dundee et al. 1991). In a more recent meta-analysis of 26 randomized controlled trials examining acupuncture for postoperative nausea and vomiting, PC6 stimulation with acupuncture, acupressure or electrical stimulation was concluded to be effective in preventing postoperative nausea (RR 0.71, 95% CI of 0.61 to 0.83). PC6 stimulation when used with anti-emetic drugs was also found to reduce the risk of nausea, but not vomiting, when compared to anti-emetic drugs alone. There was no difference in the risk of postoperative nausea and vomiting between acupuncture and anti-emetic drugs. Side effects were minimal (Lee and Fan 2009). Invasive and non-invasive acupuncture on PC6 should be considered as an option for reducing the risk of postoperative nausea and vomiting (Gan et al. 2003).

In chemotherapy-induced nausea and vomiting, similar effectiveness of acupuncture point stimulation was identified in a systematic review of eleven randomized trials (Ezzo et al. 2006). However, the review suggested that electroacupuncture effectively reduced acute chemotherapy-induced nausea and vomiting but non-invasive electroacupuncture is not effective. Acupressure may be able to prevent acute nausea. This review also questioned the clinical relevance of acupuncture approaches when state-of-the-art anti-emetic medications are used. In a more recent randomized trial of acupuncture in a small pediatric cancer population, requirement for rescue anti-emetic medications was reduced in the acupuncture and anti-emetics group compared to anti-emetics alone group. The number of vomiting episodes was also shown to be reduced significantly in the treatment group (Gottschling et al. 2008).

Based on the available evidence, acupuncture should be considered as an option for managing postoperative and chemotherapy-induced nausea and vomiting, and should be used in combination with state-of-the-art anti-emetic medications. Electroacupuncture on PC6 should be recommended, however, acupressure on PC6 is still advisable if electroacupuncture is not practical. ST36 acupuncture point can be utilized in combination with PC6 to potentially improve treatment results (Ma 2009). ST36 should also be considered in patients considered to have 'low energy' since stimulation of this point has been considered to improve overall energy of a patient. According to acupuncture practice, overall energy should first be improved before direct symptoms management; otherwise, acupuncture treatment may not be as effective.

Various acupuncture points alternatives other than PC6 have also been suggested to be effective in managing nausea and vomiting according to some published reports (Shen et al. 2000; Somri et al. 2001; Ming et al. 2002; Gottschling et al. 2008). Korean hand acupuncture points K-K9 and K-D2 have also been shown to be viable alternatives (Schlager et al. 2000; Boehler et al. 2002).

5.3.2 Moxibustion for Nausea and Vomiting

5.3.2.1 Proposed Mechanisms by Which Moxibustion May Work for Nausea and Vomiting

Possible mechanisms by which moxibustion may exert beneficial effects in nausea and vomiting managements have been proposed. However, research in this area is still very limited. Moxibustion provides heat stimulation on acupuncture points in addition to the possible absorption of herbal extract through the skin. Treatment effects are likely mediated through mechanisms similar to that of acupuncture. Like acupuncture, moxibustion may modulate the activities of cortical and subcortical regions of the brain, brain stem areas and autonomic nervous system (Hui et al. 2000; Huang et al. 2005; Napadow et al. 2008).

5.3.2.2 Limited Evidence to Suggest Moxibustion for Nausea and Vomiting

Moxibustion as a single modality in managing nausea and vomiting has not been well studied. In a meta-analysis of moxibustion in cancer care (Lee 2010b), two small randomized studies have examined indirect moxibustion on CV8 in reducing chemotherapy-induced treatment toxicities in patients with nasopharyngeal cancers and gastric cancers as one of the study endpoints. In both studies, toxicities included nausea and vomiting were found to be significantly reduced with a combined risk ratio of 0.38 (95% CI of 0.22 to 0.65) (Cao et al. 1997; Chen et al. 2000). CV8 is the acupuncture point right on the umbilicus and needling is not advised for the fear of easy infection. This point is used in Chinese medicine to aim at treating abdominal, gynaecological and urinary symptoms, particularly in patients who present with ‘cold’ pattern (Wang, 2008).

Given the limited clinical evidence today, it is inconclusive in regards to the effectiveness of moxibustion alone for chemotherapy-induced nausea and vomiting. Adoption of this treatment modality should be used for selected patients according to traditional Chinese medicine practice and with appropriate precautions.

5.4 Postoperative Urinary Dysfunction

Patient underwent pelvic surgery for cancer commonly experience with urinary retention during the postoperative period as a result of bladder detrusor muscle dysfunction and reduced bladder sensation. This may lengthen hospital stay and increase the

chance of urinary infection due to prolonged urinary catheter insertion (Chen et al. 2010).

Two publications have shown electroacupuncture on body acupuncture points including Guilai (ST29), ST36, Tiaokou (ST38), SP6 and Waiguan (TE5), was able to improve urinary flow rate, reduced residual bladder volume and shorten postoperative hospital stay compared to controls (Shi et al. 2008; Yi et al. 2011). A third study in patients who suffered from acute urinary retention after rectal cancer surgery, also showed acupuncture on body points that affect energy flow of the bladder meridian improves urinary flow and relieve retention symptoms in over 90% of patients (Dong et al. 2003).

In another randomized trial in patients who developed urinary retention after radical hysterectomy, patients who were randomized to receive acupuncture on Shuidao (ST28), ST36, SP6, scalp reproduction area plus moxibustion on CV8 showed significant improvement in bladder function ($p < 0.05$) after one and two courses of treatments, compared to acupuncture point injection on ST36 and SP6 (Yi et al. 2011). Unfortunate, the study did not have a control group. This latter study, however, provide insight in the usage of moxibustion in combination with acupuncture may enhance clinical effectiveness. Addition evidence to further support the effectiveness of indirect moxibustion on CV8 in managing urinary dysfunction was provided in another study. Stroked patients with urinary dysfunction were randomized to ginger-salt indirect moxibustion on CV8 and acupuncture. Urinary function in patients of the moxibustion group, including a reduction in urinary incontinence, was found to be significantly better than that of acupuncture group (Liu and Wang 2006).

5.5 Radiation-Induced Xerostomia (RIX)

Xerostomia, or dry mouth, remains a common complication of radiation treatment for head and neck cancers. Despite the use of more advanced radiation techniques that are able to reduce radiation dose to major salivary glands while delivering a radical dose to the cancer areas, up to 30% of patients still suffer from xerostomia and its associated symptoms that include loss of taste, difficulty in speech and swallowing. Current treatments mainly rely on symptomatic relief with saliva substitutes and pharmaceutical salivary stimulants with no long lasting effect. Recent studies have demonstrated acupuncture approaches may be viable treatment modalities for this condition with sustained benefit.

5.5.1 Acupuncture

5.5.1.1 Mechanisms of Acupuncture for RIX

Acupuncture has long been used for dry mouth symptom in traditional Chinese medicine. Recent advances in research have shed lights on the possible mechanisms

by which acupuncture can have an effect on salivary production. Acupuncture has been shown to differentially affecting the autonomic nervous system activities with activation of the parasympathetic component that increases overall salivary production and deactivation of the sympathetic component that reduces salivary viscosity (Proctor and Carpenter 2007; Sakatani et al. 2010). Increase in blood flow to parotid glands and stimulation of glandular tissue regeneration of salivary glands have also been shown (Blom et al. 1992; Blom et al. 1993; Schneyer et al. 1993). The latter finding may explain the long-term benefits of acupuncture approaches in treating xerostomia as demonstrated in several clinical studies (Blom and Lundeberg 2000; Johnstone et al. 2002; Wong et al. 2003). In a fMRI study, stimulation of Erjian (LI2), a frequently utilized acupuncture point for xerostomia, has also been found to activate the insula region of the brain, the area associated with gustatory function, suggesting that acupuncture may act *via* the central nervous system resulting in a cascade of physiological events that lead to an improvement of salivary flow (Deng et al. 2008) (Fig. 5.2).

5.5.1.2 More Supportive Clinical Evidence of Acupuncture for RIX

After Blom et al. (1992) published the first report suggesting a positive effect of acupuncture for xerostomia, there has been a growing interest of research in evaluating different acupuncture approaches for this condition, particularly related to patients with RIX. The first randomized controlled trial of 38 patients with RIX divided into two groups: deep or superficial acupuncture treatments (Blom et al. 1996). Superficial acupuncture group was chosen to be the control despite previous evidence that superficial acupuncture may have certain degree of effectiveness and that should not be used as control for acupuncture study. Individualized body acupuncture points were utilized for the study. In this study, both groups showed a more than 20% increase in salivary flow rate in over 50% of patients after acupuncture treatments. In the treatment group, 68% of patients showed an increase in salivary flow rate compared to 50% of patients in the control group at one year. Moreover, the treatment group reported significantly greater improvement in symptoms with less dryness, less hoarseness and improved taste.

In another randomized controlled trial aimed to study the usefulness of acupuncture for pain and dysfunction in patients after neck dissection for cancers (Pfister et al. 2010). Over 80% of 58 patients recruited received radiation as a component of their treatments. Xerostomia inventory was set as a secondary endpoint of the study. Limbs acupuncture points were used including LI2 for xerostomia in the treatment group. Symptoms of xerostomia in the treatment group were found to be significantly reduced compared to that of the control ($p = 0.02$). Other prospective cohort studies are confirming the clinical usefulness of acupuncture for the relief of RIX (Rydholm and Strang 1999; Blom and Lundeberg 2000; Johnstone et al. 2001; Braga et al. 2008; Cho et al. 2008).

Interestingly, results from a few studies have suggested that acupuncture treatments may provide long-term improvement in symptoms related to RIX. In Blom

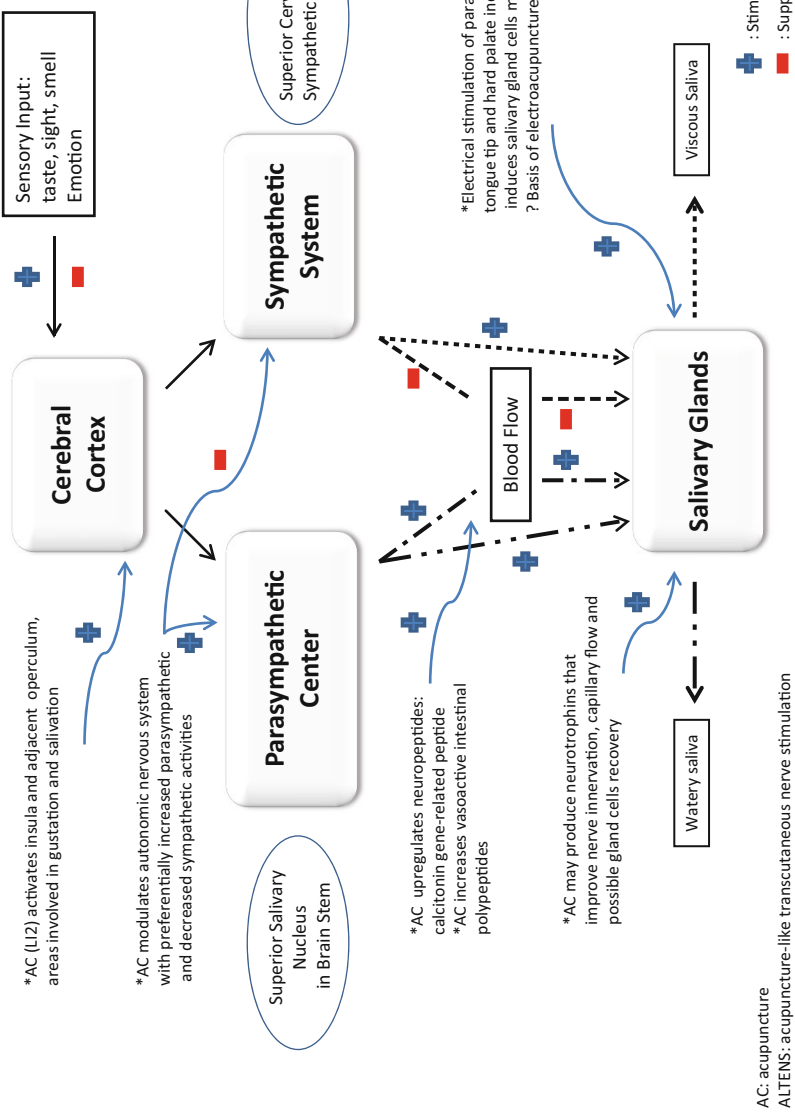

Fig. 5.2 Proposed mechanisms of action of acupuncture for xerostomia

et al's study of 70 patients with xerostomia due to either Sjögren's syndrome or radiotherapy treated with acupuncture, not only was there an increase in salivary flow rates observed immediately after acupuncture treatment, this increase were sustained up to 6 months follow up. At 3 years, patients who chose to have additional acupuncture treatment had consistently higher median salivary flow rate than those who did not have additional acupuncture. In another study (Johnstone et al. 2002), patients received initial weekly acupuncture treatments with ear points and LI2 for 3–4 weeks followed by monthly to bimonthly maintaining treatments were found to have sustained benefit.

Results of attempts in using acupuncture to prevent RIX have suggested positive outcomes. In a small randomized study involving only 24 patients who had radiation dose of greater than 5,000 cGy to over 50% of the parotid glands, the treatment group received acupuncture during radiation treatment and the control group had radiation treatment alone. Individualized body and auricular acupuncture points were used according to traditional Chinese medicine practice. Although all patients showed worsening of salivary function after radiation, there was significant difference in the mean resting and post stimulating salivary flow rates in favor of the treatment group. Xerostomia-related symptoms scores were also better in the treatment group (Braga Fdo et al. 2011). The small sample size of the study, however, had raised doubt in the study conclusion. Another larger randomized trial involving 96 eligible patients, also showed that patients received acupuncture during radiation treatment had reduced severity of xerostomia and maintained salivary flow rate better than those who did not have acupuncture (Meng et al. 2012). The beneficial effects were shown to occur as early as the third week and at 1 and 6 months after the completion of radiation. Unfortunately, the inclusion of only Chinese patients with nasopharyngeal cancers without advanced organ sparing radiation techniques made the results less generalizable. Further research in this prevention approach will be needed.

5.5.1.3 ALTENS: A Different Acupuncture Approach

Recognizing the possibility of fear for needle therapy in some patients and the possible difficulties in offering acupuncture treatments in conventional cancer clinics, at the Juravinski Cancer Centre, a different acupuncture-related approach was explored to manage RIX. In a Phase I and II study, preselected acupuncture points chosen according to traditional Chinese medicine principles were stimulated using acupuncture-like transcutaneous nerve stimulation (ALTENS) (Wong et al. 2003). Instead of needles, electrode pads applied on the skin overlying the acupuncture points were used for stimulation. Low frequency, high current intensity and random stimulation were used and treatments were given twice weekly for a total of 12 weeks. Salivary production, both basal and citric-acid primed, and xerostomia symptoms scores were all significantly improved in patients at 3 and 6 months after treatment completion. There were also improvement in swallowing, speech and taste. Built on these positive study results, a Phase II and III multicenter randomized study comparing ALTENS to oral pilocarpine, the current standard management, in

treating established RIX was initiated by the Radiation Therapy Oncology Group (Wong et al. 2012). Acupuncture points used were Chenjiang (CV24), ST36, SP6 and LI4 selected based on the results of previous mentioned Phase II trial. The study has completed the required accrual of 190 patients quickly with a rate of 6–8 patient recruited per month suggesting high acceptance of this treatment modality by both patients and care providers in conventional clinical settings. The results of the Phase II (non-randomized) component of this study were reported recently demonstrated a 94% compliance rate for ALTENS treatments. At 3 months after randomization, 84% of the evaluable 35 patients achieved a positive treatment response with an improvement of xerostomia specific quality of life scores of 35.9%.

The results of a trial to examine ALTENS in preventing RIX were disappointing. In a Phase II randomized trial involving 60 patients who were to have conventional radiation treatment for head and neck cancers, ALTENS were given concurrently during radiation in the treatment group while the control group only had standard mouth care (Wong et al. 2010). ALTENS failed to exert any detectable differences in the mean salivary flow rate or xerostomia symptoms scores in the treatment group when compared to the controls. It was postulated that the acupuncture points stimulation that may induce salivary gland tissue regeneration during radiation may, in theory, render the glandular cells more sensitive to radiation damage and negate the beneficial effect of improved salivary function. The small sample size of the study may also be a factor affecting the results and the interpretation of the study conclusion.

5.5.2 Moxibustion Is Not Indicated

In traditional Chinese medicine, moxibustion is mainly used for 'cold' patterns since the warmth of burning moxa and the 'warm' nature of the herb, *Artemisia vulgaris* can drive the 'cold' away and promote blood and energy flow. In fact, there is description that moxibustion can cause dry mouth and is not advisable to be given in patients with 'heat' symptoms. A search in the literature has failed to show any reported study to investigate the effect of moxibustion in xerostomia conditions (Gu 1996).

5.6 Radiation Proctitis

Radiation proctitis is an inflammatory condition of the rectal mucosa as a result of radiation damage. This condition is seen often in patients receiving radiation treatment for pelvic cancers, particularly for prostate and cervical cancers, since high radiation dose volume will likely include the anterior portion of the rectum. Acute proctitis will usually subside after a few months but up to 5% will become chronic. Only one study investigated acupuncture as a treatment modality for radiation proctitis has been published (Zhang 1987). Forty-four cervix cancer patients who received radiation treatment and developed radiation proctitis were treated with acupuncture. 73%

of patients had complete response and marked reduction in symptoms was seen in 9%. At the Juravinski Cancer Centre, weekly acupuncture treatment on GV20 during the third to fifth week of radiotherapy has been offered to patients with locally advanced rectal cancers undergoing chemoradiation treatment and who presented with severe symptoms of tenesmus, increased rectal mucous secretion and bleeding. Preliminary experience in 24 patients showed marked improvement in patients' reported symptoms after one to two treatments (unpublished data). A formal in-house study is being planned. GV20 is indicated in traditional Chinese medicine for treating organs prolapse and to reduce leakage symptoms.

5.7 Quality of Life in Lymphoedema

Lymphoedema is a debilitating and disfiguring condition as a result of damage to the lymphatic drainage of part of the body. It commonly occurs in the limbs of patients who have had cancer treatments that cause damage to the axilla or groins. In one study on breast cancer patients, a prevalence of 29% was reported (Moffatt et al. 2003). Acupuncture directly on the affected area should be avoided to prevent the introduction of infection that may result in serious consequences. However, there is no contraindication to acupuncture in patients who have lymphoedema (Filshie 2001).

Recent experience in using acupuncture and moxibustion in the management of lymphoedema was reported with promising results. Kanakura et al. (2002) reported that acupuncture and moxibustion applied right after surgery or after the occurrence of lymphoedema in 24 patients who underwent pelvic lymph node dissection can prevent and improve the condition. However, measurements of lymphoedema used in the study were largely subjective.

Using traditional Chinese medicine principles to develop a acupuncture treatment protocol, Alem and Gurgel (2008) conducted a study on 29 breast cancer patients who suffered from lymphoedema of the upper limbs. Eleven acupuncture points were needled, without electrical stimulation, from the upper limb down to the leg on the unaffected contra-lateral side of the body. Jianyu (LI15), Jianliao (TE14), Chize (LU5), TE5 and LI4 were used for pain, heaviness and restricted movement of the upper limb; Zhongwan (CV12), Zhongji (CV3) and Qugu (CV2) for improved energy and increase lymphatic drainage; ST36, Yinlingquan (SP9) and SP6 for reducing oedema and promote "blood" flow. Twenty-four treatments were given once a week and no other interventions were given. Compared to baseline assessments, there were significant improvements in shoulder range of motion, degree of lymphoedema and sense of heaviness and tightness at 6 months. Interestingly, the degree of lymphoedema that was based on the skin characteristics, limb consistency and visual inspection showed improvements, circumferential measurements of the lymphoedematous limbs were not found to be significant. Logically, one would not expect that acupuncture approaches can correct anatomical damage and mechanical obstruction of lymphatics. The common presence of fibrosis in the affected limb will further prevent limb volume reduction.

Further study has demonstrated the feasibility of using acupuncture and moxibustion to treat cancer patients with upper body lymphoedema. Thirty-five subjects including breast cancer patients and head and neck cancer patients were managed with individualized acupuncture and moxibustion. Overall well being status of the patients was assessed using Measure Yourself Medical Outcome Profile. There was no significant adverse effect reported. Significant better well-being profile was noted after treatments. The authors concluded that acupuncture and moxibustion can be safely delivered to patients with lymphoedema provided that needling is avoided in the affected area (de Valois et al. 2011).

5.8 Cancer-Related Fatigue

Fatigue is a very common problem experienced by cancer patients and very often patients continue to have this symptom for a long time beyond active treatments (Wagner and Cella 2004). The underlying mechanism by which cancer-related fatigue occurs is not fully known. Apart from some correctable causes, for example, anemia, there is no effective treatment. Acupuncture and moxibustion approaches have been investigated for managing this distressful condition.

5.8.1 Proposed Mechanisms

Since the mechanisms by which cancer-related fatigue occurs is still not clearly known, any proposed mechanisms that acupuncture and moxibustion may act through are only theoretical. Fatigue has been found to be associated with changes in cytokine and hormonal levels and through modulating cytokines and hormonal secretions, acupuncture can play a role in treating fatigue (Glaus 1998; Stone et al. 1998). Study on human subjects who were experiencing fatigue also showed that overactive sympathetic activities are common in fatigue state. Acupuncture can modulate autonomic nervous system activities with preferential suppression of sympathetic activities and may lead to improvement of fatigue (Li et al. 2005).

5.8.2 Evidence Is Still Limited

To date, several studies have investigated the usefulness of acupuncture and moxibustion in managing this distressful symptom with mixed results. A Phase II study examined acupuncture for post chemotherapy fatigue that had lasted on average of 2 years, showed a mean improvement of 30% on the Brief Fatigue Inventory assessment (Vickers et al. 2004). Twice per week acupuncture treatments for 4 weeks were given for one cohort. Points that are indicated for fatigue in traditional Chinese medicine were used. These included classical energy points: ST36, Guanyuan

(CV4), CV6 and also Diji (SP8), SP9 and Quchi (LI11). For a second cohort, once weekly treatment for 6 weeks were delivered. Points included CV4, CV6, ST36, Taixi (KI3), Shufu (KI27) and SP6. There was no apparent significant difference in treatment responses between the twice weekly or weekly treatment.

In a small randomized controlled trial comparing acupuncture, acupressure and sham acupuncture in treating post chemotherapy fatigue in 47 cancer patients (Molassiotis et al. 2007). Results demonstrated significant improvement of the severity of fatigue measured by Multidimensional Fatigue Inventory in both the acupuncture (36%) and acupressure group (19%) compared to the sham acupuncture group (0.6%). Acupuncture provided higher fatigue relief than acupressure. Again, like the previous study, similar acupuncture points were used: ST36, SP6 and LI4. Patients, however, were treated three times per week for 2 weeks. More treatments were found to provide more sustained fatigue improvements.

In another randomized, double-blinded, controlled trial, 27 patients undergoing radiation therapy for cancers were randomized into a acupuncture and a sham acupuncture group (Balk et al. 2009). Typical acupuncture points including ST36, SP6, LI4 and KI3 were used given once to twice a week for 6 weeks. Non-penetrating needles were used for sham treatments. Although in both sham and true acupuncture groups, there was improvement in fatigue, there was no significant difference between the responses of the two groups. The result of this trial again cast some doubt in the effectiveness of acupuncture treatments in cancer-related fatigue but the sample size of this trial is far too small to make the results conclusive.

Traditionally, moxibustion is indicated to 'tonify' or to improve energy level of an individual. Indirect moxibustion on 'energy' points, ST36, CV4, CV6 and KI3 is usually recommended (Gu 1996). Adding moxibustion to acupuncture seems to be a logical choice to increase the probability of treatment success in cancer-related fatigue. Experiences in treating chronic fatigue using this strategy have suggested greater than 80% effectiveness (Wang et al. 2008a). However, this experience may not be completely generalizable to cancer-related fatigue. There is still no reported clinical trial investigating moxibustion alone in managing cancer-related fatigue.

5.9 Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) occurs in 10–20% of patients who received neurotoxic chemotherapies including platinum compounds, vinca alkaloids, taxols and suramin (Forman 1990). With increasing indications of these chemotherapies and better survivals of cancer patients, the prevalence of CIPN is likely on the increase. Different components of the peripheral nervous system can be affected, but axonal degeneration is the commonest. Sensory neuropathy is predominant, while sensory-motor and autonomic nervous system dysfunction is less common. Patients usually present with numbness, paraesthesia, pin and needle sensation, and pain that is hard to describe but usually described in terms of burning, shooting or electric in nature. Impaired vibrational sense is common. There can be

associated ataxia, myalgia and muscle weakness. CIPN symptoms can appear during the later courses of chemotherapy and can occur weeks or months after completion of chemotherapy (Windebank and Grisold 2008). Although peripheral nerve damages can recover in most patients, the recovery is usually incomplete with persistent symptoms resulting in poorer quality of life. Treatments for CIPN are largely for symptomatic relief of pain and paraesthesia. Centrally acting drugs like tricyclic anti-depressant, ion channel blockers have been shown to be moderately effective but with significant side effects that may limit their practical usefulness. Moreover, the beneficial effects are not long lasting, symptoms reoccur once medications are discontinued.

5.9.1 Evidence from Clinical Trials Continue to Support Acupuncture Usefulness

Approach in treating syndrome pattern that includes paraesthesia, hyperalgia, pain, pin and needles in both feet and hands has been described in TCM. The symptoms presented by patients with CIPN can be considered as a state with deficiency in energy and blood, and that the body is unable to direct these essential components to the four limbs resulting in sensory and motor dysfunctions.

Acupuncture treatments that aim to improve total energy and blood in the body and direct them to the limbs have been shown to be clinically effective. In recent clinical trials, acupuncture has been shown to improve symptoms due to peripheral neuropathy in HIV and diabetic patients (Abuaisha et al. 1998; Phillips et al. 2004). The first reported study on acupuncture for CIPN was reported by Wong and Sagar (2006) at the Juravinski Cancer Centre. This prospective pilot study involved patients with CIPN after combined taxol and platinum chemotherapies for gynaecological cancers treated with a selected acupuncture protocol. Five consecutive patients with WHO grade II CIPN symptoms were recruited. Mean duration of symptoms was 18 months (ranged from 6–38 months). Pain, pin and needle sensation and numbness of the hands and feet were the main presenting symptoms. In three patients, imbalance in gait was also present. After acupuncture treatments, marked improvement in pain was noted with average pain score came down from 7.8/10–3/10. All patients had a reduction in analgesic dosage. Gait was improved in all the three patients. Numbness and pin and needle sensation were significantly better. At 6 months follow up, symptoms improvement was sustained in four patients. Although the number of patients in this study was small, the results suggested acupuncture can be useful in CIPN. A Phase II study at the Juravinski Cancer Centre examining the effectiveness of acupuncture alone or ALTENS alone in CIPN management has completed recruitment. Results of the preliminary analysis were presented at the International Scientific Acupuncture and Meridian Symposium and continued to show that acupuncture or ALTENS using a selected protocol acupuncture points improved symptoms of CIPN at three months follow-up. Complete analysis is pending to be completed in 2012.

Follow the reported study by Wong and Sagar (2006), a few other pilot studies were conducted with results supporting the effectiveness of acupuncture in CIPN. In one study (Donald et al. 2011), 18 patients were treated with individualized acupuncture treatments with core acupuncture points including SP6 and ST36 similar to Wong and Sagar's study (2006). Improvement in symptoms especially in pain, and analgesic dosage were noted in 14 patients. In another study (Schroeder et al. 2011), six patients received acupuncture and best medical care were compared to a control group of five patients who received best medical care alone. All patients had nerve conduction study prior to interventions. Five patients in the treatment group had improvement in CIPN symptoms after acupuncture and all had improved nerve conduction studies while one patient in the control group showed improvement in nerve conduction study but no improvement in symptoms. With these positive pilot studies, a well designed randomized controlled trial is justified to clarify the efficacy of acupuncture in CIPN.

5.10 Vasomotor Symptoms Reduction

Vasomotor symptoms with hot flashes and sweating are common complications as a result of hormonal ablative therapies for breast and prostate cancer. Frequent hot flashes with associated fatigue, insomnia and irritability, were shown to adversely affecting quality of life (Oldenhave et al. 1993). Management of vasomotor symptoms involves hormonal replacement therapy and non-hormonal centrally active drugs including gabapentin, venalfaxine and anti-depressants (Bordeleau et al. 2007). However, their usage are often limited by associated side effects. Treatment of vasomotor symptoms in cancer patients remains a challenge and research for optimal non-hormonal approaches is continuously advocated.

5.10.1 Acupuncture Can Be Useful in Women Suffered from Vasomotor Symptoms

Acupuncture has been found to increase secretion of central β-endorphins, thereby potentially stabilizing thermoregulation and decreasing vasomotor symptoms (Filshie et al. 2005; Mayor 2008; Lee et al. 2009b). Sense of well-being was found to increase in women who underwent acupuncture as a result of enhanced brain serotonin, norepinephrine, and oxytocin activities (Nedstrand et al. 2006).

Uncontrolled small clinical studies have demonstrated improvement in vasomotor symptoms in breast cancer women; however, results are inconsistent (Borud et al. 2009a, 2010; de Valois et al. 2010). A retrospective audit of acupuncture and self acupuncture in 194 patients with breast or prostrate cancers showed up to a 50% reduction of hot flashes in some patients who successfully continued acupuncture for up to 6 years later (Filshie et al. 2005). A systematic review, conducted in 2008, of six randomized controlled trials of acupuncture compared with sham, hormonal

replacement therapy, or Effexor XR failed to show statistical significant difference, however reported decreases of hot flashes with the use of both true acupuncture and sham acupuncture (Lee et al. 2009b).

Results from newer randomized trials continued to support the effectiveness of acupuncture in vasomotor symptoms management. In a more recent reported randomized trial comparing acupuncture plus self-care to self-care alone in postmenopausal women suffering from hot flashes, hot flashes frequencies and intensities were found to be improved significantly in the acupuncture plus self-care group. The vasomotor, sleep and somatic dimensions of the Women's Health Questionnaires were also improved (Borud et al. 2009b). In another study with similar design for perimenopausal and postmenopausal women with hot flashes, acupuncture plus usual care was also found to significantly improve hot flashes and related symptoms compared to usual care alone (Kim et al. 2010).

Frisk et al. (2012) randomized 45 breast cancer patients suffering from vasomotor symptoms to electroacupuncture for 12 weeks or hormonal therapy for 2 years. Scores in Health-related Quality of Life and Women's Health Questionnaire were improved significantly from baseline in both groups. Numbers of hot flashes per day were reduced and all sleep parameters were enhanced. The authors suggested that electroacupuncture can be considered as an alternative treatment to hormonal therapy for hot flashed in this group of patients.

Acupuncture has been suggested to be an alternative treatment for vasomotor symptoms in women with breast cancers who were refractory to, or unable to tolerate other treatments (Deng et al. 2007; Walker et al. 2010).The Society of Integrative Oncology's evidence-based clinical practice guidelines indicated that although there is no strong evidence to support the use of acupuncture for treatment of hot flashes, it is, however, a safe, tolerable treatment and could be used to treat hot flashes failing conventional treatments (Deng et al. 2009).

To answer the question regarding what are the acupuncture points and approached that should be recommended in managing vasomotor symptoms, a recent consensus building conference was held involving ten acupuncture experts. Consensus was made for eight syndromes and about five indicative symptoms for each syndrome. The choices of acupuncture points used, however, were quite different and probably reflecting the different in approaches by different acupuncture schools for the same clinical problem (Alraek et al. 2011).

5.10.2 Acupuncture Usefulness for Man with Vasomotor Symptoms Is Less Conclusive

A systematic review of acupuncture for vasomotor symptoms in prostate cancer patients has failed to show supportive evidence that acupuncture can exert a positive effect in reducing vasomotor symptoms (Lee et al. 2009c). However, this systematic review only included one randomized study and five uncontrolled studies reported prior to 2009 and that meet the study criteria. More studies, unfortunately, all uncontrolled, have been reported and suggested that acupuncture can provide relief

in vasomotor symptoms in patients who underwent androgen ablative therapies for prostate cancers (Harding et al. 2009; Beer et al. 2010; Ashamalla et al. 2011). Further well designed trials are needed to clarify acupuncture usefulness in this condition.

5.10.3 Moxibustion Can Be Useful

To date, there is only one randomized trial conducted to examine the effect of moxibustion alone in vasomotor symptoms in post menopausal women. In this trial, 51 patients were randomized into three groups: Group A in which moxibustion was based on clinical expert opinion. In this group, CV12, CV4, bilateral ST36 and SP6 were used. These points were indicated for improving physical function and to treat gynecological diseases. Group B in which moxibustion was based on published literature. In this group, Mingmen (GV4), CV4, CV6 and bilateral Shenshu (UB23) points were used. Group C was the control waiting list. Treatment groups A and B were found to have significant reduction in the frequency (60% reduction *vs* increased frequency in the control group) and severity (40–50% reduction) of hot flashes. Group B also had significant better scores on the Menopausal-Specific Quality of Life Scale compared to the other two groups (Park et al. 2009).

5.10.4 ALTENS Is Being Examined

At the Juravinski Cancer Centre, non-invasive acupuncture approach using ALTENS is being examined in treating vasomotor symptoms of breast cancer patients as a result of hormonal ablation therapies. Apart from working through mechanisms by which acupuncture may improve vasomotor symptoms, recent evidence has also suggested that ALTENS can stimulate a neuroreflex network involving the autonomic nervous system that participates in body temperature regulation (Haker et al. 2000). This Phase II randomized study will compare ALTENS plus standardized life-style interventions to standardized life-style interventions alone. Sixty-eight eligible patients with a Hot Flashes Score of > 15 will be randomized. Hot Flashes Scores, heart rate variability and quality of life will be assessed. The choice of acupuncture points to treat vasomotor syndrome was based on the traditional Chinese medicine (TCM) concept. This concept explains the occurrence of vasomotor syndrome according to its meridian and Zhangfu (organs) models. It conceptualizes that Zhangfu functions and overall meridian energy decline with increasing age. At around age 50, "kidney" function and its meridian energy start to become deficient. As "kidney" is the foundation that supports and interacts with other Zhangfus and meridians to work properly, its deficiency cascades into multiple dysfunctions and imbalances of bodily functions, particularly involving the "liver", "heart" and "spleen". In women present with vasomotor syndrome, the "liver" tends to become overactive causing symptoms of hot flashes, sweating, irritability, mood swings, headache, dizziness,

irregular menstrual flow, back discomfort and feeling of weakness in the knees. The "heart" also becomes overactive manifesting with palpitation, chest tightness, insomnia, and feeling of heat in the face, palms and soles. On the other hand, the "spleen" like the "kidney" becomes deficient resulting in decreased appetite, loose stool, cold hands and feet, fluid retention with swollen face and limbs, and generalized fatigue. The lack of "blood" during this period has also been viewed as a contributing factor to multiple symptoms.

TCM acupuncture treatment approach for vasomotor syndrome thus aims to improve "kidney" and "spleen" deficiencies and, at the same time, suppress "heart" and "liver" overactivities. The promotion of "blood" is also utilized to achieve symptom control. Selection of acupuncture points was based on a review of the published clinical studies identified through PubMed, non-PubMed and acupuncture texts describing experiences in treating vasomotor syndrome using body acupuncture points (Cheng 1987; Wyon et al. 2004; Huang et al. 2006; Zhou et al. 2006; Nir et al. 2007; Vincent et al. 2007; Avis et al. 2008; Kim et al. 2010). Shenshu (BL23), SP6, Xuehai (SP10), Taichong (LR3), Shenmen (HT7) and KI3 were selected and will be treated using ALTENS two times a week for 12 weeks. If this study results were positive, this may provide yet another approach utilizing acupuncture principles and may provide more options for patient care and further research.

5.11 Chemotherapy-induced Cognitive Dysfunction

Sixteen to fifth percent of cancer patients who received chemotherapy may develop cognitive impairment that can be long lasting for up to 10 years after treatments were completed (Tannock et al. 2004). The role of acupuncture for chemotherapy-induced cognitive impairment is not clear. In an animal study, acupuncture was shown to improve cognitive impairment caused by multi-infarcts of the brain (Yu et al. 2005). Johnston et al. (2007) has proposed that evidence exists to suggest acupuncture may be effective in managing this condition since it has been shown to provide benefit to a range of psychoneurological symptoms that are similar to those experienced by patients with chemotherapy-induced dysfunction. There was no reported study of moxibustion in this condition. Obviously, with the increasing prevalence of cancer patients who underwent successful chemotherapies, investigations for effective treatment options for this condition are increasingly necessary.

5.12 Myelosuppression

Myelosuppression is a common complication of chemotherapy treatments. It also occurs when significant amount of bone marrow is radiated to a certain dose. Patients, especially elderly who develop myelosuppression have increased risk of infection, bleeding and anaemia that not only can limit chemotherapy dosage but also can lead to

significant treatment-related morbidities, mortalities and poor quality of life. Moreover, the lowering in immunological function can adversely affect cancer treatment outcomes. Current treatment has to rely on the use of expensive recombinant human granulocyte-colony stimulating factor (G-CSF) and transfusion of blood components, all with associated side effects.

Traditional Chinese medicine views the depressed immunity and susceptibility to infection and cancer progression as the weakening of the body healthy energy or Qi and that the "kidney" function is declined leading to an inability to maintain blood elements. Multiple traditional Chinese medicine treatment approaches aim to improve body Qi and to strengthen "kidney" function has been developed including the use of herbs, acupuncture and moxibustion.

In animal studies, acupuncture and moxibustion have been shown to promote the repair of damage done to bone marrow cells by chemotherapies through the upregulation of DNA excision repair-related proteins (Lu et al. 2009a). Acupuncture and moxibustion have also been shown to improve cell cycle regulator protein, cyclin D1 resulting in shortening of the cell cycles of hematopoietic cells and increased DNA synthesis with quicker repopulation of hematopoietic cells (Lu et al. 2011).

In an interesting case report (Grass 2003) of a patient who suffered from sustained myelosuppression requiring regular blood transfusions after chemotherapy treatments for chronic lymphocytic leukaemia, the patient received electroacupuncture to Jingming (BL1), point associated with sea of blood; Geshu (BL17), influential point of "blood"; LR3, point associated with nourishment of "liver" blood and SP6 weekly for 8 treatments. After the start of treatments, all peripheral blood parameters continued to be improved and no further transfusions were required. This case demonstrated the temporal changes in blood parameters in response to electroacupuncture.

A number of clinical trials have been conducted showing promising results in using acupuncture and or moxibustion in managing chemotherapy-induced myelosuppression. A meta-analysis reported by Lu et al. (2007) reviewed 11 randomized controlled trials published from 1979–2004 that meet the study criteria. Only studies that use manual acupuncture or electroacupuncture or warm needling were included. Daily treatments were commonly employed. Effective rates of leukopenia recovery from 50–90% were reported in all studies. Electroacupuncture appeared to be more effective than manual acupuncture. Though the positive results of this meta-analysis was encouraging, the authors noted that publication bias, poor quality of study methodologies, short follow-up periods and incomplete chemotherapy deliveries in some studies seriously affect the interpretation of the results.

In a recent, though small but well designed trial (Lu et al. 2009b), 17 patients were divided into a real acupuncture group and a sham acupuncture group. In the active treatment group, acupuncture points were selected based on practitioners' experience and from literature. These points include LR3, KI3, SP6, ST36, SP10, LI4, PC6, LI11 and GV20. TDP infra-red heating to the feet were applied in place of moxibustion. Superficial needling at non-acupuncture points were used as sham control. The incidence of grade 2 or greater leukopenia in the acupuncture group (30%) was significantly less than that in the control group (90%). The adjusted absolute neutrophil counts and plasma G-CSF, however, did not show significant

different between the two groups. Larger trial is necessary to confirm the observed effectiveness.

In other controlled but non-randomized studies, acupuncture plus or minus moxibustion were all reported positive in correcting chemotherapy-induced leukopenia compared to controls that included G-CSF like drugs or no active treatment (Chen and Chen 2001; Ye et al. 2007). ST36 were used in all studies and SP6 was used in two. Daily treatments for 3–4 weeks were employed.

Indirect moxibustion alone may also be effective for chemotherapy-induced leukopenia. In a randomized trial that compared ginger indirect moxibustion to a Chinese patent medicine in 221 patients, the effective rates were improved by two folds in the moxibustion group compared to the control group after ten daily treatments. The effectiveness seemed to sustain after 15 days follow-up (Zhao et al. 2007).

It is still unclear as to when the acupuncture or moxibustion should be commenced in order to reduce the severity of chemotherapy-induced leukopenia. While in the meta-analysis mentioned above, the timing in starting the acupuncture was found to be not significant for treatment effectiveness, in the two positive randomized trials, the treatments were started one to two weeks prior to chemotherapy.

5.13 Anxiety, Depression

Anxiety is a common reaction in cancer patients. The presence of anxiety can reduce pain threshold, causes insomnia, worsen quality of life and may affect cancer treatment outcome (Jones 2001). Relief of anxiety by acupuncture was found to associate with increase in pain threshold (Widerstrom-Noga et al. 1998). Depression, though less common, is also frequently encountered by cancer patients (Jones 2001). Recent laboratory evidence has shown that the presence of tumor alone can stimulate cytokines production in behaviour related brain regions and can alter the regulation of the hypothalamic-pituitary-adrenal axis resulting in a depression-like behaviour (Pyter et al. 2009).

Adequate management of anxiety and depression in cancer patients is important to ensure better quality of life and to ensure optimum treatment outcomes. Conventionally, depression and anxiety are managed with the use of oral medications, such as amitriptyline or serotonin reuptake inhibitor drugs and inevitably, with associated side effects. Clinical studies have shown acupuncture may be a viable alternative to drugs treatments for anxiety and depression. In a recent review of conducted animal and clinical studies published in the English literature from year 2000 onwards, despite some methological issues, acupuncture was shown to have sufficient evidence to support its effectiveness for anxiety disorders (Errington-Evans 2011). The most frequently use acupuncture points among all studies were PC6, HT7, LR3, GV20 and Yintang (EX-HN3). One or three treatments per week, half hour per treatment and a total of ten treatments were the most common regime utilized.

Although a Cochrane review conducted in year 2005 concluded that there was insufficient evidence to determine the efficacy of acupuncture compared to medication, or to wait list control, or sham acupuncture in the management of depression, a

more recent extensive review done by the Department of Veteran Affairs (US) has a different conclusion (Smith et al. 2010; Williams et al. 2011). This review included all the relevant published literature from year 2006–2011 and found that acupuncture showed promise in treating depression. For major depressive disorder, acupuncture showed greater effect than sham control on depressive symptoms but did not improve response or remission rates. Moreover, it did not differ significantly from short-term use of anti-depressants. This conclusion was largely based on a meta-analysis of eight randomized controlled trial included in this review (Wang et al. 2008b).

In another randomized trial conducted in China, 80 patients with cancer-related depression and sleep disorders to an acupuncture group and a fluoxetione control group (Feng et al. 2011). The mean Self-rating Depression Scale and Hamilton Depression Rating Scale scores were decreased significantly in the treatment group (43.6 and 9.8) compared to that of control (50.7 and 13.7). Sleep disorder symptoms were also significantly improved similarly in the treatment group.

In a single-blinded placebo-controlled study comparing the addition of acupuncture to oral anti-depressant, mianserin, to mianserin alone, acupuncture was shown to improve the course of depression (Roschke et al. 2000). The benefit of acupuncture seemed to appear immediately after start of treatments and since pharmaceutical anti-depressants are not usually effective until 2 weeks after starting therapy, their combination with acupuncture may enable more rapid onset of treatment response.

5.14 Gastrointestinal Dysfunction Other Than Nausea and Vomiting

Apart from nausea and vomiting that is commonly experienced by most cancer patients, there are other gastrointestinal dysfunctions that may occur in some patients. Gastroparesis, dysfunctional gastric retention creating symptoms of postprandial fullness, bloating, nausea and vomiting, early satiety and epigastric discomfort, can be caused by cancer and non-cancer-related causes. It can present as a paraneoplastic disorders associated with breast, small-cell lung and pancreas cancers. Abdominal surgeries also precipitate gastroparesis. Current treatments mainly rely on dietary and lifestyle modification, and gastric prokinetic medications including metoclopramide and anti-emetics. Acupuncture has been shown to increase gastric emptying and reduce symptoms of gastroparesis in diabetic patients (Chang et al. 2001a, 2001b). In a recent randomized controlled trial in liver cancer patients who developed gastroparesis after abdominal surgery (Sun et al. 2010). A total of 63 eligible patients were randomized to receive acupuncture or intramuscular metoclopramide treatment. Complete recovery was defined as the absence of gastric juice drained from gastric tube, no vomiting after removal of gastric tube and patient was able to tolerate semi-liquid diet. CV12, ST36, SP6 and PC6 were needled once a day. After acupuncture treatments, 90% of patients in the acupuncture group achieved complete recovery and only 32% in the control group.

Dysphagia is another condition that many patients who received head and neck cancer radiation can experience as a result of mucosal damage of pharynx and direct

radiation damage of the swallowing muscles. Chronic dysphagia can result from fibrosis of the damaged muscles. A significant number of patients with dysphagia are at risk of aspiration pneumonia and may rely on percutaneous endoscopic gastrostomy (PEG) for feeding during treatment and, sometimes for a sustained period. Many studies have investigated acupuncture as a treatment modality for cancer-related dysphagia and have suggested moderate symptom relief (Shen and Shen 1996; Zheng and Ruan 2002; Zhou and Zhang 2006). A more recent retrospective case report in head and neck patients with post radiation dysphagia demonstrated that acupuncture treatments were able to shorten the period needed for PEG feeding (Lu et al. 2010). Nine of the ten patients treated showed various degree of improvement in swallowing. 86% of PEG tube dependent patients were able to have PEG removed after acupuncture treatments.

5.15 Hiccups and Yawning

Persisting hiccups and yawning are rarely encountered in cancer patients. Persistent hiccups have been associated with drug treatments, particularly with some types of chemotherapy, steroid and analgesics and direct tumor involvement of the brain stem area (Amirjamshidi et al. 2007; Kang et al. 2011; Tazi et al. 2011). Acupuncture has been used successfully in treating hiccups in non-cancer patients (Yan 1988; Lin 2006; Chang et al. 2008). In a recent case study of 16 cancer patients with persistent hiccups, acupuncture was shown to be an effective treatment option (Ge et al. 2010). Acupuncture points: BL17, GV14, CV12, PC6, ST36, Pishu (BL20), Weishu (BL21) and Qimen (LR14) were used. The mean hiccups severity measured by Hiccups Assessment Instruments before treatment was 5.2/10. After treatments, 13 patients had complete remission and 8 of this 13 patients achieved remission after only one treatment session. The authors reviewed laboratory evidence that acupuncture stimulation of PC6, ST36 and CV12 can activate the nucleus tractus neurons and subncucleus reticularis doraslis neurons that are implicated to be involved in hiccups reflex arc (Sun et al., 2007; Ji et al., 2009).

Persistent yawning has been linked to drugs, for example, anti-depressants, opioid and dopaminergic medications, and direct tumor involvement of the brain stem (Patatanian and Williams 2011). Radiation treatments that include the brain stem area can also induce yawning (Wong et al. 1997; Wong and Sagar 2000). One case report has shown that acupuncture on PC6 was able to abort persistent yawning in a patient receiving radiation treatment that include the brain stem for brain cancer (Wong and Sagar 2000).

5.16 Conclusion

Cancer patients suffer from a variety of cancer-related symptoms during and after cancer therapies. With recent improvement in cancer survival, increasing number of patients will also be affected by long-term and often debilitating treatment

toxicities leading to poorer quality of life. The search for effective management options for cancer-related symptoms has become more important. Among all complementary and alternative therapies, acupuncture and related techniques are increasing accepted by cancer patients and are more widely provided by health care providers. Results from recent research have suggested acupuncture and related techniques are effective options for treating both short-term and long-term cancer-related symptoms. Future effort with innovative research design involving multiple disciplines and collaborative systematic data collection will continue to provide evidence to guide optimal utilization of these treatment techniques in cancer care and to reveal the underlying mechanisms of treatment effects.

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