

# Complementary Medicine in Palliative Care and Cancer Symptom Management

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## ABSTRACT

Complementary and alternative medicine (CAM) use among cancer patients varies according to geographical area, gender, and disease diagnosis. The prevalence of CAM use among cancer patients in the United States has been estimated to be between 7% and 54%. Most cancer patients use CAM with the hope of boosting the immune system, relieving pain, and controlling side effects related to disease or treatment. Only a minority of patients include CAM in the treatment plan with curative intent. This review article focuses on practices belonging to the CAM domains of mind-body medicine, CAM botanicals, manipulative practices, and energy medicine, because they are widely used as complementary approaches to palliative cancer care and cancer symptom management. In the area of cancer symptom management, auricular acupuncture, therapeutic touch, and hypnosis may help to manage cancer pain. Music therapy, massage, and hypnosis may have an effect on anxiety, and both acupuncture and massage may have a therapeutic role in cancer fatigue. Acupuncture and selected botanicals may reduce chemotherapy-induced nausea and emesis, and hypnosis and guided imagery may be beneficial in anticipatory nausea and vomiting. Transcendental meditation and the mindfulness-based stress reduction can play a role in the management of depressed mood and anxiety. Black cohosh and phytoestrogen-rich foods may reduce vasomotor symptoms in postmenopausal women. Most CAM approaches to the treatment of cancer are safe when used by a CAM practitioner experienced in the treatment of cancer patients. The

potential for many commonly used botanical to interact with prescription drugs continues to be a concern. Botanicals should be used with caution by cancer patients and only under the guidance of an oncologist knowledgeable in their use. (*Cancer J* 2006;12:425-431)

## KEY WORDS

Cancer, palliative care, symptom management, complementary medicine

The National Center for Complementary and Alternative Medicine (NCCAM) defines complementary and alternative medicine (CAM) as "... a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine" (<http://nccam.nih.gov/health/whatisacam/>). Although complementary medicine is used together with conventional practices, alternative medicine is used in place of conventional medical practice. This article focuses on complementary medicine approaches to palliative care and symptom management in cancer treatment.

NCCAM groups CAM modalities into five major domains that are applicable to cancer-related CAM: alternative medical systems, mind-body interventions, biologically based therapies, manipulative and body-based methods, and energy therapies (<http://nccam.nih.gov/health/whatisacam/>). This review article focuses on practices belonging to the CAM domains of mind-body medicine, CAM botanicals, manipulative practices, and energy medicine because they are widely used as complementary approaches to palliative cancer care and cancer symptom management.

## CAM DEMOGRAPHICS IN CANCER AND PALLIATIVE CANCER CARE

CAM use among cancer patients varies according to geographical area, gender, and disease diagnosis. The prevalence of CAM use among cancer patients in the

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United States has been estimated to be between 7% and 54%.<sup>1</sup>

Comparisons of CAM use among patients with different cancer diagnoses have yielded many similarities. Most cancer patients use CAM with the hope to

- Boost the immune system
- Relieve pain
- Control side effects related to disease or treatment

Only a minority of patients include CAM in the treatment plan with curative intent.<sup>2</sup> A recent systematic review of motivations for cancer patients published in 500 articles on the use of CAM in cancer identified perceived beneficial response, desire for control, and strong belief in CAM as prominent motivators for the use of CAM, but not disappointment with conventional treatment.<sup>3</sup>

### **CANCER SYMPTOM MANAGEMENT**

The National Institutes of Health State of the Science expert panel in symptom management in cancer<sup>4</sup> concluded that among treatment options for common cancer symptoms, some CAM approaches may be beneficial for pain relief, such as hypnosis, whereas CAM approaches for cancer-related depression require additional research for validation of efficacy. However, the rationale for requiring evidence-based palliative cancer care has been debated, with one side questioning any other than an evidence-based approach for justification of the use of CAM in this setting, whereas others have argued the inherent difficulties and limitations that clinical research may have to face in this setting.<sup>5</sup>

A recent systematic review of clinical trials on CAM in end-of-life care identified a few case series suggesting a role of acupuncture in cancer-related pain.<sup>6</sup> Acupuncture, acupressure, and breathing exercises reduced dyspnea in several small randomized, controlled trials (RCTs).<sup>6</sup>

Although there is a paucity of well-designed randomized controlled trials examining the role of hypnosis in symptom relief of terminally ill adults with cancer,<sup>6,7</sup> the few well-designed RCTs that have been conducted provide evidence of hypnosis' beneficial effects in this population. A recent systematic review by Rajasekaran et al<sup>7</sup> examining hypnotherapy's effect in terminally ill adult cancer patients revealed 27 publications, only one of which was an RCT. Lioosi and White<sup>8</sup> examined the efficacy of clinical hypnosis in the enhancement of quality of life in 50 terminally ill cancer patients by randomly assigning participants to either standard care or standard care plus hypnosis administered once weekly for 4 weeks.

Results demonstrated that patients in the hypnosis intervention group experienced a statistically significant reduction in physical distress scores ( $P < 0.01$ ), as well as anxiety and depression scores ( $P < 0.01$ ). Although its mechanisms of action have not been fully characterized, recent neuroimaging studies suggest that hypnotic phenomena are associated with changes in brain activity within brain structures involved in the regulation of consciousness.<sup>9</sup> When used by properly trained practitioners with a therapeutic intent, hypnosis and guided imagery have potential applications in relieving cancer-related pain<sup>10</sup> and symptom-related distress, particularly in the palliative care setting.<sup>6,7,11,12</sup>

### **Cancer Pain**

**Acupuncture** Auricular acupuncture can be effective for cancer-related pain, as recently demonstrated in a study of 90 cancer patients. Pain intensity decreased by 36% at 2 months from baseline in the group receiving acupuncture, whereas there was little change for patients receiving placebo (2%). The difference between groups was statistically significant ( $P < 0.0001$ ).<sup>13</sup> However, the role of acupuncture in cancer pain has been debated because of the current lack of additional high-quality clinical trials supporting its use.<sup>14</sup> Several case reports and published series suggest a role for acupuncture in the palliation of chronic pain. Provided that caveats for the treatment as listed below are considered, acupuncture may be a helpful adjunct for cancer pain management if it is performed by a trained specialist with experience in this clinical setting.

**Energy Medicine** One RCT of the effect of reiki on opioid analgesic use in 24 cancer patients suggested improved pain, but no decreased opioid use, and improved health-related quality of life.<sup>15</sup> Therapeutic touch, as defined by Dolores Krieger, may have a role in cancer pain management. A review of 11 RCTs supported the use of therapeutic touch in cancer patients for the treatment of pain and anxiety.<sup>16</sup>

**Hypnosis** Pan et al<sup>6</sup> conducted a comprehensive systematic review of CAM therapies as symptom-relieving modalities in adults with end-stage incurable diseases. Of the 21 studies reviewed, three supported the effectiveness of hypnosis/relaxation/imagery interventions in terminally ill cancer patients.<sup>17-19</sup>

In an often-cited landmark study, Spiegel et al<sup>19</sup> conducted a RCT of 58 women with advanced breast cancer, randomly assigned to weekly group therapy with or without hypnosis. Results demonstrated that

supportive group therapy resulted in statistically significant reductions in pain sensation and suffering (both  $P < 0.01$ ) over 10 months of follow-up and that the addition of self-hypnosis provided a further reduction in pain sensation ( $P < 0.05$ ).<sup>20</sup>

Syrjala et al<sup>21</sup> studied the effect of hypnosis or cognitive behavioral therapy (CBT) on symptoms of oral pain, nausea, and vomiting in patients with hematologic malignancies undergoing bone marrow transplantation. Forty-five patients were randomly assigned to (1) hypnosis with relaxation and guided imagery; (2) CBT that included progressive muscle relaxation, cognitive restructuring, coping and problem-solving strategies; (3) therapist attention control; or (4) standard care. These researchers found that the mucositis-related oral pain was significantly relieved by hypnosis, but not in any of the other three groups an effect that persisted 3 weeks after transplantation in the hypnosis group. Nausea and emesis were not affected by any intervention in this study. A subsequent study by the same researchers in a similar cohort of patients found that patients in both the relaxation/imagery group and the CBT group had significantly less mucositis-related pain than in the standard treatment group.<sup>17</sup>

### Anxiety

**Therapeutic Touch** Therapeutic touch may be beneficial for cancer patients experiencing anxiety.<sup>16</sup> A recent systematic review of aromatherapy and massage identified four out of eight RCTs reporting a benefit of 19% to 32% reduction in anxiety, suggesting that limited evidence supports the benefit of aromatherapy and massage in patients with cancer who have anxiety.<sup>22</sup>

**Music Therapy** Numerous qualitative studies have pointed to a role of music therapy in palliative cancer care. A recent review of the empiric data suggests a benefit on anxiety as well as cancer pain based on a small number of controlled clinical trials.<sup>23</sup>

### Hypnosis-Based Methods in Acute Procedural Pain and Anxiety

In a recent review of the literature of hypnosis in cancer patients,<sup>12</sup> Lioessi et al cite nine studies that have demonstrated the effectiveness of hypnosis in relieving pain and anxiety in pediatric cancer patients undergoing painful medical procedures. An early study by Lioessi and Hatira<sup>24</sup> randomly assigned 30 children who were undergoing bone marrow aspiration to hypnosis, cognitive behavioral coping skills, or no inter-

vention. Results demonstrated that children who received either hypnosis or cognitive behavioral therapy experienced more pain relief than control patients and that those in the hypnosis group also had less anxiety and behavioral distress than the CBT group. In a randomized trial of pediatric cancer patients undergoing lumbar puncture, 80 children (aged 6–16 years) were randomly assigned into one of two hypnosis groups (direct vs indirect suggestion), an attention control group, or standard medical treatment alone. Those who received hypnotic interventions (both direct and indirect suggestion groups) experienced significantly less pain, anxiety, and behavioral distress than those who were randomly assigned to distraction or attention control.<sup>25</sup>

Similarly in adults, hypnotherapy appears to have beneficial effects in reducing acute procedural pain. Montgomery et al<sup>26</sup> randomly assigned 20 women undergoing excisional breast biopsy to either a presurgical hypnosis intervention or standard care and found that those randomly assigned to the hypnosis group reported significantly less postsurgical pain and distress than those randomly assigned to standard care.

### Fatigue

A recent study found persistent fatigue in 19% of disease-free cancer patients.<sup>27</sup> A small randomized study of acupuncture in 37 cancer patients with persistent fatigue over 2 years found a mean improvement of fatigue by 31.1% (95% CI, 20.6%–41.5%) after acupuncture.<sup>28</sup> Results of an outcome study at Memorial Sloan-Kettering Cancer Center suggest a beneficial role of massage to reduce fatigue in cancer patients.<sup>29</sup>

## SYMPTOM MANAGEMENT OF CANCER TREATMENT

### Nausea/Vomiting

**Acupuncture** Acupuncture and electroacupuncture are widely used for cancer symptom management. A number of acupuncture approaches are being practiced, including Chinese, Japanese, Korean, and French acupuncture.

The 1997 NIH Consensus Conference on acupuncture ([http://dowland.cit.nih.gov/odp/consensus/107/107\\_statement.htm](http://dowland.cit.nih.gov/odp/consensus/107/107_statement.htm)) concluded that existing evidence based on clinical trials suggests a beneficial role for acupuncture in the areas of chemotherapy-induced nausea/vomiting and dental pain. A recent study of electroacupuncture in a cohort of breast cancer patients receiving high-dose chemotherapy suggests su-

priority of a regimen combining electroacupuncture and antiemetics over antiemetics and placebo.<sup>30</sup> Clinical evidence for efficacy of acupuncture in other settings remains limited.

Commonly used acupuncture points include P 6, Neiguan point of the pericardium meridian of hand (jueyin), and St 36, Zunsali point of the stomach meridian of foot (yangming). Treatment is commonly started before administration of antiemetic drugs or chemotherapy. Both acupuncture and electroacupuncture are being used.<sup>30</sup>

**Botanicals** Ingestion of ginger root preparations may reduce chemotherapy-induced nausea and vomiting, although there is a lack of clinical research-based dosing information.<sup>31</sup> A recent comprehensive review of the use of Chinese herbal medicines for the treatment of chemotherapy side effects suggests that huangqi de-

coctions may reduce chemotherapy-induced nausea and vomiting,<sup>32</sup> although more clinical research on this preparation is needed. Because there has been increasing concern of botanical-chemotherapy interactions (Table 1), caution has to be applied to the use of botanical products with chemotherapy.

### Hypnosis/Imagery-Based Methods

Guided imagery, hypnosis, relaxation training, and emotive imagery have been effective in diminishing anticipatory nausea and vomiting in both pediatric and adult cancer patients receiving chemotherapy, reducing anxiety and distress caused by invasive medical procedures and decreasing acute pain caused by aversive medical procedures.<sup>33-35</sup> However, these interventions have not demonstrated efficacy in moderating chronic pain in cancer populations and allevi-

**TABLE 1** Drug Interactions of Five of the Top-selling Botanicals on the US Market

Botanical	Drug Interactions
Saint John's wort	5-HT1 agonists (triptans), alprazolam, aminolevulinic acid, amitriptyline, analgesics with serotonergic activity, antidepressants, barbiturates, cyclosporine, digoxin, dextromethorphan, fenfluramine, fexofenadine, irinotecan, monoamine oxidase inhibitors, narcotics, nefazodone, nonnucleoside reverse transcriptase inhibitors, nortriptyline, oral contraceptives, paroxetine, phenobarbital, phenprocoumon, phenytoin, photosensitizing drugs, protease inhibitors, reserpine, sertraline, simvastatin, tacrolimus, theophylline, warfarin
<i>Ginkgo biloba</i>	Anticoagulant-antiplatelet drugs (aspirin, heparin, indomethacin); buspirone; fluoxetine; insulin; monoamine oxidase inhibitors (MAOIs); seizure threshold lowering drugs; thiazide diuretics; trazodone; warfarin, other drugs metabolized by cytochrome P450 CYP1A2 (acetaminophen, diazepam, estradiol, ondansetron, propranolol, warfarin), CYP2D6 (amitriptyline, codeine, fentanyl, fluoxetine, meperidine, methadone, ondansetron, and others), and CYP3A4 (chemotherapeutic agents (etoposide, paclitaxel, vinblastine, vincristine, vindesine), antifungals (ketoconazole, itraconazole); glucocorticoids; fentanyl; calcium channel blockers (diltiazem, nifedipine, verapamil, and others)
<i>Panax ginseng</i>	Anticoagulant-antiplatelet drugs (aspirin, heparin, indomethacin), antipsychotic drugs, caffeine, furosemide, immunosuppressants (azathioprine, cyclosporine, tacrolimus, prednisone, others), insulin, monoamine oxidase inhibitors (MAOIs), oral hypoglycemic agents (glimepiride, glyburide), stimulant drugs, warfarin, other drugs metabolized by cytochrome P450 CYP2D6 enzyme (amitriptyline, codeine, fentanyl, fluoxetine, meperidine, methadone, ondansetron, and others)
<i>Allium sativum</i> (garlic)	Anticoagulant-antiplatelet drugs (warfarin, aspirin, heparin, indomethacin), cyclosporine, nonnucleoside reverse transcriptase inhibitors (NNRTIs), saquinavir (potentially, other protease inhibitors), oral contraceptives, other drugs: preparations containing allicin may increase the activity of the cytochrome P450 CYP3A4. Drugs that might be affected include chemotherapeutic agents (etoposide, paclitaxel, vinblastine, vincristine, vindesine), antifungals (ketoconazole, itraconazole), glucocorticoids, fentanyl, calcium channel blockers (diltiazem, nifedipine, verapamil) and others
<i>Piper methysticum</i> (kava)	Alcohol, alprazolam, central nervous system (CNS) depressants, hepatotoxic drugs (azathioprine, methotrexate, tamoxifen), levodopa, other drugs metabolized by cytochrome P450 enzymes CYP1A2, CYP2C9 (tamoxifen, warfarin), CYP 2C19 (cyclophosphamide), CYP2D6 (codeine, ondansetron, paroxetine), and CYP3A4 (cyclosporine and others)

ating postchemotherapy nausea, vomiting, and chronic pain.

**Meditation for Cancer-Related Symptoms** Cancer therapists and cancer patients have used a wide range of meditative approaches to alleviate cancer symptoms. The two most widely studied techniques are transcendental meditation and mindfulness-based meditation. Transcendental meditation uses the repetition of a specific mantra with the intent of quieting and ultimately "transcending" the practitioner's internal mental dialogue. Mindfulness-based meditation strives to develop an objective "observer role" of the practitioner for emotions, feelings, perceptions, and so on, thus creating a nonjudgmental "mindful state" of conscious awareness. Other meditative practices are usually pursued in a religious or spiritual context.

**Transcendental Meditation** Studies of transcendental meditation in cancer patients and cancer symptom management are lacking. There is weak evidence that transcendental meditation may help with reduction of anxiety and stress,<sup>36</sup> but it remains unclear how this information can be translated into the cancer setting.

**Mindfulness Meditation** The mindfulness-based stress reduction (MBSR) program was developed by Jon Kabat-Zinn.<sup>37</sup> The components of sitting meditation, body scan, and mindful movement are taught over a training period of 7 to 8 weeks.

Studies of MBSR in cancer populations<sup>38-40</sup> suggest that MBSR may result in decreased anxiety and total mood disturbance, decreased depression, anger, and confusion. MBSR may also change posttreatment total stress scores. MBSR is a highly structured, didactic program that may not be appropriate for all educational levels.

**Yoga** Deriving from the Ayurvedic medical system, yoga combines breath awareness and control with meditation, movement, and chanting. Studies have supported its benefits for stress management, anxiety reduction, and insomnia.<sup>41</sup> Although published studies are lacking that specifically used yoga alone as an intervention for persons with cancer, it is likely a safe modality except in patients with bone metastases at risk for pathological fractures.

**Distant Healing Modalities** "Distant healing" interventions include such modalities as therapeutic touch, reiki, spiritual healing, prayer, and external qi gong. Some of these interventions, such as reiki, are based on the belief that the practitioner serves as a conduit of subtle vibrational energy flow by placement of hands on the recipient, whereas others, such

as therapeutic touch, do not necessarily require direct contact with the recipient.

A number of RCTs and several reviews of beneficial effects have been published, but only a few studies have been conducted in cancer populations.

A recent meta-analysis of 23 clinical studies conducted by Astin et al<sup>42</sup> found that 16/23 were double-blinded studies: 10 positive studies used therapeutic touch versus a sham control. Two studies showed positive results of distant intercessory prayer. Four positive studies used other forms of distant healing. However, only one of the studies included in this meta-analysis was conducted in a cancer population (18 children with leukemia), showing an insignificantly higher death rate in the control group.<sup>43</sup> A recent update of this systematic review identified 17 additional controlled trials, but concluded that "... since the publication of our previous systematic review in 2000, several rigorous new studies have emerged. Collectively, they shift the weight of the evidence against the notion that distant healing is more than a placebo."<sup>44</sup>

## CAM FOR VASOMOTOR SYMPTOMS

### Botanicals for Menopausal Symptoms

A number of botanical products, including soy and soy extracts, black cohosh (*Cimicifuga racemosa*), chaste tree berry (*Vitex agnus-castus*), don quai (*Angelica sinensis*) ginseng (*Panax ginseng*), evening primrose oil (*Oenothera biennis*), red clover (*Trifolium pratense*), motherwort (*Leonurus cardiaca*) and licorice (*Glycyrrhiza glabra*), have been widely used as adjunct treatments for menopausal symptoms including hot flashes, mostly considered to be effects of the components.

A recent review of 29 RTCs of CAM therapies for menopausal symptoms<sup>45</sup> concluded that black cohosh and phytoestrogen-containing foods show promise for the treatment of menopausal symptoms, but clinical trials do not support the use of other herbs or CAM therapies for menopausal symptoms.

Limited data based on two RTCs of soy beverage<sup>46</sup> or phytoestrogen tablets<sup>47</sup> specifically used by postmenopausal women with breast cancer, respectively, concluded that soy phytoestrogens administered as a soy beverage do not alleviate hot flashes. Pure isoflavones administered as tablets do not improve menopausal symptoms. A recent comprehensive review of the effects of soy<sup>48</sup> concluded that soy isoflavone supplements may reduce hot flashes in postmenopausal women. However, no significant effect on vasomotor symptoms was found in perimenopausal women or in women who underwent breast cancer therapies.

## Acupuncture

In a recent retrospective audit at the Royal Marsden Hospital in London regimen of six weekly acupuncture treatments given initially at LI4, TE5, LR3, and SP6 and two upper sternal points was reviewed. A total of 194 patients, predominantly with breast and prostate cancer, were treated. Patients estimated the number of pretreatment hot flushes per day. After treatment, 114 (79%) gained a 50% or greater reduction in hot flushes, and 30 (21%) gained a less than 50% reduction.<sup>49</sup>

## SAFETY OF CAM IN PALLIATIVE CARE

Acupuncture is generally well tolerated. The most frequent side effects include minimal local bleeding/bruising and mild pain.<sup>50,51</sup> Acupuncture, manipulative therapies, and deep tissue massage are not advisable in patients with thrombocytopenia, bleeding disorders, or aplasia. CAM mind-body interventions are generally considered safe as long as they are administered by properly trained and experienced practitioners.

There has been increasing concern about the use of botanicals and dietary supplements by cancer patients because of mounting evidence of botanical-drug interactions. Table 1 exemplifies available information of drug interactions with the five most commonly sold botanicals in the United States. Patients with cancer should be cautioned and should discuss the use of botanicals with their oncologist.

## SUMMARY

Cancer patients often seek CAM approaches for relief of disease-related symptoms as well as reduction of treatment side effects. In the palliative care setting, CAM interventions are often useful in enabling the individual to achieve physical comfort and psychological quiescence at the end of life.

Based on this review of the literature of several systematic reviews and RCTs, a number of CAM approaches may have a role in the management of cancer and cancer treatment-related symptoms:

- Acupuncture may relieve cancer-related pain, chemotherapy-induced emesis, and vasomotor symptoms.
- Hypnosis may be helpful for pain, anxiety, and chemotherapy-induced emesis.
- Meditation may reduce anxiety, stress, and depressive symptoms.
- Black cohosh and phytoestrogen-containing foods may help reduce menopausal symptoms but do not seem to be beneficial for premenopausal women.

- Evidence for the efficacy of distant healing modalities for cancer-related symptoms and the reduction of cancer treatment side effects remains limited.
- Most CAM approaches to the treatment of cancer are safe when employed by a CAM practitioner experienced in the treatment of cancer patients.

The potential for many commonly used botanicals to interact with prescription drugs continues to be a concern and needs to be considered in any cancer patient using or inquiring about botanicals.

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