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Integrative Oncology: Complementary Therapies in Cancer Care



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Abstract and Introduction

Abstract

Cancer patients' use of complementary therapies, including massage therapy, acupuncture, mind-body therapies, music therapy, physical exercise, and herbs and botanicals has increased in recent years. In fact, complementary therapies are increasingly integrated into mainstream cancer programs and centers. Randomized controlled studies indicate that many complementary therapies control treatment-related physical and emotional symptoms including pain, fatigue, nausea, xerostomia, anxiety, and depression in both adult and pediatric cancer patients. Importantly, many of these interventions produce long-lasting improvement. Cautions are important, however, regarding the use of herbs, vitamin preparations, and other over-the-counter agents. These may be harmful as many interact with conventional pharmacologic drugs, including chemotherapy, or produce unwanted side effects. A subset of the too-numerous Internet and other sources of information contains accurate information. Cautions and resources for reliable information are given in this chapter to assist physicians in guiding their patients on the appropriate use of helpful complementary therapies as well as the often problematic products that are taken by mouth. (Cancer & Chemotherapy Rev. 2008;4:204-11)

Introduction

In addition to standard treatments, complementary therapies are increasingly being used by cancer patients in an effort to alleviate cancer symptoms and those associated with cancer treatment as well as improving their overall wellbeing and quality of life. More than 40% of breast cancer patients in the USA reported using complementary therapies,^[1] and the numbers are comparable to complementary and alternative medicine use by European cancer patients^[2].

As opposed to alternative therapies, which are used in place of conventional treatment, complementary therapies are utilized in conjunction with standard treatments and consist of noninvasive therapies. Complementary therapies include massage therapy, acupuncture, mind-body therapies, music therapy, physical exercise, and herb and botanical use. Of these, herbs are the most commonly employed complementary medicine by cancer patients^[2,3]. We review here the evidence base and appropriate application of today's popular complementary modalities for cancer, including acupuncture, mind-body therapies, physical activity, herbs, and other dietary supplements. In addition, with respect to herbs and other dietary supplements, cautions regarding harmful side effects and interactions with conventional pharmacologic drugs are presented. Finally, reliable resources that provide information pertaining to helpful and potentially harmful complementary therapies are given in this chapter.

Massage Therapy

Massage has long been used to reduce tension, anxiety, and pain in various populations including cancer patients. Surveys indicate that over 20% of cancer patients use massage therapy.^[4,5] Through the application of pressure and motion to the muscle and connective tissues of the body, massage therapy elicits both physiological and psychological responses.

In a study involving breast cancer patients, massage therapy was shown to reduce depression, anger, and pain.^[6,7] In patients undergoing bone marrow transplantation, reductions in diastolic blood pressure, distress, nausea, and anxiety

were detected immediately after receiving upper body massage.^[8] Furthermore, massage therapy reduced central nervous system/neurologic complications, which include anxiety, depression, and fatigue, in patients following bone marrow transplantation compared to those receiving therapeutic touch or friendly visits.^[9] Data from another study indicate that massage therapy and light therapeutic touch (without deep tissue stimulation) reduced fatigue and pain, resulting in decreased four-week nonsteroidal anti-inflammatory use and improved mood in cancer patients. Improvements were also reported in blood pressure, heart rate, and respiratory rate.^[10]

Although most studies have reported the effects of massage in adult patients, pediatric cancer patients also experienced reduced pain after massage therapy.^[11] Massage is one of the most commonly used pain management strategies for pediatric patients newly diagnosed with leukemia.^[12]

In addition to massage, foot reflexology offers beneficial effects such as reductions in pain, anxiety, and nausea in cancer patients.^[13] Reflexology teaching protocols have been successfully administered to caregivers, and subsequent relief in pain intensity and anxiety has been reported in metastatic cancer patients.^[14]

Most types of massage (i.e. Swedish, light touch, and foot) result in various levels of symptom relief for patients; however, those receiving Swedish or light touch massages reported a significantly greater reduction in symptoms compared to those receiving foot massages and the beneficial effects persisted for up to 48 hours.^[15]

Although the mechanism by which massage induces symptom relief is not fully known, increased dopamine and serotonin along with decreased cortisol levels have been reported following massage.^[7,16] In addition, there was an increase in natural killer cells and lymphocyte levels in breast cancer patients following massage therapy.^[6] However, conflicting results were reported in a recent study.^[17] It is possible that many factors including location of massage, massage intensity, or psychological impact of surgery, chemotherapy, or radiation may impact the efficacy of massage therapy.

Acupuncture

An important component of traditional Chinese medicine, acupuncture is the stimulation of predetermined points on the body with needles, sometimes with added heat, pressure, or electricity to enhance the therapeutic effect. The ancient theoretical underpinnings assume that "qi" (pronounced "chee"), or life energy flows through meridians said to connect the organs in the body. According to this philosophy, disease occurs when the meridians become blocked. Acupuncture was thought to relieve the blockage and permit the normal flow of qi, thereby restoring health.

Some acupuncture points coincide with trigger points, indicating enriched enervation at the anatomic location. Biophysiological research indicates that acupuncture triggers a sequence of events such as the release of neurotransmitters and endorphins and activation of the central nervous system, although full understanding of mechanisms remains under investigation.

In a study of patients with head and neck cancer, acupuncture improved xerostomia or dry mouth that is often associated with radiotherapy by improving salivary flow rates.^[18] Data from another trial showed that in cancer patients who had completed chemotherapy for at least one month prior to the study, acupuncture and acupressure reduced chemotherapy induced fatigue by 36 and 19%, respectively.^[19] Acupuncture also reduced the number of hot flashes by more than 50% in breast cancer patients receiving estrogen receptor antagonists such as tamoxifen.^[20] In addition, several small studies have reported that acupuncture and electroacupuncture, which involves electrical stimulation of the acupuncture needles, relieved neuropathic pain in cancer patients.^[21-24]

Both acupuncture and acupressure improved nausea in palliative care patients;^[25,26] acupressure also reduced nausea and vomiting in cancer patients concurrently receiving first-round chemotherapy.^[27-29] Acupressure^[30] of the P6 point reduced delayed nausea and vomiting in breast cancer patients undergoing a second or third round of chemotherapy, and electroacupuncture effectively reduced vomiting in high-risk breast cancer patients receiving high-dose

chemotherapy.^[31] In addition to relieving chemotherapy induced nausea and vomiting, electro-acupoint stimulation reduced postoperative nausea and vomiting.^[32]

Most studies have determined the short-term effects of acupuncture on cancer and cancer treatment-related symptoms. With respect to chemotherapy induced vomiting, the number of vomiting episodes was significantly reduced after five days of treatment; however, after four days of follow-up, there was no detectable improvement.^[31] Longer treatment periods may induce greater periods of relief after cessation of treatment. For example, 10 weeks of acupuncture (twice weekly for five weeks and once weekly for five weeks) reduced hot flashes in breast cancer patients, an effect that lasted three months after treatment.^[20]

Neuroimaging analysis using functional magnetic resonance imaging, positron emission tomography, and electroencephalography has revealed that acupuncture may alter cortical and subcortical activities of the brain.^[33] Specifically, acupuncture at a point used to relieve xerostomia resulted in cortical activation (as detected by functional magnetic resonance imaging), which coincided with increased salivation.^[34] Further studies in cancer patients may reveal the mechanisms by which acupuncture affects pain, increases salivation, and reduces nausea, fatigue, and hot flashes.

Mind-Body Therapies

Guided imagery, biofeedback, hypnosis, music therapy, meditation, and other relaxation approaches comprise mind-body therapies and are increasingly available in mainstream medical centers. Their value lies not only in their documented ability to relieve many symptoms, but also because patients may select these pleasant, noninvasive interventions as they prefer, and apply them to help manage their own clinical care.

Yoga

Yoga, a 5,000-year-old exercise regimen originally developed in India, also involves deep breathing, movement, and posture. Yoga is often part of general management for heart disease, asthma, diabetes, drug addiction, AIDS, migraine headaches, arthritis, and cancer. In recent years, a number of studies using Hatha yoga, the most commonly practiced yoga in the West, as well as Tibetan yoga have been reported.

In a study involving breast cancer patients in varying stages of disease, those practicing yoga experienced enhanced physical and psychological wellbeing. Specifically, improvements in mood, stress, and quality of life were detected in breast cancer survivors practicing yoga.^[35,36] Another study reported that yoga reduced anxiety, stress, and depression in breast cancer patients receiving radiotherapy.^[37] Further, yoga reduced fatigue and pain as well as increased relaxation, invigoration, and acceptance in women with metastatic breast cancer.^[38] Conversely, lower adherence to the yoga program was associated with increased fatigue and distressed mood in addition to decreased physical wellbeing.^[36]

Yoga also reduced the frequency and severity of chemotherapy induced nausea by 18%, and frequency and severity of anticipatory nausea (by 12 and 18%, respectively) as well as the severity of anticipatory vomiting by 9%.³⁹

In addition, yoga reduced sleep disturbances, increasing better sleep quality, faster sleep latency, and longer sleep duration in lymphoma patients receiving or recovering from chemotherapy.^[40] Because patients experienced fewer sleep disturbances, they reported decreased use of sleep medications.^[40]

Data from a study of women with metastatic cancer show that yoga improved symptoms as well as emotional wellbeing, and the effects were maintained the following day.^[38]

Mechanistic studies of yoga have shown that yoga may reduce chemotherapy induced immune suppression; a yoga treatment group had reduced post-radiotherapy lymphocyte DNA damage.^[37] Furthermore, in breast cancer patients receiving yoga in addition to conventional therapy, the yoga group experienced less therapy associated reduction in

natural killer cells as compared to the supportive therapy group.^[41] In addition, yoga may relieve psychological stress associated with cancer and its treatments. Decreased sympathetic and increased parasympathetic activity^[42] as well as decreased cortisol levels^[43] have also been detected in yoga participants.

Meditation

Meditation is the practice of relaxing one's mind, often by focusing on breathing or a specific object or image. It is often used to combat stress, anxiety, and depression and for symptom management such as pain control. In addition, a combination of mindfulness meditation and Hatha yoga, termed mindfulness-based stress reduction (MBSR), has proven useful for cancer patients in reducing stress, anxiety, and sleep disturbances.^[44] Furthermore, mindfulness-based art therapy, which combines mindfulness meditation and art therapy, reduces distress and improves health-related quality of life.^[45]

Mindfulness-based stress reduction reduced stress by 31% and mood disturbances, such as anxiety, depression, anger, and fatigue, by 65% in cancer outpatients.^[46]

In addition, improvements in sleep disturbance,^[47] fatigue,^[48] stress, and mood disturbance in cancer patients using MBSR have been reported.^[48] In breast and prostate cancer outpatients, MBSR also improved quality of life scores.^[49] Although multiple studies have reported the benefits of MBSR, conflicting results have been reported with respect to the necessity of home practice.^[47,50] In addition to short-term benefits, a reduction in mood disturbance affected by MBSR was maintained six months post-intervention^[46] while stress reductions were maintained for up to 12 months.^[51]

Studies suggest that MBSR may influence immunity; although MBSR did not alter lymphocyte number, it did influence cytokine production.^[49] Specifically, T-cell-derived IL-4 levels increased while interferon-gamma decreased, and reduced IL-10 production by natural killer cells was detected in patients using MBSR.^[49] Furthermore, decreased cortisol, blood pressure, and proinflammatory cytokine production were reported after 12 months of intervention.^[51]

Hypnosis

Hypnosis may be performed by a trained therapist or self-administered. Often through visualization techniques, a patient's attention is diverted in hypnosis, making them more prone to suggestion. Treatment-specific suggestions for reduced anxiety, pain, and nausea are commonly used in cancer patients.

In breast cancer patients undergoing surgery, those receiving hypnotic intervention reported less emotional distress^[52] and required less intraoperative and postoperative pain control, and their surgery time was reduced.^[53] Self-reported mental wellbeing as well as overall wellbeing was improved in hypnosis patients undergoing radiotherapy.^[54] In addition, hypnosis patients reported less pain, nausea, fatigue, discomfort, and emotional upset as compared to patients receiving empathic listening.^[53] Thus, the beneficial effects of hypnotherapy in cancer patients undergoing surgery and recovery may also be reflected in reduced cost by lowering the use of pain medication and shortening the length of hospital stay.^[55]

In addition to benefiting adult cancer patients, hypnotherapy may also reduce anxiety and nausea in children undergoing standard cancer treatment. Specifically, pediatric cancer patients receiving hypnosis experienced less anticipatory and post-chemotherapy nausea as compared to those receiving non-hypnotic distraction and relaxation or individual attention.^[56] In addition, hypnosis as a primary treatment instead of standard antiemetic therapy resulted in less supplemental antiemetic medication use and reduced anticipatory nausea in children receiving chemotherapy.^[57] Pediatric cancer patients receiving hypnosis combined with a local anesthetic experienced a reduction in anticipatory anxiety in addition to reduced pain and anxiety during lumbar punctures compared to those receiving local anesthetic alone or supportive attention.^[58]

Music Therapy

Music is a powerful tool that can evoke latent emotions. Individuals may associate a particular music to his/her life experience. Music therapy, which can be receptive or participatory, is provided by professional musicians who are also trained music therapists. Along with patient preferred music, music therapists often use passive listening, lyrical creativity, and relaxation techniques such as progressive muscle relaxation and imagery.

In patients undergoing autologous stem cell transplantation for hematologic malignancies, a 37% reduction in mood disturbance was detected in those receiving music therapy compared to patients receiving standard treatment.^[59] Furthermore, music improved postoperative pain and pain-associated distress^[60] as well as reducing fear and anxiety in patients receiving chemotherapy;^[61] participation in recreational music also improved mood.^[62] In addition, increased use of music was correlated with a reduction in distress in cancer patients undergoing radiotherapy, indicating a possible dose-response effect.^[63]

Few studies have assessed the long-term benefits of music therapy in cancer patients. In one study, improvements in mood disturbance mediated by music therapy were maintained throughout the length of hospital stay in patients undergoing autologous stem cell transplantation.^[59] Furthermore, in patients undergoing radiotherapy, treatment-related distress continued to decline over an average of 4.4 weeks.^[63]

Physical Activity

Because cancer survivors are at increased risk of developing other chronic diseases such as cardiovascular disease and osteoporosis in addition to secondary tumors, diet and exercise intervention programs have been recently initiated with the goal of improving lifestyle behaviors in cancer patients.^[64,65] Exercise guards against loss of muscle mass, which eventually impairs physical performance and diminishes physical and emotional quality of life. Regular exercise helps reduce fatigue and improve stamina, agility, muscle tone, and flexibility. Several studies have assessed the possible benefits of aerobic and resistance exercise programs for cancer patients.

Both aerobic and resistance exercise regimens improved self-esteem as well as physical fitness and body composition in breast cancer patients receiving chemotherapy.^[66] In addition, continued exercise further improved their quality of life compared to the usual care group.^[67] In prostate cancer patients undergoing radiotherapy, participation in an exercise program improved quality of life and reduced fatigue compared to a control group,^[68] and exercise reduced sleep disturbances in older breast cancer patients receiving hormonal therapy.^[69]

Recent studies have found that specific benefits may be associated with the type of physical exercise program implemented (i.e. aerobic versus resistance training). For example, progressive resistance exercise training improved shoulder function and pain in head and neck cancer patients who underwent surgical management compared to those in a standardized exercise program.^[70] In addition, weight-bearing aerobic exercise limited bone mineral density decline in breast cancer patients receiving chemotherapy compared to the resistance exercise or usual care groups.^[71]

In addition to the short-term benefits of exercise, long-term improvements have also been reported in cancer patients. Benefits from both aerobic and resistance exercise programs were not only maintained after six months, but additional benefits, such as anxiety reduction that were previously absent, emerged.^[67]

Herbs and Other Dietary Supplements

Medicinal plants, used alone or in combination with other plants, have long been used in traditional medical systems, including traditional Chinese medicine and Ayurveda. Over the last two decades, the use of herbs and other botanicals in Europe and the USA has increased; nearly 20% of individuals in the USA reported using herbs to treat a specific health condition.^[72] Herbs are the most commonly used complementary medicine in European cancer patients,^[2,3] and among Japanese cancer patients using complementary medicine, most used herbs, mushrooms, and shark cartilage.^[73]

Because botanicals are considered dietary supplements, they are sold over the counter without regulation by the Food and Drug Administration (FDA). However, lack of regulatory oversight poses many safety concerns. For example, poor quality control may result in contamination with other plant materials, pesticides, heavy metals, etc. Due to a lack of standardization, variability in product quality or levels of botanical agents may occur.

In addition to safety issues surrounding the lack of regulation, botanicals contain pharmacologically active compounds that may induce serious side effects, such as renal and hepatic failure, or may interact with prescription drugs.^[74] Some herbs contain components that interfere with drugs metabolized via the cytochrome P-450 pathway.^[75] These interactions can influence oncologic drug concentrations, thereby reducing their efficacy or increasing their toxicity. In fact, analysis of cancer patients using dietary supplements while receiving chemotherapy estimated that 27% were at risk for harmful drug-herb interactions.^[76] In addition, certain botanicals may be harmful to some patients. For example, garlic, ginger, ginkgo, and ginseng possess anticoagulant effects or anti-platelet activities.^[77] Therefore, patients using heparin, warfarin, aspirin, and other anticoagulants should avoid these botanicals. In addition, botanicals with estrogenic properties such as red clover, Dong quai, and soy should be avoided in patients with hormone-sensitive cancers.^[78]

The use of other kinds of dietary supplements, such as vitamins, minerals, amino acids and enzymes, also has increased in recent years; 56-73% of cancer patients reported regular use of multivitamins,^[79-81] although it is not necessarily clear whether these were USDA-level supplements or extremely high doses. Because many patients believe that anticancer therapies deplete them of important dietary vitamins and minerals, and because high doses of vitamins are promoted by many purveyors of related products, cancer patients often utilize megadoses of these agents, some of which are potent antioxidants (i.e. vitamin C, vitamin E, selenium, etc.). In addition, patients believe antioxidant supplementation will relieve radiotherapy and chemotherapy associated side effects.^[82] However, clinical evidence regarding the safety and efficacy of antioxidant therapy is conflicting.^[83] A recent review of randomized, controlled clinical studies in cancer patients found that antioxidant supplementation decreased chemotherapy associated side effects.^[84] Conversely, antioxidant supplementation has been associated with increased mortality in cancer patients,^[85] perhaps by reducing the efficacy of antineoplastic drugs.

The mechanism by which antioxidant supplements interact with chemotherapeutic drugs is not fully known. Many chemotherapy agents such as cisplatin and doxorubicin generate reactive oxygen species (ROS), so addition of potent antioxidants may reduce the efficacy of these drugs. For example, vitamin C reduces the efficacy of antineoplastic drugs whose cytotoxic effects are mediated by ROS; however, it also affects the efficacy of those that do not involve ROS production.^[86] Therefore, vitamin C interacts with a wide range of chemotherapeutic agents, inhibiting mitochondrial membrane depolarization and perhaps cell death.^[86] Thus, until studies determine the safety of antioxidant supplementation as well as appropriate dosage, cancer patients receiving chemotherapy and radiotherapy and those undergoing surgery should approach antioxidant supplements with caution.

Healthy individuals also use antioxidant supplementation as a means to prevent diseases such as cancer and cardiovascular disease, despite the absence of scientific proof. In fact, harmful rather than beneficial effects have been found in some studies that assessed the use of antioxidant supplementation for cancer prevention; there is increasing evidence that antioxidant supplementation may be linked to increased risk of developing certain cancers. For example, in male smokers, higher lung cancer incidence and mortality due to lung cancer was reported with beta carotene supplementation,^[87] and long-term vitamin E supplementation may also increase lung cancer incidence.^[88] Furthermore, antioxidant supplementation, which included a combination of vitamin C, vitamin E, beta carotene, selenium, and zinc, increased skin cancer in women.^[89] In addition, a recent meta-analysis found that antioxidant supplementation, particularly beta carotene, may increase not only gastrointestinal cancer incidence but also all-cause mortality.^[90,91] Subsequent *in vitro* and *in vivo* animal studies have reported tumor cell growth in response to various antioxidants. Specifically, beta carotene stimulated cellular proliferation in a pancreatic ductal adenocarcinoma cell line^[92] and in lung cancer cell lines.^[93] In an *in vivo* tumor model, vitamin C enhanced tumor growth.^[94] Thus, the use of antioxidant supplementation for cancer prevention may be unwarranted, and antioxidant supplementation should be approached with caution in both healthy individuals as well as cancer patients.

Despite the lack of scientific data, most individuals consider botanicals as "natural" and "safe" as compared to conventional treatments. Of the individuals who reported using herbs (excluding Echinacea and ginseng), only one-third used them in accordance with evidencebased studies;^[72] most received information pertaining to a specific herb from a friend and initiated herbal use without consulting their doctor.^[73] Therefore, increased patient education on the appropriate use of dietary supplements by healthcare professionals is necessary. The Memorial Sloan-Kettering Cancer Center "AboutHerbs" Web site, <http://www.mskcc.org/aboutherbs>, is free to access, provides evidence-based and clinically useful information about more than 235 herbs and other botanicals as well as vitamins, other dietary supplements, and unproved cancer therapies, and is continually updated.

Summary

Cancer patients are increasingly using complementary therapies to alleviate symptoms caused by the disease as well as those induced by surgery, chemotherapy, and radiotherapy. Complementary therapies are not used for primary treatment of the cancer, but to manage symptoms and to control side effects from conventional treatments. They also offer patients the opportunity to select and participate in their own recovery. Although many of these therapies have been practiced over time as components of traditional medical systems, efforts to subject complementary therapies to rigorous scientific research started only in the past decade or so. Accumulating evidence supports the use of complementary therapies to reduce physical and emotional symptoms.

Due to a lack of regulatory oversight and therefore many safety concerns, dietary supplement use, including that of herbs and other dietary supplements, should be approached with caution. Patient-physician communication about dietary supplement use is important.

Sidebar: Table 1. Reliable Sources of Information on Complementary Therapies

Medline Plus:

<http://www.nlm.nih.gov/medlineplus/druginformation.html>

British Medical Journal:

<http://biomedcentral.com/bmccomplementaltermmed/>

Memorial Sloan-Kettering Cancer Center:

<http://mskcc.org/aboutherbs>

National Center for Complementary and Alternative Medicine (NCCAM):

<http://nccam.nih.gov>

Sidebar: Key Issues

- Many symptoms associated with cancer and cancer treatments are difficult to treat with standard means.
- Accumulating evidence from randomized clinical trials supports the use of complementary therapies including massage, acupuncture, mind-body therapies, music therapy, and physical exercise for symptom control and to improve cancer patients' quality of life.
- Cancer patients should be informed of safety issues concerning dietary supplements, including herbs and other botanicals.

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