

Review

Complementary and alternative medical therapies for children with cancer

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Received 10 May 2004; accepted 10 May 2004

Available online 19 August 2004

Abstract

Complementary and alternative medical therapies (CAM) are treatments that generally fall outside of the mainstream of conventional medicine. CAM therapies are used by 31–84% of children with cancer, including many children enrolled on clinical trials. CAM therapies are often used for the treatment of side-effects of cancer or cancer therapy, and only rarely as an alternative to conventional therapy. Regulation of CAM therapies varies worldwide, and many therapies have not been subject to scientifically conducted analyses. Adverse events have been described, especially from the contamination of herbs. Only rare reports of interactions of CAM therapies with conventional anticancer treatments have been reported. Several research studies of CAM in children with cancer are underway. In the interim, non-pharmacological therapies such as mind–body medicine, manipulative and body-based therapies and energy therapies may be used for supportive therapy. Research is needed before biologically based CAM therapies may be recommended in conjunction with conventional therapy.

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Keywords: Complementary; Alternative; Cancer; Child; Supplements; Unconventional

Complementary and alternative medicine (CAM) is a broad domain of healing resources that encompasses all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period [1]. The US National Center for Complementary and Alternative Medicine (NCCAM) defines CAM therapies in five categories (Table 1) [2]. CAM therapies are popular among adults with cancer [5,6], and it has become increasingly clear that children with cancer are frequent users of these therapies too [3–16].

1. Children with cancer and the use of CAM therapies

Recent surveys have shown that 31–84% of children with cancer use CAM therapies (Table 2) [3–16]. CAM therapies are mostly used as an adjunct to conventional

therapy, and primarily as supportive therapies to alleviate pain and symptoms of cancer, and especially to reduce actual or potential side-effects of cancer treatment. The factors associated with CAM use among children with cancer are varied. Parents' desire to try to do everything possible to improve their child's health likely plays a major role in their decision to use CAM therapies for their child [9,11,16]. Poor prognosis, prior CAM use, higher parental education, older age and religiosity are other factors associated with CAM use [9,10,15].

Disclosure of the use of CAM therapies to the treating physician occurs only half the time [6,8,11,15], although health care providers are beginning to routinely question their patients about the use of dietary supplements. A high rate of CAM use was noted among participants of cooperative group clinical trials for childhood cancer for which CAM use is not routinely ascertained [11]. Most users of biologically based CAM use more than one therapy, thereby creating the possibility of complex interactions with conventional chemotherapy and radiation therapy.

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Table 1

Categorisation of CAM therapies by the National Center for Complementary and Alternative Medicine [2]

Type of CAM	Definition	Examples
Alternative medical systems	Complete systems of theory and practice	Homeopathy, naturopathy, traditional chinese medicine, ayurvedic medicine
Mind–body medicine	Variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms	Meditation, prayer, mental healing, art, music, or dance
Biologically based therapies	Substances found in nature	Dietary supplements, herbal products, and the use of other so-called “natural”, but as yet scientifically unproven therapies
Manipulative and body-based methods	Manipulation and/or movement of one or more parts of the body	Chiropractic or osteopathic manipulation, massage
Energy therapies: Biofield therapies	Are intended to affect energy fields that purportedly surround and penetrate the human body	Qi gong, reiki, therapeutic touch
Bioelectromagnetic-based therapies	Involve the unconventional use of electromagnetic fields	Pulsed fields, magnetic fields or alternating current or direct current fields

CAM, complementary and alternative medicine.

Table 2

Surveys of CAM use among paediatric patients with cancer

References	Location/year of study	Number surveyed	Prevalence of CAM use (%)	Most common types
[3]	Texas, USA, 1977	69	8.7	Laetrile, faith healers
[4]	Washington, USA, 1981	106	16	Faith healers
[5]	Texas, USA, 1983	66	6	Tea, herbs, curanderos
[6]	Australia, 1994	48	46	Hypnotherapy, imagery, relaxation
[7]	Finland, 1997	15	40	Micronutrients
[8]	Florida, USA, 1997	81	65	Prayer, exercise, spiritual healing
[9]	British Columbia, Canada, 1998	366	42	Herbal teas, plant extracts, vitamins, relaxation/imagery, massage, therapeutic touch
[10]	Netherlands, 1998	84	31	Homeopathy, anthroposophy, macrobiotics
[11]	New York, USA, 2000	75	84	Diet changes, nutritional supplements, herbs, mind–body
[12]	Saskatchewan, Canada, 2000	44	36	Echinacea, essiac, garlic, selenium, herbs
[13]	Taiwan, 2000	63	73	Functional foods, temple worship/shamanism, traditional Chinese medicine, herbs, diet supplements
[14]	Washington, USA, 2001	75	73	Herbs, high-dose supplements, alternative provider
[15]	North Carolina, USA, 2003	195	47	Faith healing, megavitamins/minerals, massage, dietary supplements, relaxation techniques, herbal medicines/teas
[16]	Massachusetts, USA, 2003	118	46	Not specified

USA, United States of America.

2. Controversies of CAM therapies

For most health-care providers, the challenge is in counselling patients on the use of the biologically based CAM therapies. There have been few clinical trials of safety and efficacy especially as herbs and other biologically based CAM therapies are usually marketed as dietary supplements. Regulation of herbs and other dietary supplements varies from country to country [17], but the supplements are generally not subject to the same regulations that apply to conventional drugs. As with conventional therapies, CAM therapies are not risk-free. The majority of published serious adverse events associated with CAM use in children and adolescents are with the use of herbs, and are frequently

caused by contamination of the therapy [18]. The potential for contamination is particularly high with herbs and supplements imported from developing countries [19].

The major concern among paediatric oncologists is the potential for interactions among biologically based therapies and conventional treatments, especially chemotherapy and radiation therapy. The concomitant use of irinotecan with St. John's wort, an herb often used for mild depression, results in low levels of irinotecan through induction of cytochrome P450 CYP3A4 [20]. Few other actual herb-drug interactions have been reported in humans undergoing cancer treatment, so that the potential for interaction still must be regarded as theoretical. However, concomitant administration may

affect chemotherapy levels or increase toxicity that may ultimately impact upon outcome. Examples of potential herb or supplement interactions with conventional drugs are listed in Table 3.

The controversy surrounding antioxidants in combination with conventional therapy has focused on regimens that are believed to achieve their cytotoxic effects by generating free radicals, such as alkylating agents, anthracyclines, platinum compounds, and topoisomerase II inhibitors, and radiation. In theory, antioxidants may decrease the efficacy of these agents by quenching free radicals. However, certain adjunctive agents, such as Mesna, exert their effects through the quenching of free radicals and do not appear to decrease the efficacy of chemotherapy. Individuals treated with conventional agents that deplete the antioxidant status may require replenishment of antioxidants after treatment, just as patients receiving high-dose methotrexate require leucovorin rescue to minimise toxicity. Antioxidant supplements may reduce the short- and long-term side

effects of chemotherapy and radiation therapy, and thereby allow the administration of higher and possibly more effective doses of chemotherapy. However, the published clinical reports do not clearly define the role of antioxidant supplementation [21].

Immunomodulators are a broad category of CAM therapies that purportedly affect the immune system. Mistletoe, Asian mushrooms (maitake, reishi, shiitake, coriolus versicolor, polysaccharide K (PSK)), and astragalus are examples of immunostimulants used by patients with cancer, and these supplements generally increase either cytotoxic T lymphocytes or natural killer cells, or endogenous production of interferon, interleukins, or other cytokines [19]. No well-designed clinical trials of immunomodulators have been performed in children with cancer. Use of supplements with immunomodulatory effects should be particularly discouraged in children with haematological malignancies and in those children undergoing stem cell transplantation [19].

Table 3
Examples of potential herb and supplement-drug interactions [19,41]

Drug/effect	Herbs and supplements
<i>Anticoagulants (warfarin)</i>	
Supplements that may increase bleeding potential	Angelica root, anise, arnica flower, black cohosh, bogbean, boldo, asafoetida, capsicum, celery, chamomile, clove, denshen, devil's claw, dong quai, evening primrose, fenugreek, feverfew, garlic, ginger, ginkgo biloba, panax ginseng, guarana, horse chesnut, horseradish, licorice, meadowsweet, onion, papain, parsley, passion flower, pau d'arco, poplar, prickly ash, quassia, quinine, red clover, sweet clover, sunflower seeds, turmeric, wild carrot, wild lettuce, willow, vitamin E
Supplements that may decrease the effectiveness of anticoagulation	Alfalfa, broccoli, eicosapentenoic acid, γ -linolenic acid, garlic, ginseng, green tea, inositol hexaphosphate (IP-6), plantain, Saint John's wort, turmeric
<i>Immunosuppressants (corticosteroids, cyclosporin)</i>	
Supplements that may reduce the immunosuppression	Cordyceps (with prednisolone); country mallow, ephedra, marshmallow (with dexamethasone)
Supplements that may increase immunosuppression	Cordyceps, fish oils, garlic, grapefruit, grapefruit seed extract, L-arginine, red yeast, St. John's Wort (with cyclosporin)
Supplements that may increase cyclosporin toxicity	Licorice (with corticosteroids) alfalfa sprouts, astragalus, cat's claw, echinacea, licorice, Saint John's wort, vitamin E, zinc
<i>Methotrexate</i>	
Supplements that may increased hepatotoxicity	Grapefruit juice
<i>Tamoxifen</i>	
Supplements that may decrease efficacy	Black cohosh, soy
<i>Cisplatin</i>	
Supplements that may increase toxicity	Selenium, squalamine
<i>Etoposide</i>	
Supplements that may decrease efficacy	Glucosamine hydrochloride, glucosamine sulphate, N-acetyl glucosamine, quercitin, Saint John's wort
Supplements that may increase toxicity	
<i>Itraconazole</i>	
Supplements that may decrease efficacy	Grapefruit juice
<i>Penicillins</i>	
Supplements that may decrease efficacy	Khat

Adverse events have also been reported with non-biologically based therapies. Chiropractic upper spinal manipulation has been associated with serious adverse events including cerebrovascular accidents, acute necrosis of a holocord astrocytoma and vertebral artery dissection [18]. Acupuncture is generally considered safe with an overall underlying adverse event rate of zero to 1.1 per 10 000 treatments [22], although anecdotal reports of serious complications including cardiac tamponade, epidural abscess formation and HIV infection have been described [18]. Local reactions such as bruising, pain or bleeding are rarely observed. There is a general consensus that acupuncture in children may be used safely above the age of 10 years [23].

3. Potential benefits of CAM therapies

Many CAM therapies have the potential of improving quality of life. CAM therapies may be considered in the management of symptoms of cancer and conventional treatment and for psychological support associated with the diagnosis of cancer. CAM therapies may also be useful for end of life care. Several programmes integrate CAM therapies into the conventional care of a child with cancer [24,25].

3.1. Non-pharmacological therapies

Mind–body medicine and biofield therapies may be of particular use for supporting a child through cancer treatment, especially for the management of symptoms for which conventional therapy is often ineffective. Hypnosis and imagery reduced anticipatory nausea and vomiting and pain in children and adolescents with cancer [26–29]. Music therapy may affect a child's emotional state [30], as well as immune function [31].

Manipulative or body-based therapies, such as massage, have been related to improvements in mood and anxiety [25], and increases in neutrophil recovery rates [32]. Acupuncture has been associated with reductions in nausea and vomiting [33] and improvements in white blood cell recovery in adolescents receiving chemotherapy [34].

3.2. Pharmacological therapies

Biologically based therapies must be used with caution. Some therapies may be integrated as supportive care; the homeopathic remedy TRAUMEEL S® was associated with significant reductions in the severity and duration of stomatitis in children undergoing stem cell transplantation [35] and is currently being evaluated in a large follow-up study (Table 4). However, there is insufficient clinical evidence to support or discourage the use of most types of CAM therapies in children with cancer, especially in conjunction with conventional therapy. The safest time to use such unstudied therapies may be after completion of therapy, when the risk of drug interactions has passed.

3.3. Research of CAM therapies

Few research studies have evaluated the safety and efficacy of CAM therapies, especially among children with cancer. Numerous barriers to conducting research in CAM and cancer exist [36]. Complex therapeutic systems, such as Traditional Chinese Medicine, are difficult to study in a controlled design. The lack of regulation of herbs and nutritional supplements lead to problems with the standardisation of the product. Biases in patient recruitment to CAM trials exist because of emotional issues, in that patients strongly supportive of CAM therapies may refuse randomisation to a placebo.

Table 4
Active randomised clinical trials of paediatric CAM therapies

Trial	Sponsor	Contact
A randomised double-blind placebo-controlled clinical trial to assess the efficacy of TRAUMEEL S® for the prevention and treatment of mucositis in children undergoing haematopoietic stem cell transplantation	Children's Oncology Group, USA	Susan Sencer, M.D.
A randomised study of electro-acupuncture treatment for delayed chemotherapy-induced nausea and vomiting in patients with paediatric solid tumours	National Center for Complementary and Alternative Medicine, USA	Patrick Mansky, M.D.
A pilot study of Silymarin during maintenance therapy in children with acute lymphoblastic leukaemia and abnormal liver function tests	Herbert Irving Comprehensive Cancer Center, Columbia University, NY, USA	Kara Kelly, M.D.
A pilot study of aromatherapy to reduce anxiety and nausea in children undergoing stem cell and bone marrow transplants	Herbert Irving Comprehensive Cancer Center, Columbia University, NY, USA	Kara Kelly, M.D.
Aromatherapy as an intervention for nausea and vomiting in children receiving chemotherapy for cancer	Children's Hospitals and Clinics, Minneapolis, MN, USA	Janice Post-White, RN, PhD
Massage therapy in childhood cancer	Children's Hospitals and Clinics, Minneapolis, MN, USA	Janice Post-White, RN, PhD

Difficulties also exist in determining an adequate placebo for some CAM therapies, such as acupuncture. CAM providers may have little incentive for the scientific evaluation of CAM therapies [37]. Paediatric trials also need to account for developmental differences in the acceptance of CAM therapies [25]; for example, massage may be well accepted by an adolescent patient, but may provoke increased anxiety in an infant or young child when administered by a provider other than a parent. Yet, an increasing number of randomised controlled trials are being completed [38]. However, the quality of reports of paediatric randomised clinical trials in CAM appears to be inferior to those found for conventional medicine [39]. Several randomised clinical trials of CAM in children with cancer are currently in progress in the US (Table 4).

4. Conclusions

Many children with cancer are using CAM, and usually in conjunction with conventional chemotherapy and radiation therapy. Health-care providers need to inquire about the use of CAM and discuss its use in a non-judgmental way. Non-conventional therapies that are physically or psychologically harmful should be discouraged. However, non-harmful complementary therapies that may have a supportive role should not be routinely dismissed [40]. Further research is necessary to evaluate the safety and efficacy of CAM, especially in children with cancer where the outcome with conventional therapies is generally good.

CAM therapies may have a stronger role in supporting children through the side-effects and stress of conventional therapy. Non-pharmacological therapies, such as mind–body medicine, biofield therapies, and manipulative and body-based methods may be integrated. More information is needed before biologically based therapies can be routinely recommended.

Conflict of Interest: I have no conflict of interest to disclose.

Funding Sources: Paediatric Cancer Foundation, American Institute for Cancer Research and support to Carol Ann's Library from the Lerner and Schwartz Family.

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