Oncology Issues

ISSN: 1046-3356 (Print) 2573-1777 (Online) Journal homepage: https://www.tandfonline.com/loi/uacc20

Complementary and Alternative Medicine in the Treatment of Cancer: Current Research and Future Directions

Omer Kucuk

To cite this article: Omer Kucuk (2000) Complementary and Alternative Medicine in the Treatment of Cancer: Current Research and Future Directions, Oncology Issues, 15:6, 17-19, DOI: 10.1080/10463356.2000.11905170

To link to this article: https://doi.org/10.1080/10463356.2000.11905170

Complementary and Alternative Medicine in the Treatment of Cancer: Current Research and Future Directions

by Omer Kucuk, M.D., F.A.C.N.

The term "alternative cancer therapy" refers to clinically unproven treatments that are used in place of conventional cancer treatments, while the term "complementary therapy" is attributed to such treatments when they are used as adjuncts to conventional therapy. These treatments may enhance, interfere, or have no interactions with standard cancer therapy. Some complementary and alternative medicine (CAM) treatments may provide symptom control and palliation with minimal or no side effects. However, CAM treatments may have dangerous adverse effects or potentially interfere with standard therapy. In addition, if used alone, they may indirectly harm the patient by delaying clinically proven standard treatments.

Complementary cancer therapies have recently received considerable attention in the scientific and medical community. The National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH) is dedicated to research investigating these therapies. Although CAM therapies have been used for many years, few well-designed, properly conducted clinical studies have investigated their efficacy and adverse effects. Many physicians treating cancer patients have little knowledge of alternative therapies and, therefore, frequently discourage their use by patients. More recently, however, reports of CAM treatments have begun to appear in medical journals, and research programs for CAM therapy have been developed by several comprehensive cancer centers.

Omer Kucuk, M.D., F.A.C.N., is professor of medicine and oncology, Division of Hematology and Oncology, Barbara Ann Karmanos Cancer Institute, in Detroit, Mich. Dr. Kucuk can be reached at 313-745-2357, or e-mail him at: kucuko@karmanos.org

NIH listed the following CAM research areas in a recent Request for Applications (RFAs):

- Alternative medical systems, which include traditional oriental medicine (acupuncture, herbal medicine, oriental massage, and *qi gong*, or vital energy); ayurveda (India's traditional system of medicine that places equal emphasis on body, mind, and spirit, and strives to restore the innate harmony of the individual); other traditional medical systems such as those developed by Native American, Aboriginal, or African cultures; homeopathy; and naturopathy
- Manipulative and body-based systems, such as chiropractic, osteopathic, or unconventional applications of integrated conventional and physical therapies, including massage therapy
- Biofield therapy, such as energy healing and intentional effects on living systems
- Bioelectromagnetics, such as diagnostic and therapeutic application of electromagnetic (EM) fields, including pulsed EM fields, magnetic fields, direct current fields, and artificial light therapy
- Pharmacologic therapies, such as metabolic therapies and immunoaugmentative therapies as used by CAM practitioners or the public, including antineoplastons (medium- or small-size peptides and amino acid derivatives that are taken orally or injected, and are said to form a defense against cancer), enzyme therapies, the Revici system (which focuses on improving the balance between anabolic and catabolic activities, using injectable selenium, calcium, and copper), or 714X (a camphor rich in nitrogen) therapy
- Herbal medicine, such as echinecea, gingko biloba, and other herbals
- Mind-body medicine, such as transcendental meditation, imagery, hypnosis, biofeedback, music therapy, yoga, spirituality, and biological effects of consciousness
- Orthomolecular medicine, such as the use of products that may be used as nutritional and food supplements, such as ultra-high doses of magnesium, co-enzyme Q-10 (an antioxidant), carnitine (an amino acid), melatonin, or vitamins, when investigated for therapeutic or preventive purposes.

Despite the widespread use of CAM treatments,[1] little data are available to demonstrate the safety, efficacy, and mechanisms of these therapies. The U.S. Office of Technology Assessment issued a report urging a systematic analysis of alternative treatments and their effects on major disease, health, and wellness (U.S. Office of Technology Assessment, OTA-H-405, 1990, p. 225). To promote high-quality research of CAM, the National Center for Complementary and Alternative Medicine (NCCAM), the National Cancer Institute (NCI), and the National Heart, Lung, and Blood Institute (NHLBI) recently funded 11 centers for CAM research. Such centers will provide the resources necessary for the rigorous scientific investigation of CAM. Research conducted at these centers is expected to examine the

potential efficacy, effectiveness, safety, and validity of CAM practices, as well as the physiological or psychological mechanisms underlying or contributing to the effects of these practices.

Some of the research topics for CAM therapies listed in the NIH RFA include: prevention; modification of disease course; supportive care or symptom management (including pain control); management of chemotherapy, surgery, or radiation induced side-effects; and issues involved in improving quality of life of cancer survivors. Multidisciplinary approaches to study the molecular and cellular basis of the mechanism of action of CAM therapies in cancer are needed, and collaborations between clinical investigators and basic scientists are crucial. Areas of CAM research include:

- Unconventional adjuvant nutritional approaches that either augment the therapeutic effect of conventional therapies or ameliorate side effects
- Elucidation and systematic evaluation of the mechanisms of action and potential clinical significance of drug-botanical interactions
- Comparative analyses of therapeutic indexes of whole botanical products versus specific isolated compounds from these products with known anticancer activity
- Studies of the potential effect of mind-body modalities (e.g., relaxation, imagery, meditation, psychosocial support groups, or psychotherapy) on physiologic end points (e.g., immune parameters) or disease parameters, such as response rate to conventional therapy, disease-free survival, or overall survival
- Cancer chemoprevention studies that are oriented to unpurified, whole natural substances, such as soy products or herbal extracts
- Studies to evaluate the potential interaction of antioxidant compounds and conventional chemotherapy and/or radiation therapy.

Oncologists are aware that their patients use CAM. As cancer incidence rates and survival time increase, use of CAM will likely increase. Richardson and colleagues[2] assessed the prevalence and predictors of CAM use among cancer patients attending the outpatient clinics at The University of Texas M.D. Anderson Cancer Center, Houston, Tex. Of the 453 participants, 99 percent had heard of CAM. Of those, 83 percent had used at least one CAM approach. Use was greatest for spiritual practices (81 percent), vitamins and herbs (63 percent), and movement and physical therapies (59 percent). The researchers found that women, younger patients, and those who had undergone cancer surgery or who were poor were more likely to use alternative treatments. Most of the participants expected CAM to improve their quality of life (77 percent), boost their immune system (71 percent), prolong life (63 percent), or relieve symptoms (44 percent). However, about 38 percent expected CAM therapies to cure their disease. Despite high hopes for CAM, about 60 percent of participants said that they had not discussed the topic of alternative and complementary medicine with a physician. The authors concluded that "given the number of patients combining vitamins and herbs with conventional treatments, the oncology community must improve patient-provider communication, offer reliable information to patients, and initiate research to determine possible drug-herb-vitamin interactions."

Nam and colleagues[3] determined the prevalence and patterns of the use of complementary therapies among patients with prostate cancer and those at high risk for the disease. Of the patients presenting to urology clinics and the support group, 27.4 and 38.9 percent with, and 25.8 and 80 percent at high risk for prostate cancer, respectively, used some form of CAM. Since some CAM therapies used by prostate cancer patients may include herbs, such as PC-SPES,[4] and phytochemicals, such as lycopene[5] and soy isoflavones[6] with potent biological effects, obtaining accurate information from patients regarding their CAM use is important.

PHYTOCHEMICALS IN CANCER PREVENTION AND TREATMENT

One area of active CAM research is the use of phytochemicals in the prevention and treatment of cancer. The rationale for the use of phytochemicals in cancer prevention comes from epidemiological studies demonstrating decreased cancer risk associated with increased consumption of fruits, vegetables, and specific phytochemicals. Fruits, vegetables, and other plants contain many potentially cancer-preventive compounds.

Large clinical studies have been conducted and more trials are planned to study the cancer-preventive effects of specific micronutrients and phytochemicals. Well-designed clinical trials are necessary to determine whether a micronutrient confers benefit or risk in the target population. The importance of conducting clinical chemoprevention trials has become very clear recently when several clinical trials showed that the agents hypothesized to prevent cancer did exactly the opposite.[7,8] A large chemoprevention study conducted to determine whether beta-carotene and/or alpha-tocopherol would prevent lung cancer showed that beta-carotene supplementation *increased* the risk of lung cancer.[7] These unexpected results highlight the importance of conducting well-designed, prospective, randomized clinical trials before making recommendations to the public regarding the use of supplements.

BETA-CAROTENE PARADOX

Epidemiological studies have consistently shown that increased intake of fruits and vegetables, which are rich in carotenoids, is associated with decreased risk of lung cancer. Since lung cancer is caused by smoking, which is a pro-oxidant, and since smokers have decreased serum levels of beta-carotene and other antioxidants, supplementing the diet with beta-carotene in smokers to prevent the development of lung cancer was a reasonable strategy. However, a well-designed, large clinical study conducted in Finland found just the opposite.[7] This unexpected result might have been due to the paradoxical pro-oxidant effect of beta-carotene in lungs where the oxygen tension is high. This information became available only recently and was not known at the time the study was designed. Studies have shown that beta-carotene, at high concentrations, has a pro-oxidant effect when the oxygen pressure is also high.[9] Therefore, in lungs where the oxygen tension is high,

administering large doses of beta-carotene may lead to oxidative DNA damage and higher incidence of cancer. Furthermore, beta-carotene and tobacco smoke interact to increase activator protein-1 (AP-1) production in ferret lungs.[10] Overexpression of AP-1 is positively associated with squamous metaplasia in lung tissue. This increased production of AP-1 may also explain the increased risk of lung cancer with beta-carotene supplementation in current smokers but not in current non-smokers.

ANTIOXIDANT USE DURING CHEMOTHERAPY OR RADIATION

Recent articles have cautioned and discouraged the use of antioxidant supplements during radiation and chemotherapy primarily because of the theoretical possibility that antioxidants may interfere with the therapeutic efficacy of radiation and chemotherapy.[11] Since antitumor effects of radiation therapy and certain chemotherapeutic agents have been attributed to generation of oxygen free radicals, there is some concern regarding potential interference that may be caused by antioxidant micronutrients taken by patients during therapy. Although theoretically plausible, no reported human clinical trials have yet shown this potential adverse effect. To the contrary, there are examples of antioxidants preventing the toxicities of radiation[12] or chemotherapy[13] while not affecting their antitumor effects. Since supplement use is prevalent among cancer patients and there is potential for negative interactions between supplements and anticancer therapy, clinical trials investigating these potential interactions should be conducted. Until clinical data become available, recommendations should not be made one way or another, and caution should be exercised in the use of any high-dose chemical that has the potential to interact with chemotherapy or radiation therapy.

SOY ISOFLAVONES: TO USE OR NOT?

Similarly, some physicians discourage the use of soy products by women who have breast cancer, because of possible estrogenic effect of soy isoflavones. However, many physicians prescribe tamoxifen and/or estrogen replacement therapy for the same women. The concerns about soy phytoestrogen use in the breast cancer setting are not based on clinical data, since no clinical studies have shown increased risk of cancer or poor outcome in women with breast cancer who are taking dietary soy products. To the contrary, in Japan, where soy consumption is much higher than the United States, the risk of breast cancer is lower, and the outcome of treatment is better than that in the United States in similarly treated women.[14]

Because of the U.S. Food and Drug Administration approval of soy products as "heart disease preventive" foods in October 1999, the consumption of soy products is likely to increase in the U.S. population. This increase will likely include a substantial number of women who are at risk for breast cancer or have active breast cancer or had cured breast cancer. Some women will be on tamoxifen or raloxifene for prevention or treatment of breast cancer. Since soy isoflavones bind to estrogen receptors, potential interactions with tamoxifen, raloxifene, or other molecules that bind to estrogen receptors are possible. Thus, it is important to investigate the soy isoflavone compounds in breast cancer as well as prevention and treatment in other cancers. Keep in mind that soy isoflavones are not only antiestrogenic/proestrogenic, but they also have antioxidant, antiproliferative, anti-inflammatory, and pro-apoptotic effects in cancer cells, which may provide additional mechanisms for their potential anticarcinogenic effects. Current recommendations to healthy individuals as well as patients include caution in using soy isoflavone supplements until clinical trials are completed. However, there is no good reason to discourage people from eating whole soy products, such as roasted soy nuts or tofu, or drinking soy milk. Clinical research with soy foods and/or soy isoflavones in patients with breast cancer or in individuals at high risk for breast cancer should be a high priority.

REFERENCES

[1]Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*. 1998;280:1569-1575.

[2]Richardson MA, Sanders T, Palmer JL, et al. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *J Clin Oncol*. 2000;18:2505-2514.

[3]Nam RK, Fleshner N, Rakovitch E, et al. Prevalence and patterns of the use of complementary therapies among prostate cancer patients: an epidemiological analysis. *J Urol*. 1999;161:1521-1524.

[4]DiPaola RS, Zhang H, Lambert GH, et al. Clinical and biologic activity of an estrogenic herbal combination (PC-SPES) in prostate cancer. *N Engl J Med*. 1998;339:785-791.

[5]Kucuk O, Sakr W, Sarkar F, et al. Lycopene supplementation decreases serum PSA, PIN and tumor volume in early stage PCa. *Proc AACR*. 1999.

[6]Davis JN, Muqim N, Bhuiyan M, et al. Inhibition of prostate specific antigen expression by genistein in prostate cancer cells. *Int J Oncol*. 2000;16:1091-1097.

[7]Albanes D, Heinonen OP, Taylor PR, et al. Alpha-tocopherol and beta-carotene supplements and lung cancer incidence in the alpha-tocopherol, beta-carotene cancer prevention study: effects of base-line characteristics and study compliance. *J Natl Cancer Inst*. 1996;88:1560-1570.

[8]Omenn GS, Goodman GE, Thornquist MD, et al. Risk factors for lung cancer and for intervention effects in CARET, the beta-carotene and retinol efficacy trial. *J Natl Cancer Inst*. 1996;88:1550-1559.

[9]Palozza P, Luberto C, Calviello G, et al. Antioxidant and prooxidant role of beta-carotene in murine normal and tumor thymocytes: effects of oxygen partial pressure. *Free Radic Biol Med*. 1997;22:1065-1073.

[10]Wang XD, Liu C, Bronson RT, et al. Retinoid signaling and activator protein-1 expression in ferrets given beta-carotene supplements and exposed to tobacco smoke. *J Natl Cancer Inst*. 1999;91:60-66.

[11]Labriola D, Livingston R. Possible interactions between dietary antioxidants and chemotherapy. *Oncol*. 1999;13:1003-1008.

[12]Planting AS, Catimel G, de Mulder PH, et al. Randomized study of a short course of weekly cisplatin with or without amifostine in advanced head and neck cancer. EORTC Head and Neck Cooperative Group. *Ann Oncol*. 1999;10:693-700.

[13]Hensley ML, Schuchter LM, Lindley C, et al. American Society of Clinical Oncology clinical practice guidelines for the use of chemotherapy and radiotherapy protectants. *J Clin Oncol*. 1999;17:3333-3355.

[14]Nemoto T, Tominaga T, Chamberlain A, et al. Differences in breast cancer between Japan and the United States. *J Natl Cancer Inst*. 1977;58:193-97.