

Approach to Communicating with Patients About the Use of Nutritional Supplements in Cancer Care

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Abstract: In recent years, complementary and alternative medicine has become popular among the general population in the Western world. Cancer patients have joined this global trend, often seeking supplements to conventional oncologic care, usually without their physicians' knowledge. Among the most common forms of complementary and alternative medicine used by cancer patients are natural products such as herbs and megavitamins. The extensive use of nutritional supplements by cancer patients raises multiple questions and challenges for the physician. Since there are limited scientific data on the efficacy and safety of many nutritional supplements, advising patients about when to use them during the course of illness is difficult. This is true for each stage of cancer care: prevention, acute active care (radiation, chemotherapy, surgery), and post-acute care (follow-up visits and prevention of recurrence). The authors describe a patient-centered approach to the use of nutritional supplements in cancer care.

Key Words: alternative medicine, antioxidants, cancer care, cancer prevention, dietary supplements, green tea, integrative medicine, lycopene, nutritional supplements, patient-centered care

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Many studies have confirmed that a majority of patients undergoing cancer therapy also use self-selected forms of complementary and alternative medicine (CAM), including over-the-counter biological products.^{1,2} Nutritional supplements are one of the easiest and most accessible modes of CAM therapies. Previous reports estimate that these products are used by 20 to 55% of cancer patients.³⁻⁷ Patients may take nutritional supplements to reduce side effects and organ toxicity, to protect and stimulate immunity, or to prevent further cancers or recurrences (Table).

Patients often do not report their use of supplements or other CAM therapies to their provider.⁸ This gap in communication may result from (1) patient perception that their physician is indifferent or negative toward CAM⁹ or (2) physician emphasis on scientific studies and evidence-based medicine rather than patient preferences, in the selection of such therapies.

The failure of physicians to communicate effectively with patients on CAM topics may result in a loss of trust within the therapeutic relationship and in the selection by patients of harmful, useless, or ineffective and costly nonconventional therapies when effective CAM therapies may exist. Poor communication may also lead to a diminishment of patient autonomy and self-efficacy and thereby interfere with the self-healing response.⁹

Key Points

- Nutritional supplement use is popular among patients who are concerned about cancer care.
- The extensive use of nutritional supplements by patients with cancer raises multiple questions and challenges for the physician.
- A patient-centered approach to the use of nutritional supplements in cancer care is suggested; this approach makes use of all available scientific data relating to safety and efficacy of these supplements, combined with an open discussion with the patients about their needs and expectations.

Table. Some nutritional and herbal supplements commonly used by patients with cancer^a

Vitamins
Vitamin A (including beta carotene),
Vitamin B ₆
Vitamin C
Vitamin D
Vitamin E
Minerals
Calcium
Selenium
Zinc
Botanicals
Esslac
Green tea
Lycopene
Mistletoe
Soy
Others
Bioflavonoids
Coenzyme Q ₁₀
Glutathione
Melatonin

^aFrom References 1–4, 6, 16–24, 26–29.

Although scientific and evidence-based thinking is fundamental to contemporary medical practice, failure to recognize that patients often do not reason in this way interferes with the physician's ability to address the unspoken needs of the patient who has cancer. Psychologic, social, and spiritual dimensions of care may be ignored if the physician cannot adapt to the individual needs of the patient or provides care without compassion. Particularly when physicians are faced with unfamiliar information from a CAM field, they may feel "deskilled" by being forced outside their zone of comfort and competence. This discomfort can lead to defensiveness and a breakdown in communication with the patient. In contrast, the physician who is receptive to patient inquiries and aware of subtle, nonverbal messages can create an environment of safety in which a patient feels protected⁹ and can openly discuss potential CAM choices.

This article will focus on the challenges facing clinicians in addressing patient questions about the use of nutritional supplements and herbals in cancer care. The authors will consider related issues about physician-patient communications and offer a useful model for developing a therapeutic relationship with patients who request advice about the use of these supplements in their struggle to overcome cancer.

Patient Perspective

The physician faces multiple questions and challenges in approaching a patient with cancer who is using nutritional

supplements; the most important issues are likely to be safety and efficacy.¹⁰ Often, no adequate studies of a particular supplement have been reported. If no safety issues are documented and there are clinical clues that suggest possible effectiveness, should we discourage the patient from using those supplements despite the limited evidence? Even though we try to base our work on reliable scientific evidence, one cannot overlook the patient perspective in this equation. Patients frequently see natural product consumption as an avenue that they can use to try to take control over their health and increase their quality of life.¹¹

Most patients do not consult with their physician before the decision to use these supplements.^{5,12} Many believe that the physician has limited knowledge on this topic or has no interest in discussing the use of supplements. However, some patients expect their physician to study the appropriate use of the supplements that are specific to their situation, so they can obtain educated advice and cooperation in decision-making.¹¹ If their physician is not a responsive and reliable source of information, patients obtain and collect information on supplements from a variety of sources, such as advice from friends and relatives, nonprofessional literature, popular magazines, journals, daily newspapers, the Internet, advertisements, and other information provided at the health food store. At times this information is not accurate and occasionally it may even be dangerous.¹³

To be open to the patient's perspective and sensitive to his or her need for autonomy and empowerment, physicians may need a shift in their own perspectives. Today's informed patients truly value physicians who appreciate them as empowered participants in making their own health care choices. The physician or other health care provider is an informed intermediary, an expert guide, a consultant. Ultimately, the patient must be encouraged and supported to make his or her own choices, informed by the best knowledge of the doctor. To help cancer patients be truly informed and autonomous, we need to (1) identify the patient's beliefs, fears, hopes, and expectations; (2) learn what conventional treatments have been tried, have failed, or have been rejected because of safety, quality of life, cost, or other issues; (3) make sure the patient understands prognostic factors associated with the stage of the disease and also understands the potential benefit of conventional therapy as well as its potential harm; (4) acknowledge the patient's spiritual and religious values and beliefs, including views about the end of life, and seek to understand how these impact health care choices; (5) discover what levels of support the patient relies on from family, community, faith community, and friends.

The bottom line is that before we can assess the value of specific alternative therapies, we must determine why the patient is seeking them in the first place. By creating a trusting relationship based on good communication between physician and patient, misunderstandings are avoided on both

sides.¹⁴ Perhaps the optimal approach is to discuss both the facts and the uncertainty with the patient in order to reach a mutually informed decision.¹⁵

Use of Nutritional Supplements Across the Continuum of Cancer Care

It is appropriate to raise the question of CAM use with patients and decide together on therapeutic management options at each stage of cancer care, from prevention, to acute active care (radiation, chemotherapy, surgery), to post-acute care (follow-up visits and prevention of recurrence). In the following discussion, we offer several examples of controversial uses of nutritional supplements in cancer care. Our purpose is not to prove or disprove the efficacy of these supplements, but to sharpen and refine the questions that physicians may ask when faced with uncertain information about CAM therapies. We believe that asking the right questions, particularly when final answers are not available, will lead to improved patient-doctor communication and a rational strategy to address patients' needs and expectations in the face of uncertainty.

Prevention

Many publications report on the potential usefulness of nutritional supplements in preventing cancer. The US Preventive Services Task Force, in its recent update of the evidence from randomized controlled trials, concluded that so far, the data do not show any consistent association between vitamin supplementation and risk for cancer.¹⁶ On the other hand, in a recent article by one of the medical officers of the Task Force, it was mentioned that with the exception of vitamins for which there is compelling evidence of harm (eg, β -carotene supplements in smokers), there is little reason to discourage people from taking vitamin supplements.¹⁷

Some of the studies on which the US Preventive Services Task Force bases its recommendations are epidemiologic in nature, raising multiple questions about the validity of extrapolating that data to preventive and therapeutic applications. How should we respond to patients' requests to add those products to their care? Should we use a different approach for specific high-risk populations, such as women with specific genes for breast cancer or family members of patients with colorectal or prostate cancer? There are no clear answers to these questions, and the current medical literature offers limited guidance. To sharpen such questions and to address such uncertainty, let us look at a commonly used supplement called lycopene.

Lycopene is a red pigment, a fat-soluble carotenoid, and a very strong antioxidant that is found mostly in tomatoes. In a review of the epidemiologic literature by Giovannucci,¹⁸ 57 of 72 studies revealed an inverse association between serum lycopene levels and the incidence of prostate, lung, and stomach cancer. No side effects were observed with high serum

lycopene. To apply this data to the individual patient, we need to ask: Is the evidence sufficient to recommend this supplement to a patient who would like to reduce his risk for development of prostate cancer? Since 72 studies have shown no known harm or major side effects from lycopene treatment, we probably don't need to wait for a large, randomized, controlled clinical trial to establish definitively the safety of this supplement. Hence, with current knowledge, it would be appropriate to bring this option of care to the patient who is very concerned about this type of cancer, but only after a proper discussion about the limitations of currently available studies.

Active Phase of Cancer Care: Surgery, Chemotherapy, Radiation

What happens beyond prevention? Should we or should we not add supplements in the acute stage of treatment? Should we give supplements during and after surgery, during radiotherapy, or add some supplements to the chemotherapy protocol? What supplements have the potential to reduce or enhance the safety and efficacy of our conventional treatments? Would chemotherapy be more effective and have fewer side effects if we added these agents? Are they going to improve quality of life and extend survival, or maybe the opposite? Should we object to the use of these therapies, and support or ignore patients that bring such an option of care to the patient-doctor encounter?

In this instance, let us consider the case of green tea. As in the case of lycopene, epidemiologic studies of green tea suggest that it has anticancer properties, reducing the risk of breast, prostate, colon, and pancreatic cancers.¹⁹ Green tea (*Camellia sinensis*) originates from the same plant as the black tea that is consumed worldwide. Because green tea is less processed than black tea, it is thought to have stronger medicinal properties.

Green tea has multiple flavonoids, including epi gallo catechin gallate. These substances are reported to induce apoptosis in some tumors without affecting normal cells. Another effect of the epi gallo catechin gallate is the inhibition of urokinase, an enzyme important in cancer cell development.²⁰ Moreover, a research group from Japan evaluated the effects of adding green tea to doxorubicin in the treatment of mice with ovarian sarcomas and found that this combination increased the efficacy of the chemotherapy. Adriamycin concentrated 2.7 times more in the tumor cells, whereas its concentration was reduced in the normal cells.²¹ So, do we need to change some protocols of care and consider adding green tea to increase the efficacy of chemotherapy and reduce its side effects and toxicity? Unfortunately, animal studies cannot answer this question; human clinical trials are required to obtain definitive answers.

In another clinical trial, lycopene was used as a supplement to treat prostate cancer in 33 patients for whom surgery was the suggested plan of care. This study was a randomized,

controlled trial in which the active group received lycopene for 3 weeks while they awaited surgery. The patients who received lycopene had significant reduction in prostate-specific antigen by the end of the study. In the lycopene-treated group, tumors were smaller, with a lower degree of malignancy.²² Since it is common for patients to wait for surgery, especially in countries with socialized medicine, it would make sense to use this waiting period to test the efficacy of other nutritional supplements.

Another major controversy relates to the use of antioxidants during the active chemotherapy treatment phase. Some argue that while concurrent use of antioxidants might reduce treatment-related side effects, it also runs the risk of reducing the cancer fighting power of chemotherapy.²³ A recent study evaluated the addition of glutathione, a natural antioxidant compound that consists of three amino acids, to a chemotherapy regimen using oxaliplatin to treat patients with advanced colorectal cancer. The researchers found that adding glutathione did not reduce the effectiveness of chemotherapy: The overall response rate was 23.1% in the placebo-added group compared with 26.9% in the glutathione-added group. Moreover, by the eighth cycle of the regimen, 15 of the 19 patients (78.9%) who received oxaliplatin plus placebo had nerve damage (neurotoxicity), compared with just 9 of the 21 patients (42.9%) who received oxaliplatin plus glutathione. The results were even more dramatic for patients who had serious to severe neuropathy: 11 of 19 patients (57.9%) in the oxaliplatin-plus-placebo group had serious neuropathy, compared with 2 of 21 (9.5%) in the oxaliplatin-plus-glutathione group, a 6-fold reduction. After a full 12 cycles, serious to severe nerve damage was seen in 8 of 19 patients (42.1%) in the oxaliplatin-plus-placebo group, compared with 3 of 21 patients (14.3%) in the group receiving glutathione. These differences were all statistically significant. The authors of this study concluded that glutathione is “a promising drug for the prevention of oxaliplatin-induced neuropathy” and that “it does not reduce the clinical activity of oxaliplatin.”²⁴ This one study does not resolve the controversy of antioxidant use during chemotherapy,^{25,26} but it highlights the need to look at this issue more carefully.

The controversy that surrounds the use of antioxidants during the active treatment phase also involves supplements to radiotherapy. The same questions arise here: will antioxidants reduce radiation-related side effects, or is there risk of reducing the cancer fighting power of the therapy? A recent review article reported that multiple studies demonstrate that high dose dietary antioxidant micronutrients (vitamins A, C, and E and carotenoids) selectively enhance the inhibitory effect of irradiation on growth cancer cells, and in some cases they protect normal cells against such damage.²⁷ Although this review cannot in itself resolve the controversy of antioxidant use concomitant with radiation treatment, it brings another perspective that needs to be considered in care planning for patients undergoing radiotherapy.

Typically, the data that support the efficacy of specific supplements come from small studies that do not allow one to extrapolate to the general population. Although these studies are insufficient to change the standard of care, they do bring clinical clues that may be informative when we are considering common, safe and easily available nutritional supplements. As we talk with the individual patient, we face this basic question: At what point do we refuse to accept or actively discourage the use of substances that the patient hopes will increase the efficacy of oncologic treatment? If a high level of uncertainty is present, we should involve the patient in the decision-making, clarifying risks and benefits as well as possible.

Tertiary Prevention

Once a patient has finished the acute course of cancer treatment, what should we do at the next stage? Would selected nutritional supplements be useful? Would they increase or decrease the recurrence rate, or have no effect at all? What should we do if there are clinical observations suggesting that cancer recurrence rates are lower when a supplement is added? If safety is not in question, should we wait until a large, randomized, clinical trial is done to recommend use of this supplement?

The following research study illustrates the relevance of these questions. In Japan, a clinical trial was conducted for 10 years among 1,160 women who had surgical removal of breast cancer. A statistically significant decreased rate for recurrence was observed with consumption of three or more daily cups of green tea, particularly for women with stage I and II cancers.²⁸ With this study in mind, should we routinely recommend to breast cancer survivors that they add green tea to their daily life? How do we approach the patient who wants to use this supplement to reduce her risk for recurrence? Although we cannot base our treatment strategy on one study alone, the results of the Japanese study may be shared with patients to add another perspective in their consideration of treatment options.

Suggested Approach

The examples discussed above demonstrate that reviewing the current literature is often not sufficient to answer questions about nutritional supplements with a high level of certainty from the perspective of evidence-based medicine. The challenge for the clinician is how to deal with an issue that has a high level of uncertainty. Physicians urgently need to approach supplement use in cancer in a systematic way. When limited scientific data in the medical literature support the use of a particular nutritional supplement, these data cannot be considered proofs of efficacy, but they do offer clinical clues that support the use or avoidance of specific supplements. Such clues can provide a basis for honest and open discussion with the patient. When physicians use a patient-centered approach, they can promote informed decision making by the patient in collaboration with the physician. This combined effort can provide a base for an improved patient-doctor relationship and can empower the patient in his or her own healthcare.

We suggest a rational strategy for approaching nutritional supplement use by patients that suffer from cancer (Figure). The first step is to increase one's knowledge about the supplement in question, mainly by searching reliable web sites²⁹⁻³¹ as well as MEDLINE. In this step, one has to examine two main issues: safety and efficacy.

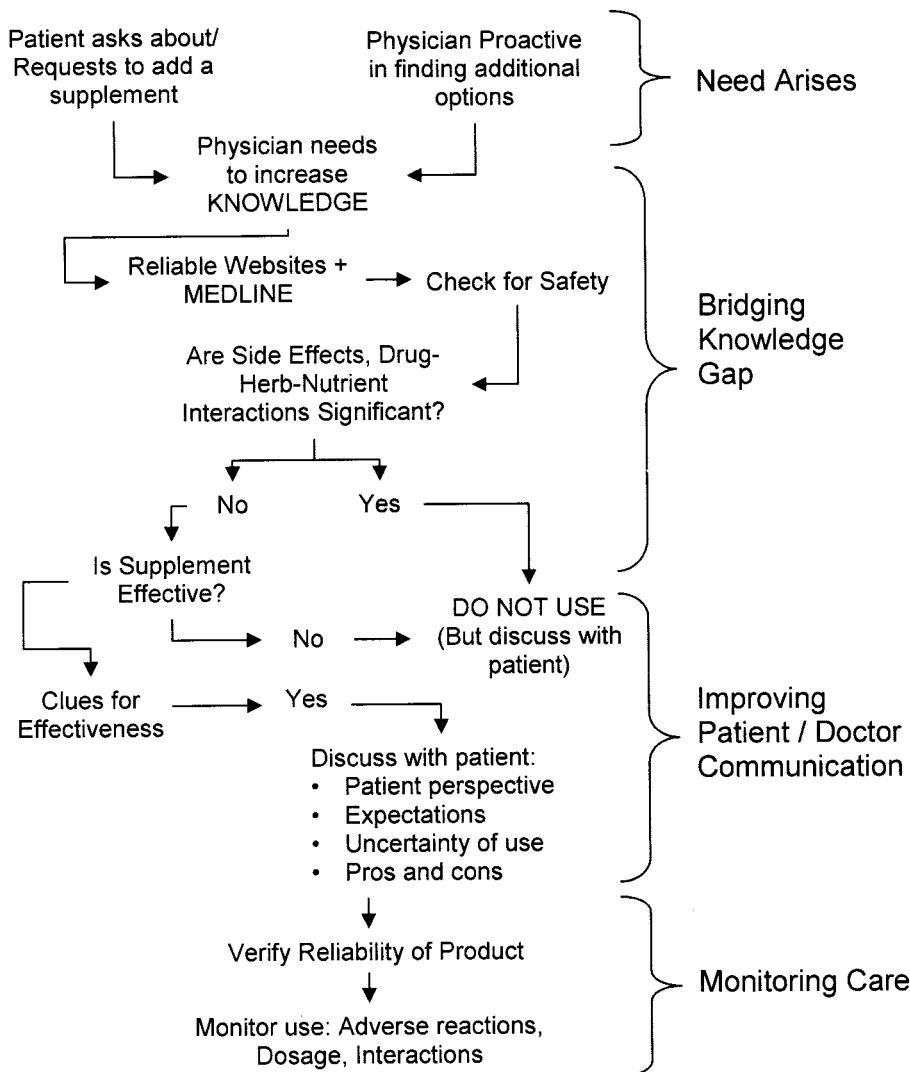
The most crucial elements are the safety of the product in question, side effect profile, and possible interactions with other nutrients and medications. *Primum non nocere* is the dictum of physicians: First of all, to do no harm. Ignorance of this information is no longer excusable, as it is widely available in medical journals, texts, reliable web sites, and databases. A corollary to this dictum may be stated as "prevent the patient from harming himself."

Frank, nonjudgmental discussion with the patient is necessary to inform the patient effectively about the known risks and benefits of these supplements.

No matter how safe a therapy is, if it is ineffective, the

patient must be so informed. Complementary therapies, by definition, have generally not reached the level of evidence of many conventional therapies. They exist at the interface of science and healing. Note, however, that many cancer therapies, including chemotherapy, radiotherapy, and a number of plant-based agents, were considered "alternative" before they were accepted as the standard of care. Moreover, arguing with the patient that they should not try an unproven therapy that they are convinced would be helpful is not productive; it is likely to damage the therapeutic relationship and drive the communication process underground. It may even be considered cruel if no better conventional therapy is available.

If it appears that a product is safe and there are clinical clues that it may have some effectiveness, the next step is to discuss the level of uncertainty of the product with the patient. A realistic view may be that more complete information will not be available in the near future and that we may need to make a decision that balances risk and benefit. The higher the patient's



Strategy for approaching the use of nutritional supplements by cancer patients.

expectations, the higher the degree of disappointment when the course of care does not go as expected. An informed discussion should give basic hard data on the supplement in question in order to minimize unrealistic expectations. This discussion can also be used as a tool to improve the doctor-patient communication and empower the patient in his or her own care at a critical juncture in the cancer care journey.

If a decision is reached to add a nutritional supplement to the treatment of cancer, the physician's role has not ended. The physician still has the responsibility of verifying, with some degree of certainty, the reliability of the specific commercial product in question. A physician with some market knowledge can verify a product's reliability by referencing independent websites.³² Once product selection and dosage is determined, regular follow-up is needed to monitor adverse effects and effectiveness, and make dosage adjustments, as with any medication.

Conclusion

The role of nutritional supplements in cancer care is controversial. There is a high level of uncertainty about their efficacy, and also doubts, in some cases, about their potential adverse interactions with conventional therapies. Nonetheless, with the increased use of these supplements by cancer patients, physicians need to use a rational approach to advising patients and monitoring their use of supplements. The approach recommended in this article might help the physician address the challenges of CAM treatments through systemic knowledge acquisition and open discussion with the patient. One can disagree with a patient's choices while compassionately engaging and supporting them. In this way, we fulfill our roles of caring, comforting, and healing, even if a cure is not possible.

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