Nutritional and Lifestyle Modification to Augment Oncology Care: An Overview

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Introduction

By the year 2000, cancer will emerge as the number one cause of death in the United States. Despite the enormous effort to combat cancer, the number of new cases of nearly every form of cancer has increased annually over the last century. Still worse, from 1930 to the present, despite the introduction of radiation therapy, chemotherapy, and immunotherapy with biological response modifiers, despite CT scans, MR scans, and all the other new medical technology – lifespans for almost every form of adult cancer except cervical cancer and lung cancer have remained constant, which means that there has been no significant progress in cancer treatment. The successes in the treatment of cancer plateaued in the 1970s, and no real advances have been made since then. Chemotherapy and radiation therapy continue to have a role in cancer treatment but produce morbidity. Nutritional modification, including the use of certain nutrients, and proper lifestyle can dramatically decrease the morbidity and side effects of chemotherapy and radiation therapy. There have even been some reports that nutritional and lifestyle modification actually increase survival. Numerous studies show that nutrients used with chemotherapy and radiation therapy can enhance tumor killing and preserve normal tissue.

Vitamins and Minerals Used With Chemotherapy and Radiation Therapy

Do vitamins or minerals interfere with chemotherapy and/or radiation therapy? This is a question I am asked frequently by patients because they have been advised not to take supplements during treatment. Many studies have been done to address this. The early clinical studies were performed at the National Cancer Institute using an antioxidant called N-acetyl cysteine which was found to protect the heart from the cardiac toxicty of adriamycin, but did not interfere with the tumor-killing capability of adriamycin.

A series of studies ensued to investigate the protective effects of antioxidants used concomitantly with adriamycin. An antioxidant called dexrasonane (formerly called ICRF-187) offered significant protection against cardiac toxicity caused by adriamycin without affecting the antitumor effect.[1-6] Cellular studies,[7-10] animal studies,[11-21] and human studies[22,23] demonstrate that vitamins A, E, and C, as well as beta-carotene and selenium, as single agents or in combination, all protect against the toxicity of adriamycin and, at the same time, actually enhance its cancer-killing effects.

Animal Studies

Vitamins and minerals have also been studied with other chemotherapies and radiation. Studies using beta-carotene and other retinoids, vitamin C, or vitamin K show that normal tissue tolerance was improved in animals undergoing both chemotherapy and radiotherapy and that tumors regressed.[24-33]Vitamin E produced similar findings: Tumors in animals showed regression when either radiation or chemotherapy was used concomitantly with vitamin E.[17-21,34-41] Animals given both beta-carotene and vitamin A with radiation and chemotherapy had more tumor killing than with chemotherapy and radiation alone, normal tissues were more protected, and there was a longer period of time without tumor recurrence.[42,43] Selenium and cysteine also heighten tumor killing by

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chemotherapy and radiation, and at the same time protect normal tissue.[44,45]

Cellular Studies

All cellular studies using vitamins (C, A, K, E, D, B_6, B_{12}), beta-carotene, minerals (selenium), or cysteine as single agents or in combination given concomitantly with chemotherapy, or tamoxifen, or interferon alpha-2b, or radiation, or combinations of these modalities show the same effect: increased tumor killing and increased protection of the normal tissues.[46-65]

Human Studies

In human studies, vitamin E reduced the toxicity without affecting the cancer-killing performance of 13-cis-retinoic acid, used in the treatment of patients with head and neck, skin, and lung cancers.[66] Vitamin E also reduced the toxicity of adriamycin and did not interfere with the cancer killing ability of adriamycin[22,23,67] At 1,600 IU of vitamin E per day, hair loss in patients receiving chemotherapy was reduced from the expected 30-90%.[68] Treating 190 head and neck cancer patients with vitamin A, 5FU, and radiation resulted in more-than-expected tumor killing while preserving normal tissue.[69] Vitamin A combined with chemotherapy for postmenopausal patients with metastatic breast cancers significantly increased the complete response rate.[70] In thirteen patients with different cancers receiving 42 different chemotherapies, vitamin K decreased tumor resistance.[71] Vitamin B_6 at 300 milligrams per day decreased radiation therapy toxicity.[72] In twenty patients receiving chemotherapy with vitamins A, C, and E, there was a greater response rate.[73] Glutathione, part of the selenium complex, protected 150 women with ovarian cancer against cisplatin toxicity with no loss of anticancer effects as shown in double-blind studies at nine British oncology centers. In fact, more women treated with glutathione had an objective response (73% vs. 62%) and completed more cycles of cisplatin (58% vs. 39%) than those who were not so treated.[74] Studies show that amifostine (WR-2721), an antioxidant, protects against the harmful side effects of chemotherapy and radiation without the loss of antitumor activity.[75-86]

An increase in survival for cancer patients, which is uncommon with any treatment, has been shown using antioxidants combined with chemotherapy or radiation. In fact, eleven patients who were given beta-carotene and anthaxanthin while undergoing surgery, chemotherapy and radiation lived longer with an increase in disease-free intervals.[87] Antioxidant treatment with chemotherapy and radiation prolonged survival for patients with small cell lung cancer compared with patients who did not receive antioxidants.[87,88]

The effects of one chemotherapeutic agent, methotrexate, can be reversed with folinic acid, which is an analog of the vitamin folic acid. Folic acid itself does not reverse methotrexate's effects.[89,90] In order to reverse the effects of methotrexate, folinic acid must be prescribed in high doses.

Studies of supplements all show that vitamins and minerals do not interfere with the antitumor effects of chemotherapy or radiation therapy. In fact, on the contrary, some vitamins and minerals used in conjunction with chemotherapy and/or radiation therapy have been shown to potentiate the destruction of cancer cells and also protect normal tissue.

Lifestyle modification to augment oncology care

Using Quality of Life Scales, fifty patients with early staged breast cancer evaluated treatment side effects of radiation and/or chemotherapy while taking therapeutic doses of nutrients.[91,92] Quality of Life Scales are an acceptable way of evaluating any treatment or side effect not by the physician, but rather by the patient. The patient decides whether the treatment is beneficial or not in terms of side effects in-

curred. These scales have been successfully used to evaluate treatments for cardiovascular disease, cancer, and other chronic illnesses.[93-102]

The scoring system for the Quality of Life Scales is simple. The patient decides if the nutrients used during the radiation and/or chemotherapy treatments has improved, worsened, or has made no change in her life during the treatment period. The qualities of life tested were: physical symptoms, performance, general well being, cognitive abilities, sexual dysfunction, and life satisfaction. Fifty consecutive patients with early staged infiltrating ductal adenocarcinoma of the breast were treated with lumpectomy (re-excisional lumpectomy if indicated), axillary node dissection, and radiation therapy. Depending upon the nodal status, chemotherapy was used. In Group I, twenty-five women with T1 or T2, N0, M0 were treated with primary radiation therapy, receiving 4500 cCy to the whole breast, and a total dose of 6000 cGy to the tumor bed. In Group II, twenty-five patients with T1 or T2, N1, MO were treated with primary radiation therapy to the same doses as with Group I and also received modified CMF chemotherapy consisting of cytoxan and 5-FU (methotrexate was omitted until radiation was completed). A total of six cycles of this modified regimen was given. Each patient was instructed to follow the pertinent aspects of the Simone Ten-Point Plan as an adjunct to treatment. These points are:

1. Nutrition. Maintain an ideal weight—lose even five or seven pounds if needed. Low-fat (about 20 percent of calories), high-fiber (25 gm) diet. Eliminate salt, food additives, and caffeine. Nutrients taken 30 to 60 minutes before oncological therapy:
beta-carotene 30 mg
vitamin A 5000 IU
vitamin D 400 IU
vitamin E 400 IU
vitamin C 350 mg
folic acid 400 mcg
vitamin B_1 10 mg
vitamin B_2 10 mg
niacinamide 40 mg
vitamin B_6 10 mg
vitamin B_{12} 18 mcg
biotin 150 mcg
pantothenic acid 20 mg
iodine 150 mcg
copper 3 mg
zinc 15 mg
potassium 30 mg
selenium (organic) 200 mcg
chromium (organic) 125 mcg
manganese 2.5 mg
molybdenum 50 mcg
inositol 10 mg
L-cysteine 20 mg

In addition, the women took the following at bedtime:
calcium carbonate 1000 mg
magnesium 280 mg
potassium bicarbonate 100 mg
boron 2 mg
l-lysine 2 mg
l-threonine 2 mg
silicon 2 mg.

2. Tobacco. Do not smoke, chew, snuff, or inhale other's smoke.
3. Alcohol. Avoid all alcohol.
4. Radiation. Avoid unnecessary x-rays; sunscreens to be used. Avoid electromagnetic fields.
5. Environment. Keep air, water, and work place clean.
6. Hormones, Drugs. Avoid all estrogens and unnecessary drugs.
7. Know the seven warning signs of cancer: lump in breast; non-healing sore; change in wart/mole; change in bowel or bladder habits; persistant cough or hoarseness; indigestion or trouble swallowing; unusual bleeding.
8. Exercise
9. Stress modification, spirituality, and sexuality.
10. Have executive physical annually.

Table 1 (p.200) presents the responses of the fifty patients. Most patients indicated improvement, a few indicated no change,

Table 1. Patient responses to Qualities of Life.

	GROUP I* Number			GROUP II* Number		
Life Quality	Improve	Change	Worsen	Improve	Change	Worsen
Physical symptoms†	25			24	1	
Performance	23	2		23	2	
General well-being	25			25		
Cognitive abilities	25			22	3	
Sexual dysfunction	25			15	10	
Life satisfaction	25			25		

* Group I patients had radiation only; Group II had radiation and chemotherapy.
† skin reaction; fatigue; mouth sores; nausea/vomiting; dizziness; vertigo; lightheadedness; muscle cramps

and none indicated worsening. This study demonstrates that patients who followed the Ten-Point Plan and used certain vitamins and minerals had few side effects from chemotherapy and radiation therapy.

The Hoffer-Pauling Study

Researchers Hoffer and Pauling asked whether therapeutic nutrition helped cancer patients.[103] All 129 cancer patients in their study were to follow a low-fat diet supplemented with therapeutic doses of vitamins C, E, A, niacin, and a multiple vitamin/mineral supplement, in addition to following the advice and treatment of traditional oncology care. Those who did not follow nutritional modification (31 patients) lived an average of six months less. The other 98 patients fell into three categories: 32 patients with breast, ovarian, cervix, and uterus cancer had an average life span of over 10 years; 47 patients who had leukemia, lung, liver, and pancreas cancer had an average life span of over six years; and 19 patients with end-stage terminal cancer lived an average of 10 months.

Other Clinical Studies

Patients who undergo conventional oncology therapy generally live longer and/or have a lower recurrence rate if they modify their lifestyle, which includes diet changes, nutrient supplementation, and other lifestyle changes.[104-109]

The effect of vegetable consumption was examined over a period of six years in 675 patients with lung cancer. Those who lived longer ate more vegetables.[104] In another study, 200 patients who made significant dietary changes, experienced regression of their cancers without conventional treatment: 87 percent changed their diet dramatically to mainly vegetables, fruits, and whole grains; 65 percent consumed nutrient supplements; and 55 percent used a detoxification method.[105]

The effect of eating a macrobiotic diet on survival was studied in 1490 patients with pancreas cancer and 18 patients with prostate cancer.[106] Twenty-three matched patients with pancreas cancer changed to a macrobiotic diet and 12 (52%) were alive after one year; 1467 continued their high-fat, low-fiber diet and of these, 146 (10%) were alive after one year. Similarly, nine patients with prostate cancer who ate a macrobiotic diet were matched to nine patients with prostate cancer who ate their "normal" high-fat diet. Those eating the macrobiotic diet lived longer (median survival 228 months) than those who did not

(median survival 45 months).

Tumor recurrence rate was decreased by 50 percent in patients with transitional cell bladder cancer who took higher than Recommended Dietary Intake (RDI) doses of certain vitamins compared to matched controls taking RDI doses.[108] Sixty-five matched patients were randomized into two groups. The first group took a vitamin supplement providing the RDI doses, and the second group took that plus 40,000 IU vitamin A, 100 mg vitamin B_6, 2000 mg vitamin C, 400 IU vitamin E, and 90 mg zinc. Tumor recurrence at 10 months was 80 percent in the first group (RDI supplement only) and 40 percent in the second group (RDI supplement plus the extra higher doses). The projected recurrence rate at 5 years was 91 percent for the controls and 41 percent for the second group taking the higher doses.

And finally, an increased survival was demonstrated for patients with small cell lung cancer who received antioxidants concomitantly with chemotherapy and radiation therapy compared to matched controls who did not receive the antioxidants.[109]

It has also been found that patients who undergo chemotherapy develop lower serum levels of antioxidant vitamins and minerals.[110,111] The decreased levels of these antioxidants result from lipid peroxidation.

Japanese Experience

The older generation of Japanese women rarely get breast cancer, but when these women do, they live longer than American women, stage for stage,[112-119] because of only two reasons: (1) they are less obese, and (2) they eat a low-fat, high-fiber diet with vitamins and minerals. This is not necessarily true for younger Japanese women who have now adopted a more Western culture and diet.[115]

Obese breast cancer patients have a greater chance of early recurrence and a shorter life span compared to non-obese patients.[120-124] And breast cancer patients who have a high-fat intake and an high serum cholesterol also have a shorter life span than patients with normal or low-fat intake and low serum cholesterol.[125] Fat can initiate and also promote a cancer, especially a dietary cancer like breast cancer. If cholesterol intake is dramatically limited, cancer cell growth is severely inhibited.[126]

U.S. National Cancer Institute Effort

Armed with this information, the US National Cancer Institute, National Institutes of Health in Bethesda, Maryland conducted a research protocol in the mid 1980s to see if a low-fat diet would increase the life span of breast cancer patients. However, in January 1988, after only a brief time and an expenditure of about $90 million, the Board of Scientific Counselors of NCI's Division of Cancer Prevention and Control decided to end the proposed ten year study because: (1) physicians did not "believe" that there was a relationship between breast cancer and fat or other nutritional factors and, subsequently, did not refer patients to the study; and (2) once a woman was enrolled in the protocol, she subsequently "failed out" because she did not want to give up pizza, ice cream, and other high-fat foods. In 1991, NCI decided to try, in the near future, another low-fat cancer study in women aged 45 and 69.

Conclusion

Many of the nutrients used in the above studies are antioxidants. Antioxidants neutralize free radicals. Most cancer modalities exert their cancer killing effects by generating free radicals. Therefore it would seem inconsistent that these nutrients can help the cancer patient. However, *in vitro* and *in vivo* studies, including many clinical studies have repeatedly shown that certain vitamins and minerals can enhance the killing capabilities of cancer therapeutic modalities while at the same time can protect normal tissues and decrease side effects from these modalities.

Cancer cells accumulate excessive amounts of antioxidants due to a loss of the homeostasis control mechanism for the uptake of these nutrients. Normal cells do not have this membrane defect and do not accumulate large amounts of antioxidants. It has been postulated[127] that the accumulation of excessive nutrients in cancer cells can:

1. Shut down the oxidative reactions necessary for generating energy.
2. Inhibit protein kinase C activity[128] = which normally increases cell division and increases cell proliferation.
3. Inhibit oncogene expression.[129,130]
4. Increase the amount of growth inhibitory growth factors.[131]

With higher levels of cancer intracellular accumulation of nutrients, more of these cellular alterations occur. These changes can lead to a higher rate of cancer cell death, and a reduction in the rate of cell proliferation and induction of differentiation. These acquired changes of cancer cells due to high doses of nutrients actually override any protective action that antioxidants have against free radical damage on cancer cells.

Cancer patients should alter their lifestyles (Ten Point Plan), which includes modifying nutritional factors and taking certain vitamins and minerals in doses outlined, especially if they receive chemotherapy and/or radiation.

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