

Mega-dose Vitamins and Breast Cancer

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In December 2002, M. L. Lesperance and colleagues published a study of patients with nonmetastatic breast cancer who had been treated with a course of beta-carotene, niacin, vitamin C, selenium, coenzyme Q10, and zinc at an alternative cancer clinic under the directorship of Abram Hoffer, MD, who also served as one of the authors of the article.¹ Dr Hoffer obtained data from medical charts of his patients to provide a treatment group, which we will refer to as the orthomolecular medicine group. Lesperance and colleagues obtained a control group from the British Columbia Cancer Agency–Vancouver Island Centre (BCCA-VIC).

The orthomolecular group consisted of female patients with unilateral breast cancer who had been prescribed a course of varying amounts of the supplements, and who had been followed for at least 2 months. They were advised to take the supplements whether or not they had radiation or chemotherapy. From a group of 271 breast cancer patients initially identified by Hoffer, a group of 90 was selected, made up of those with nonmetastatic unilateral breast cancer who had outcome records in the files of the BCCA-VIC, were diagnosed between 1989 and 1998, were followed for at least 2 months, and began the supplementation within 180 days of diagnosis. Supplementation levels were as follows: most patients took approximately 25,000 IU daily of beta-carotene, over 1 g niacin, approximately 12 g of vitamin C daily, coenzyme Q10 (amount not given), between 1 and 750 mcg selenium, and approximately 50 mg zinc. Not all patients were prescribed the same supplementation levels.

The control group (n = 180) was selected from 2360 women with nonmetastatic breast cancer referred to BCCA-VIC during the same time period. Two control patients were selected for each of the 90 supplement patients. Controls were matched on the basis of tumor-node-metastasis stage; age (within 5 years); year of diagnosis (within 2 years); number of positive nodes for N1 patients; presence of lymphatic, vascular, or neural invasion; histopathology; estrogen receptor status; and whether systemic treatment (chemotherapy or hormonal therapy) was prescribed for the

DOI: 10.1177/1534735403253905

patient. Statistical methods used to compare the 2 groups included chi-square tests of homogeneity, Kaplan-Meier survival curves, log-rank tests, and Cox proportional hazards analysis.

The 2 groups proved to be matched on most prognostic variables, with the exception that a larger number of the supplemented patients did not have radiation therapy after lumpectomy (16% of the supplemented vs 7% of the controls), whereas a larger percentage of the control patients had total mastectomy without radiation therapy. The general patterns of local treatment between the 2 groups were significantly different ($P = .04$).

Results of statistical analysis indicated that there was no difference between the 2 groups in breast cancer-specific survival (BCSS) or disease-free survival (DFS) ($P = .16$ for BCSS and $P = .07$ for DFS). Survival of the supplemented group appeared somewhat lower than that of the control group; however, the sample size was not large enough to determine this difference reliably. The overall survival at 5 years was 72% for the supplemented group and 81% for the control group.

This study had many good features. It provided a very tight control for a relatively large cohort of patients who sought alternative therapy soon after being diagnosed with cancer. Cases and controls both received local treatment (surgery and radiation therapy) at a single regional cancer center with established clinical practice guidelines. The authors also pointed out several problems with the study. Power calculations had been made on an estimate of a 25% to 30% increase in BCSS and DFS in the supplemented group over that of the control group. The resulting sample size, however, was too small to detect differences of the magnitude that were actually observed. The higher percentage of supplemented patients who did not receive radiation therapy after lumpectomy could have led to a higher rate of local, or perhaps systemic, recurrence. Whether patients in either group were taking other supplements was not known. Although

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the 2 groups were matched on whether chemotherapy or hormonal therapy had been prescribed for them, it is not known whether they followed up on these prescriptions—and the lower use of radiation therapy in the supplemented group suggests that some of them may have omitted these therapies also. Finally, there are no data on whether psychological factors such as anxiety and depression differed in the 2 groups, which might have affected survival.

This very interesting study raised some controversy in the press, chiefly about whether it implied that supplements may have lowered survival time among the patients who took them simultaneously with radiation or chemotherapy. The study, of course, was not powered to detect the small (nonsignificant) decrease in survival among the supplemented patients. Because of this press attention, however, the *Integrative Cancer Therapies (ICT)* staff felt that it would be appropriate to explore the study in more depth in our Point-Counterpoint format. For this issue, we have changed the format of the section. Rather than having experts in similar areas explore the same questions, we have asked interested parties to give us their own perspectives on the study, addressing their own questions of interest in separate short articles.

This Point-Counterpoint begins with an *ICT* staff article on the history of the various trials of high-dose ascorbic acid that have been conducted. The supplementation regimen studied by Lesperance and colleagues included 12 g daily vitamin C for most

patients, and is thus in the range of several of these studies. A great deal of effort and energy in the alternative cancer treatment community was devoted to some of these vitamin C studies, and their findings, and the controversies they engendered, underlie some of the debates and sensitivities surrounding the question of vitamin supplementation to this day. Dr David Golde, a prominent vitamin C researcher at Memorial Sloan-Kettering Cancer Center in New York, briefly summarizes his research findings on vitamin C, its transport into the cancer cell, and its role in cancer therapy. Dr Hoffer has been kind enough to give us his perspectives on this study and its conduct. Finally, Dr Debu Tripathy, of the University of Texas Southwestern, examines the Lesperance study from the point of view of an oncologist with an active interest in the design and execution of clinical studies of alternative and traditional medicine systems. He offers some particularly interesting thoughts and insights on the potential directions that trials of integrative cancer care may need to take in the future. Finally, as is usual for the Point-Counterpoint feature, the *ICT* editor offers a summary and perspective on the different contributions.

Reference

1. Lesperance ML, Olivetto IA, Forde N, et al. Mega-dose vitamins and minerals in the treatment of non-metastatic breast cancer: an historical cohort study. *Breast Cancer Res Treat.* 2002;76:137-143.