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Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and Coenzyme Q10 for the Prevention and Treatment of Cancer

Summary

Overview

The objective of this report by the research team from the Southern California Evidence-based Practice Center (EPC) was to conduct a search of the published literature on the use of supplement forms of the antioxidants, vitamin C, vitamin E, and coenzyme Q10, for the treatment and prevention of cancer and, on the basis of that search, to evaluate the evidence for the efficacy of these antioxidants. A broad search revealed sufficient literature to support a detailed review of the use of two of these antioxidants for cancer.

Patients with cancer commonly try a variety of nontraditional treatments that fit the broad category known as Complementary and Alternative Medicine (CAM). However, evidence is lacking for the effectiveness of most CAM therapies for cancer. Among the CAM therapies publicized by the popular press for cancer treatment are several supplementary antioxidants: vitamin C, vitamin E, and coenzyme Q10.

It has long been argued that the adequacy of the vitamin supply to cells and tissues influences the development, progress, and outcome of cancers. A major challenge to the integrity and function of cells and tissues is thought to come from the uncontrolled formation of free radicals. Free radicals may, alone or in combination, attack cell membranes and DNA. The body has evolved antioxidant defenses to protect against free radical-induced damage. It is postulated that the antioxidant vitamins E and C and coenzyme Q10 are potentially involved in these antioxidant defenses and that some diseases might be prevented by increasing intake of antioxidants, either through increasing the dietary intake of antioxidant-rich foods or taking antioxidant supplements. However, it should be noted that while free radicals have been implicated in over 100 human diseases, this implication does not constitute proof of their role in disease formation or that preventing the formation or function of free radicals can prevent or cure disease.

Methodology

A panel of technical experts representing diverse disciplines was used by the Southern California Evidence-based Practice Center to advise on the search and inclusion criteria. The technical experts represented diverse disciplines including acupuncture, Ayurvedic medicine, chiropractic, dentistry, general internal medicine, gastroenterology, rheumatology, integrative medicine (the practice of combining alternative and conventional medicine), neurophysiology, pharmacology, psychiatry, psychoneuroimmunology, psychology, sociology, botanical medicine, and traditional Chinese medicine. The aim was to perform a meta-analysis whenever the literature was appropriate for such an analysis.

Search Strategy

Thirteen biomedical databases were searched through early 2002: Allied and Complementary Medicine, BIOSIS Previews®, CAB HEALTH®, CANCER LIT®, Cochrane Library, Elsevier Biobase, EMBASE, MANTIS™, MEDLINE®, SciSearch® Cited Ref Sci 1974-1989, Social SciSearch® 1972-2002, SciSearch® Cited Ref Sci

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1990-2002, and TGG Health & Wellness DB. Limiting the output to human studies, the team searched using the terms coenzyme Q10, vitamin E, and vitamin C, and their many pharmacological synonyms; the condition of interest (cancer); and study design or article type (randomized controlled trials, clinical controlled trials, meta-analyses, and systematic reviews).

Selection Criteria

Trials were included in the synthesis of evidence if they focused on vitamins C or E or coenzyme Q10 as supplements for the treatment or prevention of cancer and if they presented the results of clinical trials on human subjects or were a meta-analysis or systematic review or if they provided descriptive or background information about antioxidants. Language of publication was not a barrier to inclusion.

Reporting the Evidence

Searches of the literature yielded 1,337 articles, of which researchers were able to obtain 1,125. Based on a review by two physicians working independently, 432 articles were selected for screening, including clinical trials, meta-analyses, reviews, and reports that contained supplemental information. Twenty-two unique trials that met the inclusion criteria were included in the systematic review. Of these 22 trials, 19 included vitamin C, 14 included vitamin E, and none included coenzyme Q10 either for treatment or prevention of cancer. After reviewing the available evidence, the EPC research team focused on three primary outcomes: death from cancer, new tumors, and effect on colonic polyps, because these were the clinical outcomes that were most relevant and reported most frequently in the trials.

Data Collection and Analysis

All selected titles, abstracts, and articles, in all languages, were reviewed independently by two physician reviewers who were fluent in the appropriate language, and all disagreements were resolved by consensus. Information was collected about patient demographics, disease state, intervention, study design, and outcomes. Sufficient numbers of homogeneous trials did not exist to permit a meta-analysis of the efficacy of vitamins C or E or coenzyme Q10 for the outcomes of death or new tumor development. A meta-analysis was possible only for assessing the effect on colonic polyps. Additional qualitative reviews were done for trials that could not be pooled and for studies with intermediate outcomes.

Findings

Researchers identified 35 relevant articles corresponding to 37 studies. These 37 studies correspond to 22 unique trials, because many studies presented data on the same trial. The quality of the trials varied greatly as judged by the Jadad criteria. The distribution of trials across the three selected outcomes was as follows: 20 studies reported mortality outcomes; 15 studies reported the effect on new tumor development; and 8 studies reported the effect on colonic polyps. From these studies, the researchers were able to include data from six trials for the death analysis; four trials for the tumors analysis; and four trials for the pooled polyps analysis. Only the studies on colonic polyps were homogeneous enough to perform a meta-analysis. Seven studies also reported on a variety of intermediate outcomes.

Based on their analyses, the researchers made the following observations:

- No evidence was found for assessing the efficacy of coenzyme Q10 for prevention or treatment of cancer.
- Three large trials assessed the potential of vitamin C and vitamin E in various combinations to prevent cancer when given to persons without cancer. No trial reported a statistically significant beneficial effect on death due to cancer, nor did any trial show benefit for prevention of new tumor development, except for one arm of the ATBC trial, which showed a decrease in the development of new prostate tumors.
- Seven trials assessed the use of vitamin C in patients with advanced cancer. No trial reported a statistically significant mortality benefit: Vitamin C did not decrease the risk of death from advanced cancer.
- Six trials assessed the effect of combinations of vitamin C and vitamin E with and without beta-carotene on the development of colonic polyps. No trial reported a statistically significant beneficial effect.
- A number of intermediate outcomes studies reported positive results.
- A single trial of vitamin E in combination with omega-3 fatty acids showed increased survival of patients severely ill with a variety of malignancies.
- In a single trial of patients with bladder cancer who were also treated bacillus Calmette-Guerin (BCG) tuberculosis vaccine, Vitamin C was found to be beneficial in reducing the occurrence of new tumors.

This systematic review of the literature does not support the hypothesis that supplements of vitamins C or E or coenzyme Q10 generally help prevent or treat cancer. Isolated findings of benefit require confirmation.

Future Research

Results of the literature synthesis show generally disappointing results for the efficacy of antioxidant supplementation to prevent or treat cancer. Because this finding is in contrast to observational studies reporting benefits, additional research is needed to understand why these two

sources of evidence disagree. The positive findings from single clinical trials also need to be verified by further research.

Several factors should be considered when planning future research. Clinical trials should focus on populations not heretofore included—specifically, women with breast, cervical, and ovarian cancer—and study populations should be homogeneous with respect to condition and intervention. Additional research is needed to assess the benefit of antioxidant supplements for the secondary prevention of common cancers or for the modification of premalignant states. Based on the present analysis, the most promising antioxidants for future research are vitamins E and C. For coenzyme Q10, preliminary research is needed before a large clinical trial would be recommended. Finally, validated intermediate outcomes could be used as end points in future research, as they would provide a cost-effective method to gauge the efficacy of any planned clinical intervention.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Southern California Evidence-based Practice Center (EPC) under Contract No. 290-97-0001. Printed copies may be obtained free of charge from the AHRQ Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 75, *Effect of the Supplemental Use of Antioxidants Vitamin C, Vitamin E, and the Coenzyme Q10 for the Prevention and Treatment of Cancer*.

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