

Vitamin E and C Still Safe to Take at Higher Doses!

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The authors of three recent studies, each of which received unprecedented media attention, suggested that vitamin E supplementation at or above 400 IU per day may produce dangerous and life-threatening side-effects. One study also suggested that vitamin C supplementation may also increase death from cancer. These reports have generated a significant amount of concern and confusion among members of the general public, many of whom take vitamin E supplements at or above 400 IU and/or vitamin C supplements for the purpose of reducing risk of degenerative diseases, and to derive other health and anti-aging benefits. Upon review of these three recently reported studies, researchers from the Council for Responsible Nutrition and researchers associated with leading nutrition-based research universities published a review article in the *American Journal of Clinical Nutrition*,¹ to set the record straight on these issues.

In their review of the totality of experimental and clinical trials pertaining to vitamin E and vitamin C, these authorities challenge the conclusions of these three highly popularized recent studies. Moreover, these leading nutrition authorities indicate that the established tolerable upper-intake level (UL) for vitamin E and vitamin C, as established in the year 2000 by the Food and Nutrition Board (FNB) of the Institute of Medicine, part of the U.S. National Academies, remains a safe guideline for healthy adults to follow. Based upon all available data, the Institute of Medicine indicates that vitamin E is safe to ingest in doses up to 1,000 mg per day (1492.5 IU) and vitamin C is safe to ingest in doses up to 2,000 mg per day. They also indicate that many clinical trials show the safety of combinations of vitamin E and vitamin C at the amounts identified for their individual UL values.

It is estimated that approximately 70 percent of the U.S. population uses dietary supplements at least occasionally, and approximately 40 percent uses supplements on a regular basis. The most commonly used supplements are multivitamins, vitamin C, vitamin E and calcium. As such, it is important for health practitioners to have accurate information upon which to make recommendations in regards to the use of these supplements by their patients.

Vitamin E and All-Cause Mortality

In one of the recent studies, the authors indicated that a meta-analysis, which combined the results of 19 clinical trials of vitamin E supplementation for various diseases, including heart disease, end-stage renal failure, and Alzheimer's disease, showed that adults who took vitamin E supplements at or above 400 IU per day were 6 percent more likely to die of any cause than those who did not take vitamin E supplements.² In criticism of these findings, researchers from the Council for Nutrition and from leading American universities indicate that further breakdown of the risk by vitamin E dose, and adjustment for other vitamin and mineral supplements, found that the increased risk of death in this meta-analysis was significant only for a dose of vitamin E at 2,000 IU/day, which is higher than the UL for vitamin E, as set by the Institute of Medicine.

Reporting in the April issue of *The American Journal of Clinical Nutrition*, these authorities further

point out that three other meta-analyses, which combined the results of randomized controlled trials designed to evaluate the efficacy of vitamin E supplementation for the prevention or treatment of cardiovascular disease, found no evidence that vitamin E supplementation of up to 800 IU per day significantly increased or decreased risk of cardiovascular disease or all-cause mortality. They conclude that at present, the evidence is not convincing that vitamin E supplementation of up to 1,000 mg per day increases the risk of death due to cardiovascular disease or other causes, including cancer. They also point out that numerous studies suggest that vitamin E and/or vitamin C supplement use may contribute to lowering the risk of specific chronic degenerative diseases, such as Alzheimer's disease, age-related macular degeneration, some types of cancer, cataracts, and ischemic heart disease.

A review of all studies involving vitamin E supplementation indicates that few reports have cited adverse side-effects of long-term use of vitamin E at intakes up to many times the recommended dietary allowance (RDA). More than 20 published clinical trials involving over 80,000 subjects have documented the safety of vitamin supplements in doses ranging from 100 IU to 3,200 IU per day. The Institute of Medicine, however, suggests that doses of vitamin E above 1,000 mg per day may increase the risk of bleeding complications. However, a large trial of patients taking long-term warfarin (an anticoagulant drug), who also took 800-1,200 mg of vitamin E per day showed no changes in coagulation variables that would suggest an increased risk of bleeding at a daily dosage as high as 1,200 mg, when combined with other anticoagulants.

Vitamin E and Heart Disease

Media attention has also recently focused on the Heart Outcomes Prevention Evaluation Study (HOPE Study), which also reported that vitamin E supplementation at 400 IU per day may pose a health threat. This study was an evaluation of the angiotensin-converting enzyme inhibitor (ACE-inhibitor) drug known as ramipril, vitamin E at 400 IU/d, or both, in 9,541 patients with multiple cardiovascular risk factors. Although media reports suggested that vitamin E was associated with negative outcomes in this study, the authors conclude that vitamin E was "well tolerated" because the number of adverse events associated with the vitamin E treatment was not significantly greater than that with the placebo over the mean follow-up of 4.5 years.

Antioxidants and Cancer

In criticism of the recent meta-analysis by Bjelakovic, et al.,⁴ which suggested that there is no evidence that antioxidant supplements prevent gastrointestinal cancers, but instead, seem to increase overall mortality, researchers from the Council for Responsible Nutrition and from leading U.S. nutrition-based research universities indicate that this meta-analysis was strongly biased by including studies that were not scientifically combinable. In contrast to this report, these researchers indicate that when proper scientific protocol is followed (regarding what are acceptable studies to combine in a meta-analysis), the most highly aggregated meta-analysis on this subject shows a nonsignificant protective effect for antioxidants against cancer when all trials, all treatments, and all types of cancer are considered.

Summary

In conclusion, the body of evidence continues to suggest that vitamin E and vitamin C can be taken safely across a broad range of intakes. The Institute of Medicine indicates that daily supplementation of up to 1,000 mg of vitamin E and 2,000 mg of vitamin C is safe for use by the general population. The three recently cited studies that received a great deal of media attention for their suggestion that commonly used doses of vitamin E and vitamin C supplements increase risk of cardiovascular and cancer death, have been shown to have inherent flaws in their study

designs and/or have drawn unsubstantiated conclusions from the actual study findings. Health practitioners and the general public alike should be aware of the flawed conclusions of these widely popularized recent studies, and be aware of the recommendations set out by the Institute of Medicine in regards to safe intake levels of vitamin E and vitamin C, which more accurately reflect the totality of experimental and clinical evidence to date.

References

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