WHAT THE EXPERTS SAY

VITAMIN E AND THE HEART

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Clinical Scenario:

You have a 55-year-old patient with coronary artery disease in your clinic. You have explained to him his condition and discussed the plans for management which includes lifestyle modification and combination therapy of antithrombotic and anti-ischemic agents. Before he leaves, he tells you that he has supplies of vitamin E from his relatives abroad and is told that it is good for his heart problem. He now wants your opinion about this.

You are thus faced with the clinical question: Among those with coronary artery disease, can vitamin E reduce the risk of mortality and cardiovascular (CV) events?

There has been substantial progress in the management of CV disease - largely due to the use of combination therapy of antithrombotic and anti-ischemic agents proven in clinical trials to reduce the risk of cardiovascular (CV) events. Oxidative injury has been implicated in atherosclerotic CV disease thus making antioxidants, like vitamin E, an attractive agent in CV disease management.

Several large randomized clinical trials (RCT) evaluated the effect of vitamin E on mortality and morbidity among patients who are at high risk of developing CV events. One of the earlier trials was the Cambridge Heart Antioxidant Study (CHAOS) published in 1996. It involved 2,002 patients with coronary disease. They received vitamin E 800 mg/day or placebo for 510 days. It showed significant reduction in the risk of non-fatal myocardial infarction (MI) with vitamin E (RR=0.23 [0.11-0.47]; p<0.001) but no effect on CV (RR=1.18 [0.62-2.27], p=0.61). Actually, total mortality was slightly but not significantly greater in the vitamin E group than in the placebo group 3.5% vs. 2.7%, p=0.31. The study has some limitations such as unbalanced randomization, mid-study change in dose (changed to 300 mg/day), and short follow-up period. The authors stated that whether there is a true adverse effect on mortality cannot be ascertained.

Larger RCTs were subsequently done to validate the effect of vitamin E in the reduction of CV events. In addition to the bigger sample size, they have longer duration of follow-up and similar baseline characteristics between their comparison groups.

GISSI-P trial was published in 1999. This involved 11,324 patients who had MI. They received 300 mg vitamin E or placebo daily for 3.5 yrs. No significant differences in risk for CV outcomes of CV death, MI, stroke (RR=0.98; 95% CI, 0.87–1.10) were demonstrated.

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The Women’s Antioxidant Cardiovascular Study (WACS) was published in 2000 involved 9,541 patients with coronary artery disease, other occlusive arterial disease, or DM. They were treated with 600 mg of vitamin E or placebo for 5 yrs. Similarly, there were no significant reductions in total mortality and CV events with Vitamin arm.

This year, HOPE-TOO (HOPE–The Ongoing Outcomes) was published. To assess whether longer duration of treatment would prevent CV events, HOPE was extended in 7030 patients monitored for a total of 7 yrs. The results still showed no differences in major CV events (RR, 1.04; 95% CI, 0.96-1.14; P=0.34), but importantly, there were higher rates of heart failure (RR, 1.13; 95% CI, 1.01-1.26; P=0.03) and hospitalizations for heart failure (RR, 1.21; 95% CI, 1.00-1.47; P=0.045). The authors concluded that in patients with CV disease or DM, long-term vitamin E supplementation does not prevent major CV events and may increase the risk for heart failure.

A meta-analysis by Vivekananthan, et al, on the use of antioxidant vitamins for the prevention of CV disease was published in 2003. The vitamin E trials involved a total of 81,788 patients in the all-cause mortality analyses. Vitamin E did not provide benefit in mortality compared with control treatment (11.3 vs. 11.1%, OR 1.02 [95% CI 0.98-1.06] p=0.42).

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In summary, most of these RCTs failed to confirm a role for vitamin E supplementation in cardiovascular events prevention. The more recent large trials had consistently shown that vitamin E supplementation does not reduce mortality and CV events in high-risk patients. One large trial even showed an increased risk for heart failure.

REFERENCES:


HOPE-TOO. Effects of Long-term Vitamin E Supplementation on Cardiovascular Events and Cancer A Randomized Controlled Trial. JAMA. 2003;290:1338-1347.
