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FROM THE FAMILY PRACTICE INQUIRIES NETWORK

Do antioxidants (vitamins C, E) improve outcomes in patients with coronary artery disease?

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EVIDENCE-BASED ANSWER

Antioxidant supplements of vitamins E and C do not reduce cardiovascular death in people with coronary artery disease. Vitamin E supplementation, in a variety of doses, does not decrease the incidence of cardiovascular or all-cause mortality (grade of recommendation: A, 4 high quality randomized controlled trials [RCTs]). There is no evidence that vitamin C decreases mortality in patients at risk for coronary disease (grade of recommendation: A, meta-analysis of 3 small RCTs). Combination antioxidant regimens (Vitamins E, C, and betacarotene) seem safe, but do not decrease mortality or incidence of major coronary and vascular events (grade recommendation: A, 1 high-quality RCT).

EVIDENCE SUMMARY

Four large, well-designed RCTs with a combined enrollment of nearly 25,000 individuals with known coronary artery disease (CAD) or high risk for CAD receiving vitamin E (50–800 IU/d) collectively demonstrated no change in all-cause mortality or incidence of total cardiovascular events.[1] Three of these studies were double-blind, placebo-controlled and the fourth was an open-label design with central randomization and 4 treatment arms.[2-5] Two of the studies did suggest that vitamin E may reduce the incidence of non-fatal myocardial infarctions. One study of 2002 persons receiving 400–800 IU/d showed a statistically significant reduction of non-fatal coronary events (relative risk [RR], 0.62)[2] In a subgroup analysis of another, 1862 men with history of MI also had reduced risk of non-fatal MI (RR, 0.23).[3] However, in both of these groups, the increase in coronary death was not significant.[1]

Three small RCTs enrolling a total of 1034 geriatric patients, with follow-up of less than 2 years, evaluated vitamin C (50–200 mg/d) versus placebo and showed no mortality benefit.[1] Meta-analysis of these studies

showed a non-significant increase in the relative risk of death (RR, 1.08).[6]

A randomized, placebo-controlled study of simvastatin 40 mg and antioxidants (vitamin E 600 mg, vitamin C 250 mg, beta-carotene 20 mg) enrolled 20,536 adults aged 40 to 80 years with known CAD or high risk for CAD. No significant difference was found in all-cause mortality (RR, 1.04), major coronary events (RR, 1.02), any stroke (RR, 0.99), or any major vascular event (RR, 1.00).[7] The investigators found no evidence of an adverse affect of the antioxidants on the substantial outcome benefits demonstrated with 40 mg daily of simvastatin. This finding eases some concern from a smaller prior study, which had suggested a negative interaction between simvastatin plus niacin and antioxidant supplementation (composed of vitamins E and C, beta-carotene, and selenium).[8]

RECOMMENDATIONS FROM OTHERS

A 2002 systematic review of antioxidant vitamins (carotene, tocopherol, and ascorbic acid) in primary and secondary prevention of cardiovascular disease concluded simply that "antioxidant vitamins as food supplements cannot be recommended in the primary or secondary prevention against cardiovascular disease."[9]

The American Heart Association guidelines do not advocate antioxidant vitamin supplements, rather a well-balanced diet "with emphasis on anti-oxidant rich fruits and vegetables and whole grains."[10]

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