In patients with a previous CVA, do antioxidants protect against subsequent stroke?

EVIDENCE-BASED ANSWER Most recent randomized controlled clinical trials have not found a benefit in antioxidants (vitamin C, vitamin E, and/or beta-carotene) for preventing cardiovascular disease, including stroke. These recent clinical studies have not confirmed earlier observational studies that suggested a benefit. No studies have assessed only stroke patients and stroke outcomes. (Grade of recommendation: A, based on randomized controlled clinical trials and a systematic review of antioxidants and cardiovascular disease.)

EVIDENCE SUMMARY The Heart Outcomes Prevention Evaluation (HOPE) trial was a 4.5-year randomized controlled clinical trial of vitamin E or placebo in 9541 patients aged 55 years or older with a history of coronary artery disease, stroke, peripheral vascular disease, or diabetes and other cardiovascular disease risk factors. No difference was noted between vitamin E and placebo for the outcomes of stroke, death, or other cardiac outcomes for these high-risk patients.[1] In a randomized controlled clinical trial of 29,133 Finnish male smokers, the overall net stroke morbidity and mortality with antioxidants was not significantly different from placebo. However, a trend toward higher rates of subarachnoid hemorrhages was found (relative risk [RR] = 1.5; 95% confidence interval [CI], 0.97–2.32; numbers needed to harm [NNH] = 833), while the cerebral infarction rate was decreased (RR = 0.86; 95% CI, 0.75–0.99; numbers needed to treat = 239) by vitamin E. Beta-carotene increased intracerebral hemorrhage (RR = 1.61; 95% CI, 1.10–2.36; NNH = 546).[2] Subsequent subgroup analysis showed a significant decrease in cerebral infarction (RR = 0.33; 95% CI, 0.14–0.78) without increasing subarachnoid hemorrhage in hypertensive, diabetic men taking vitamin E.[3] Given the inherent methodological perils of subgroup analysis, this association requires further study before clinical implementation.

The Italian GISSI study of 11,324 patients with a recent myocardial infarction showed no effect of vitamin E on the combined outcomes of death, myocardial infarction, and stroke.[4] In the Heart Protection Study, 20,536 adults between the ages of 40 and 80 years with cardiovascular disease, stroke, or diabetes were given vitamin E, vitamin C, beta-carotene, or placebo for 5 years. No significant differences were noted between vitamins and placebo in fatal or nonfatal stroke (RR = 0.99; 95% CI, 0.87–1.12).[5]

Although prior observational studies have hinted at a link between antioxidants and improved cardiovascular outcomes, the recently published Health Professionals Follow-up Study found no benefit to vitamin C or E in preventing strokes, based on the dietary assessment of 43,738 men, aged 40 to 75 years, who were not known to have cardiovascular disease or diabetes.[6]

RECOMMENDATIONS FROM OTHERS The American Heart Association Science Advisory and Coordinating Committee commented on antioxidant use in 1999. While their emphasis was on coronary heart disease, they concluded that the general population should "consume a balanced diet with emphasis on antioxidant-rich fruits and vegetables and whole grains," noting that "the absence of efficacy and safety data from randomized trials precludes the establishment of population-wide recommendations regarding vitamin E supplementation."[7] Some authors argue that the failure to demonstrate a benefit from antioxidants is due to inadequate antioxidant dosing, treatment length, or type of antioxidant.[8]

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Does postcoital voiding prevent urinary tract infections in young women?

EVIDENCE-BASED ANSWER Healthy women who urinate within 15 minutes of sexual intercourse may be slightly less likely to develop a urinary tract infection (UTI) than women who do not urinate afterward (grade of recommendation: D, extrapolation of single case-control study with nonsignificant findings).

EVIDENCE SUMMARY A literature review revealed only 1 small case-control study. The goal of this study was to identify possible risk factors for developing UTIs among young, healthy women who presented to the University of California at Los Angeles student health center.[1] A total of 225 women were enrolled in the study. Exclusion criteria included pregnancy, diabetes, vaginitis, candidiasis, a history of more than 1 prior UTI, hospitalization, or catheterization 4 weeks before study enrollment. The women were surveyed regarding their dietary habits, clothing, sexual and urinary habits, and birth control methods used. From midstream urine samples, the authors identified 44 cases of UTI and 181 controls presenting to the health center without urinary symptoms or a history of UTI. A UTI was defined as the presence of more than 50,000 colony forming units of a single species of bacteria per milliliter of urine and the report of 1 or more of the following symptoms: painful urination, frequent urination, urination at night, and urgent need to urinate, or blood in the urine. A primary UTI case was further defined as a not having had a prior history of UTI; a secondary UTI case was defined as a patient who reported 1 prior UTI.

Women who urinated < 15 minutes after intercourse had an estimated relative risk (RR) of 0.40 (95% confidence interval [CI], 0.09–2.17) for developing a primary case of UTI, and an estimated RR of 0.92 (95% CI, 0.18–4.88) for developing a secondary UTI. These findings were not statistically significant, but the power was too low to rule out a potential effect.

This single small case-control study had several limitations. It was not a randomized controlled trial, which would be required to prove that postcoital voiding is an effective intervention. The study included only young, healthy women and excluded women with recurrent UTIs, a subpopulation of sexually active patients who may particularly benefit from the intervention. Finally, the study lacked adequate sample size to detect a small-to-moderate effect of postcoital voiding.

RECOMMENDATIONS FROM OTHERS A major urology text does not specifically address the prevention strategy of postcoital voiding.[2] However, *Griffith's 5 Minute Clinical Consult* recommends that women with frequent or intercourse related UTIs should "empty [their] bladder immediately before and following intercourse and consider post-coital antibiotic treatment."[3] Furthermore, the American College of Obstetricians and Gynecologists District II NYS recommends urinating after sexual intercourse to prevent recurrent cystitis.[4]

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Decreasing your chance of a urinary tract Do

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

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 beta-carotene) 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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