Serial Coronary Angiographic Evidence That Antioxidant Vitamin Intake Reduces Progression of Coronary Artery Atherosclerosis

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Objective.—To explore the association of supplementary and dietary vitamin E and C intake with the progression of coronary artery disease.

Design.—A subgroup analysis of the on-trial antioxidant vitamin intake database acquired in the Cholesterol Lowering Atherosclerosis Study, a randomized, placebo-controlled, serial angiographic clinical trial evaluating the risk and benefit of colestipol-niacin on coronary artery disease progression.

Setting.—Community- and university-based cardiac catheterization laboratories.

Subjects.—A total of 156 men aged 40 to 59 years with previous coronary artery bypass graft surgery.

Intervention.—Supplementary and dietary vitamin E and C intake (nonrandomized) in association with cholesterol-lowering diet and either colestipol-niacin or placebo (randomized).

Outcome.—Change percent in the percentage of vessel diameter obstructed because of stenosis (%) determined by quantitative coronary angiography after 2 years of randomized therapy on all lesions, mild/moderate lesions (<50%), and severe lesions (≥50%).

Results.—Overall, subjects with supplementary vitamin E intake of 100 IU per day or greater demonstrated less coronary artery lesion progression than did subjects with supplementary vitamin E intake less than 100 IU per day for all lesions (P<0.04) and for mild/moderate lesions (P=0.01). Within the drug group, benefit of supplementary vitamin E intake was found for all lesions (P=0.02) and mild/moderate lesions (P=0.01). Within the placebo group, benefit of supplementary vitamin E intake was not found. No benefit was found for use of supplementary vitamin E exclusively or in conjunction with supplementary vitamin E, use of multivitamins, or increased dietary intake of vitamin E or vitamin C.

Conclusions.—These results indicate an association between supplementary vitamin E intake and angiographically demonstrated reduction in coronary artery lesion progression. Verification from carefully designed, randomized, serial arterial imaging end point trials is needed.

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A LARGE body of experimental data support the hypothesis that peroxidative processes play a role in atherogenesis. This experimental evidence includes data demonstrating that anoxi-

dants prevent peroxidative damage to low-density lipoprotein (LDL) and that atherosclerosis as well as peroxidative products found in blood and the arterial wall can be reduced with antioxidant compounds.

Additionally, there is accumulating epidemiological evidence of an association between antioxidant vitamin intake and reduced risk for heart disease (CHD). In the direct association of antioxidant vitamin intake on the progression of coronary atherosclerotic lesions has been determined in humans.

The Cholesterol Lowering Atherosclerosis Study (CLAS) was a ran-

domized controlled trial that demonstrated that aggressive cholesterol (LDL-C) reduction with niacin and cholesterol-lowering therapy reduces progression of coronary atherosclerosis. In an analysis using the extensive diet and nutritional supplement database collected in CLAS, we have reported the beneficial effect of reducing total fat intake on coronary atherosclerosis.

In this article, we use the dietary and nutritional supplement database to explore the association of supplementary vitamin E intake with the progression of coronary artery disease (CAD) in the CLAS study.

METHODS

Study Design

Detailed descriptions of the CLAS design and methods have been previously. Between September and October 1984, 188 non-smoker, 50-year-old, normotensive, men with normal renal function and cholesterol levels between 4.79 mmol/L (185 and 360 mg/dL) were enrolled in the study. The men were randomly assigned to C, A, or P treatment groups. After 2 years of intervention, 107 subjects (80%) had a rest