



Vitamin Supplements and Cardiovascular Disease

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Even with the aggressive treatment of traditional risk factors, such as LDL-cholesterol lowering, atherosclerosis continues to progress in about half of the individuals who receive such treatment. Other potential interventions such as antioxidant vitamin supplementation and the use of vitamin supplementation to reduce plasma homocysteine levels have come under close scrutiny. Homocysteine, a naturally occurring amino acid depends upon folate, vitamin B₆, and vitamin B₁₂ to be metabolized. Each 5 $\mu\text{mol/L}$ increase in plasma homocysteine concentration, equal to one standard deviation in the normal population, is associated with a 60 percent increase in coronary heart disease risk in men and an 80 percent increase risk in women. The same increment rise in the plasma homocysteine level is associated with a 90 percent increase risk for cerebrovascular disease in men and women. Like plasma cholesterol levels, the cardiovascular risk from homocysteine is continuous and graded over the entire range of plasma homocysteine levels. The coronary heart disease risk for each 5 $\mu\text{mol/L}$ increase in plasma homocysteine is equivalent to the effect of a 20 mg/dL rise in plasma cholesterol. The cardiovascular risk may be particularly important in the elderly population, because there is often inadequate intake and/or poor absorption of the B vitamins that regulate the plasma homocysteine concentration. This provides an area of research opportunity, especially because accumulating evidence indicates that homocysteine lowering with folate, vitamin B₆, and vitamin B₁₂ may reduce atherosclerotic vascular disease.

A large body of experimental and animal data suggests that atherosclerosis results from a series of oxidative processes. In general, observational studies support these data by indicating an inverse relationship between vitamin E, vitamin C, carotenoid intake, and cardiovascular disease risk. On the other hand, except for 2 trials of short duration (1.4 years), randomized controlled trials designed to determine the effects of antioxidant vitamin supplementation on cardiovascular disease have demonstrated no effect. These trials have been predominantly conducted in individuals with preexisting cardiovascular disease or in those at very high risk for cardiovascular disease. However, the Vitamin E Atherosclerosis Prevention Study conducted in younger, healthier individuals at low risk for cardiovascular disease also demonstrated no effect of vitamin E on atherosclerosis progression. The completed trials seem to indicate that in vitamin-replete individuals, further antioxidant vitamin supplementation appears to have no effect on atherosclerotic vascular disease. However, these trials also seem to indicate that cardiovascular benefit may be afforded to those individuals with low plasma and/or tissue antioxidant concentrations. This is an important area of research opportunity. Several randomized controlled trials will be completed over the next few years and will provide the necessary evidence as to whether antioxidant vitamin supplementation and the lowering of plasma homocysteine levels with vitamin B supplementation will reduce the progression of atherosclerosis and its clinical sequelae.

References

Clarke R, Collins R. Can dietary supplements with folic acid or vitamin B₆ reduce cardiovascular risk? Design of clinical trials to test the homocysteine hypothesis of vascular disease. *J Cardiovasc Risk* 1998;5:249-255.

Hodis HN, Mack WJ, LaBree L, Mahrer PR, Sevanian A, Liu CR, Liu CH, Hwang J, Selzer RH, Azen SP. Alpha tocopherol supplementation in healthy individuals reduces low-density lipoprotein oxidation but not atherosclerosis: the Vitamin E Atherosclerosis Prevention Study (VEAPS). *Circulation* 2002;106:1453-1459.