Abstract

JAMA. 1995 Oct 4;274(13):1049-57.

A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes.

Boushey CJ, Beresford SA, Omenn GS, Motulsky AG.

Northwest Prevention Effectiveness Center, University of Washington, Seattle 98195-7236, USA.

OBJECTIVES: To determine the risk of elevated total homocysteine (tHcy) levels for arteriosclerotic vascular disease, estimate the reduction of tHcy by folic acid, and calculate the potential reduction of coronary artery disease (CAD) mortality by increasing folic acid intake.

DATA SOURCES: MEDLINE search for meta-analysis of 27 studies relating homocysteine to arteriosclerotic vascular disease and 11 studies of folic acid effects on tHcy levels.

STUDY SELECTION AND DATA EXTRACTION: Studies dealing with CAD, cerebrovascular disease, and peripheral arterial vascular disease were selected. Three prospective and six population-based case-control studies were considered of high quality. Five cross-sectional and 13 other case-control studies were also included. Causality of tHcy's role in the pathogenesis of vascular disease was inferred because of consistency across studies by different investigators using different methods in different populations.

DATA SYNTHESIS: Elevations in tHcy were considered an independent graded risk factor for arteriosclerotic vascular diseases. The odds ratio (OR) for CAD of a 5-mumol/L tHcy increment is 1.6 (95% confidence interval [CI], 1.4 to 1.7) for men and 1.8 (95% CI, 1.3 to 1.9) for women. A total of 10% of the population's CAD risk appears attributable to tHcy. The OR for cerebrovascular disease (5-mumol/L tHcy increment) is 1.5 (95% CI, 1.3 to 1.9). Peripheral arterial disease also showed a strong association. Increased folic acid intake (approximately 200 micrograms/d) reduces tHcy levels by approximately 4 mumol/L. Assuming that lower tHcy levels decrease CAD mortality, we calculated the effect of (1) increased dietary folate, (2) supplementation by tablets, and (3) grain fortification. Under different assumptions, 13,500 to 50,000 CAD deaths annually could be avoided; fortification of food had the largest impact.

CONCLUSIONS: A 5-mumol/L tHcy increment elevates CAD risk by as much as cholesterol increases of 0.5 mmol/L (20 mg/dL). Higher folic acid intake by reducing tHcy levels promises to prevent arteriosclerotic vascular disease. Clinical trials are urgently needed. Concerns about masking cobalamin deficiency by folic acid could be lessened by adding 1 mg of cobalamin to folic acid supplements.

PMID: 7563456