Folic acid, pyridoxine, and cyanocobalamin combination treatment and age-related macular degeneration in women: the Women's Antioxidant and Folic Acid Cardiovascular Study.

Christen WG, Glynn RJ, Chew EY, Albert CM, Manson JE.

Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 900 Commonwealth Avenue E, Boston, MA 02215-1204, USA.

BACKGROUND: Observational epidemiologic studies indicate a direct association between homocysteine concentration in the blood and the risk of age-related macular degeneration (AMD), but randomized trial data to examine the effect of therapy to lower homocysteine levels in AMD are lacking. Our objective was to examine the incidence of AMD in a trial of combined folic acid, pyridoxine hydrochloride (vitamin B(6)), and cyanocobalamin (vitamin B(12)) therapy.

METHODS: We conducted a randomized, double-blind, placebo-controlled trial including 5442 female health care professionals 40 years or older with preexisting cardiovascular disease or 3 or more cardiovascular disease risk factors. A total of 5205 of these women did not have a diagnosis of AMD at baseline and were included in this analysis. Participants were randomly assigned to receive a combination of folic acid (2.5 mg/d), pyridoxine hydrochloride (50 mg/d), and cyanocobalamin (1 mg/d) or placebo. Our main outcome measures included total AMD, defined as a self-report documented by medical record evidence of an initial diagnosis after randomization, and visually significant AMD, defined as confirmed incident AMD with visual acuity of 20/30 or worse attributable to this condition.

RESULTS: After an average of 7.3 years of treatment and follow-up, there were 55 cases of AMD in the combination treatment group and 82 in the placebo group (relative risk, 0.66; 95% confidence interval, 0.47-0.93 [P = .02]). For visually significant AMD, there were 26 cases in the combination treatment group and 44 in the placebo group (relative risk, 0.59; 95% confidence interval, 0.36-0.95 [P = .03]).

CONCLUSIONS: These randomized trial data from a large cohort of women at high risk of cardiovascular disease indicate that daily supplementation with folic acid, pyridoxine, and cyanocobalamin may reduce the risk of AMD.

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