

Abstract

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Circulating unmetabolized folic acid and 5-methyltetrahydrofolate in relation to anemia, macrocytosis, and cognitive test performance in American seniors.

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BACKGROUND: Folate deficiency has serious consequences for the fetus. Folic acid fortification of food addresses this problem. However, clinical consequences of vitamin B-12 deficiency may be worsened by high folic acid intakes, perhaps as a direct result of unmetabolized folic acid, which does not occur naturally in body tissues.

OBJECTIVE: We attempted to attribute associations that we previously found between higher folate status and anemia and cognitive test performance to circulating unmetabolized folic acid or 5-methyltetrahydrofolate (5MeTHF).

DESIGN: The subjects (n = 1858) were senior participants in the US National Health and Nutrition Examination Survey (1999-2002) who had normal renal function and reported no history of stroke, recent anemia therapy, or diseases of the liver, thyroid, or coronary arteries. Subjects had undergone a phlebotomy, a complete blood count, and cognitive and dietary assessments.

RESULTS: Circulating unmetabolized folic acid was detected in approximately 33% of the subjects and was related to an increased odds of anemia in alcohol users. In seniors with a serum vitamin B-12 concentration <148 pmol/L or a plasma methylmalonic acid concentration > or =210 nmol/L, the presence compared with the absence of detectable circulating unmetabolized folic acid was related to lower cognitive test scores and lower mean cell volume. In the same subgroup, higher serum 5MeTHF was related to an increased odds of anemia and a marginally significantly decreased odds of macrocytosis. In seniors with a normal vitamin B-12 status, a higher serum 5MeTHF concentration was related to higher cognitive test scores.

CONCLUSION: Results of this epidemiologic study were somewhat consistent with reports on the folic acid treatment of patients with pernicious anemia, but some findings were unexpected.

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