LETTER

Reply to Quinlivan: Postfortification, folate intake in vitamin B12 deficiency is positively related to homocysteine and methylmalonic acid

With cross-sectional data, causes and effects are difficult to distinguish, and Quinlivan suggests that high circulating concentrations of homocysteine (Hcy), methylmalonic acid (MMA), and folate observed among vitamin B12-deficient survey participants all resulted from a lack of vitamin B12 (1). However, we observed the interaction between vitamin B12 status and folate status in the current, postfortification era, when high folic acid intake is common (2).

Because folic acid can be directly converted to tetrahydrofolate (3), polyglutamation should have occurred even in the vitamin B12-deficient subjects. Furthermore, dietary data from the survey support the hypothesis that high folate intake is associated with high metabolite levels in vitamin B12-deficient people. We defined higher folate intake as dietary intake ≥531 μg/d (the 80th percentile) or use of folic acid supplements and found that this variable also interacted significantly with vitamin B12 status in relation to circulating metabolite levels (P < 0.01). Specifically, among those with serum vitamin B12 >148 pmol/liter, multivariate-adjusted geometric mean Hcy for those with lower and higher folate intakes were 8.1 μmol/liter and 7.3 μmol/liter (P < 0.001), respectively, as compared with 10.2 μmol/liter and 12.3 μmol/liter for those with serum vitamin B12 P < 0.05).

Corresponding MMA values were 137 nmol/liter and 128 nmol/liter (P < 0.001) for subjects with normal serum vitamin B12, and 224 nmol/liter and 337 nmol/liter (P = 0.021) for the vitamin B12-deficient subjects. Vitamin B12 deficiency should not increase folate intakes; consequently, these results likely reflect different effects of high folate intakes on circulating metabolite levels in people with normal and low vitamin B12 status.

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