Abstract


Pyridoxine supplementation does not alter in vivo kinetics of one-carbon metabolism but modifies patterns of one-carbon and tryptophan metabolites in vitamin B-6-insufficient oral contraceptive users.

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BACKGROUND: Low chronic vitamin B-6 status can occur in a subset of women who use oral contraceptives (OCs) with uncertain metabolic consequences. An insufficiency of cellular pyridoxal 5'-phosphate (PLP), which is the coenzyme form of vitamin B-6, may impair many metabolic processes including one-carbon and tryptophan metabolism.

OBJECTIVE: We investigated the effects of vitamin B-6 supplementation on the in vivo kinetics of one-carbon metabolism and the concentration of one-carbon and tryptophan metabolites in vitamin B-6-deficient OC users.

DESIGN: A primed, constant infusion of [(13)C5]methionine, [3-(13)C]serine, and [(2)H3]leucine was performed on 10 OC users (20-40 y old; plasma PLP concentrations <30 nmol/L) before and after 28 d of supplementation with 10 mg pyridoxine hydrochloric acid/d. In vivo fluxes of total homocysteine remethylation, the remethylation of homocysteine from serine, and rates of homocysteine and cystathionine production were assessed. Targeted metabolite profiling was performed, and data were analyzed by using orthogonal partial least-squares-discriminant analysis and paired t tests adjusted for multiple testing.

RESULTS: Pyridoxine supplementation increased the mean ± SD plasma PLP concentration from 25.8 ± 3.6 to 143 ± 58 nmol/L (P < 0.001) and decreased the leucine concentration from 103 ± 17 to 90 ± 20 nmol/L (P = 0.007) and glycine concentration from 317 ± 63 to 267 ± 58 nmol/L (P = 0.03). Supplementation did not affect in vivo rates of homocysteine remethylation or the appearance of homocysteine and cystathionine. A multivariate analysis showed a clear overall effect on metabolite profiles resulting from supplementation. Leucine, glycine, choline, cysteine, glutathione, trimethylamine N-oxide, and the ratios glycine:serine, 3-hydroxykynurenine:kynurenine, 3-hydroxykynurenine:3-hydroxyanthranilic acid, and 3-hydroxykynurenine:anthranilic acid were significant discriminating variables.

CONCLUSIONS: Consistent with previous vitamin B-6-restriction studies, fluxes of one-carbon metabolic processes exhibited little or no change after supplementation in low-vitamin B-6 subjects. In contrast, changes in the metabolic profiles after supplementation indicated perturbations in metabolism, suggesting functional vitamin B-6 deficiency. This study was registered at clinicaltrials.gov as NCT01128244.

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