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Abstract

Is the Generation of Active Vitamin B6 Dependent upon Riboflavin Status? New Analysis of Data from RCTs of Riboflavin Supplementation †

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Abstract: Background and objectives: Riboflavin in the form flavin mononucleotide (FMN) acts as a cofactor for the pyridoxine phosphate oxidase required to generate pyridoxal 5′-phosphate (PLP), the active form of vitamin B6 in tissues. Few human studies have investigated this metabolic interaction between riboflavin and vitamin B6. The primary objective of this study was to examine the response of plasma PLP to riboflavin supplementation in individuals with the *MTHFR* 677TT genotype. A secondary objective was to consider whether the dose of riboflavin (1.6 mg/d vs. 10 mg/d) affects the PLP response. Methods: Data from four randomised controlled trials (RCTs) of riboflavin supplementation previously conducted at this centre were accessed to identify 209 participants of 19–60 years meeting the inclusion criteria (≤60 years, *MTHFR* 677TT genotype, not taking a vitamin B6 supplement). In the original RCTs, participants were randomly assigned to receive a placebo (n = 85) or 1.6 mg/d of riboflavin (n = 87) for 16 weeks. In one trial only, a higher riboflavin dose, 10 mg/d (n = 37), was administered. Plasma PLP was measured via reversed phase HPLC with fluorescence detection. Riboflavin status was assessed using the functional assay, erythrocyte glutathione reductase activation coefficient (EGRac). Results: riboflavin supplementation resulted in a decrease ($p < 0.001$) in the mean EGRac values, from 1.34 (1.32, 1.37) to 1.21 (1.19, 1.22). Correspondingly, PLP increased ($p = 0.027$), an effect driven by those with a sub-optimal riboflavin status at baseline (EGRac > 1.26), whereby PLP increased by 5.2 nmol/L, from 44.9 (40.3, 49.4) to 50.1 (44.6, 55.6) nmol/L ($p = 0.042$), while with the optimal baseline riboflavin (EGRac ≤ 1.26), there was no significant PLP response to the intervention. Although 10 mg/d vs. 1.6 mg/d of riboflavin resulted in a greater EGRac response ($p = 0.012$), there was no significant effect of riboflavin dose on the PLP response. Discussion: These results provide randomised trial evidence that optimising riboflavin status leads to an increase in plasma PLP, confirming the metabolic dependency of vitamin B6 on FMN. The findings indicate that riboflavin intake may need to be considered when setting dietary recommendations for vitamin B6 in adults. Further work is needed to explore the impact of the common *MTHFR* C677T polymorphism of the interrelationship of these B vitamins.

Keywords: riboflavin; vitamin B6; pyridoxal 5′-phosphate; one-carbon metabolism

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