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Abstract

Early Pregnancy Folic Acid Supplement Use and Folate Status in the Alberta Pregnancy Outcomes and Nutrition (APrON) Study †

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Abstract: Background and Objective: Periconceptional supplementation with 400 µg/day of folic acid (FA) is recommended for primary prevention of neural tube defects, such as spina bifida. In Canada, where higher-dose prenatal FA supplement use is highly prevalent, there is increasing concern over possible excess maternal FA supplementation. The objective of this study was to assess the association between prenatal FA supplementation and circulating folate forms at <20 gestational weeks (GW) in Canada. Methods: For the EpiBrain Project, a transnational collaboration investigating B-vitamin-related early programming of neurodevelopment, we used data on a subsample of apparently healthy, non-fasting pregnant women from the Alberta Pregnancy Outcomes and Nutrition (APrON) Study (n = 250P). Self-reported FA supplement intake was assessed using a questionnaire. Plasma folate, red blood cell (RBC) folate, and plasma total homocysteine (tHcy) concentrations were measured using LC-MS/MS, and plasma total vitamin B12 (tB12) concentration was measured using an immunoassay. Descriptive statistics are presented as medians (25th percentile and 75th percentile). Results: The median maternal age was 31 (28, 33) years. At 15.4 (13.4, 17.4) GW, the RBC total folate, plasma total folate, and plasma tB12 and tHcy concentrations were 1333 (1027, 1652) nM, 49 (40, 61) nM, 247 (184, 321) pM, and 4.5 (3.8, 5.4) µM, respectively. Most participants reported FA supplement use of 1000 µg/day (45%); about 23% reported >1000 µg/day, 21% reported 400–<1000 µg/day, 8% reported <400 µg/day, and 3% presented no data. FA supplement dose was correlated (Bonferroni-adjusted $p < 0.05$) with plasma and RBC total folate (Spearman's ρ = 0.26 and 0.28, respectively), plasma and RBC 5-methyltetrahydrofolate (ρ = 0.20 and 0.24, respectively), and plasma unmetabolized FA (ρ = 0.21). RBC total folate concentration differed among the supplement groups (Kruskal–Wallis test, $p < 0.05$) and was higher in those supplementing with >1000 µg/day (1259 (885, 18,444) nM; Dunn's test, $p < 0.05$) compared to the lower-dose groups. FA supplement dose was not associated with the contribution of each RBC or plasma folate form to total folate. Discussion: These preliminary findings from the APrON cohort indicate that FA supplement use at <20 GW is associated with circulating folate forms. These findings will be compared with data from pregnancy studies in Northern Ireland and Spain for the EpiBrain Project. The EpiBrain Project will provide evidence that can inform health policies and recommendations regarding the use of folate and other B vitamin supplementation during pregnancy.

Keywords: pregnancy; folic acid; supplements; folate; biomarkers

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