

The Amount of Folic Acid in Weekly Iron-Folic Acid Supplements Should Be Increased From 0.4 to 2.8 mg to Reduce Neural Tube Defects (NTD)

Kaitlyn Samson,¹ Su Peng Loh,² Siew Siew Lee,² Dian Sulistyoningrum,³ Geok Lin Khor,² Zalilah Binti Mohd,² Irm Zarina Ismai,² Lisa Yelland,³ Shalem Leemaqz,³ Maria Makrides,³ Jennifer Hutcheon,⁴ Marion Roche,⁵ Homero Martinez,⁵ Crystal Karakochuk,¹ and Tim Green³

¹The University of British Columbia; ²Universiti Putra Malaysia; ³South Australia Health and Medical Research Institute; ⁴Obstetrics and Gynaecology; and ⁵Nutrition International

Objectives: Weekly iron-folic acid (IFA) supplements are recommended for all menstruating women in countries where anaemia prevalence is > 20%. Anaemia caused by folate deficiency is low worldwide, and the need to include folic acid is in question. Including folic acid might reduce the risk of a neural tube defect (NTD) should a woman become pregnant. Most weekly supplements contain 0.4 mg folic acid; however, WHO recommends 2.8 mg because it is seven times the daily dose effective in reducing NTDs. There is a reluctance to switch

to supplements containing 2.8 mg of folic acid because of a lack of evidence that this dose would prevent NTDs. Our aim was to investigate the effect of two doses of folic acid, compared with placebo, on red blood cell (RBC) folate, a biomarker of NTD risk.

Methods: We conducted a three-arm double-blind efficacy trial in Malaysia. Non-pregnant women (n = 331) were randomized to receive 60 mg iron and either 0, 0.4, or 2.8 mg folic acid once weekly for 16 weeks.

Results: At 16 weeks, women receiving 0.4 mg and 2.8 mg folic acid per week had a higher mean RBC folate than those receiving 0 mg (mean difference (95% CI) 84 (54 to 113) and 355 (316 to 394) nmol/L, respectively). Women receiving 2.8 mg folic acid had a mean RBC folate 271 (234 to 309) nmol/L greater mean RBC folate than those receiving 0.4 mg. Moreover, women in the 2.8 mg group were seven times (RR 7.3, 95% CI 3.9 to 13.7) more likely to achieve an RBC folate > 748 nmol/L, a concentration associated with a low risk of NTD, compared with the 0.4 mg group.

Conclusions: IFA supplements containing 2.8 mg folic acid increases RBC folate more than those containing 0.4 mg. Increased availability and access to the 2.8 mg formulation is needed.

Funding Sources: Nutrition International (Ottawa, Ontario).