Potential health risks of folic acid supplementation of 5 mg per day during pregnancy

To the Editor: We would like to express our concern regarding current prescriptions for folic acid supplementation for pregnant women in state hospitals. The current practice is that these women are advised to take a supplement containing 5 mg folic acid daily, which is over 10 times the recommended daily allowance (RDA) for pregnant women, i.e. 400 µg per day from supplements, and 5 times higher than the upper tolerable limit of 1 mg per day. Intake of such high amounts of folic acid may lead to delayed diagnosis of vitamin B_{12} deficiency, thereby causing irreversible neurological damage and compromised immune function.

Since folic acid is a water-soluble vitamin it is often thought that a person can hardly consume too much of it, because it will be excreted in the urine. However, this is not entirely true. Folic acid used for supplements is in the oxidised form, which differs from the natural folate forms in our bodies. It has been shown that people consuming folic acid either through supplements or through food fortification have small amounts of unmetabolised folic acid in their blood. Although folic acid has no acute toxicity, it is not yet known what damage it could do in the longer term.

Plasma folate concentrations > 7 nmol/l are considered normal. It has been shown that unmetabolised folic acid is present in plasma after exposure to supplements or fortified foods at intake levels > 200 µg/d.[1] It has also been assessed that the level of unmetabolised folic acid in plasma after a dose of 5 mg folic acid is frequently higher than 300 nmol/l for several hours.[2]

A major concern with regard to the presence of unmetabolised folic acid in body fluids and cells is delayed diagnosis of vitamin B_{12} deficiency and its related neurological damage. Normally, vitamin B_{12} deficiency results in megaloblastic anaemia because of blocked uptake of folate in cells. However, unmetabolised folic acid is taken up in body cells even if there is vitamin B_{12} deficiency, thereby preventing megaloblastic anaemia but not neurological damage.[3] Recently it has been shown that the presence of unmetabolised folic acid in fasting plasma samples of on average 2.3 nmol/l was associated with reduced natural killer cell cytotoxicity, which is a measure of immune function.[4]

Supplementation during pregnancy with 5 mg folic acid per day poses unfavourable health risks to pregnant women and their growing children. We therefore recommend that the prescribed folic acid regimen should be lowered to 400 µg per day, which has been shown to prevent neural tube defects adequately if taken from 1 month before conception,[5] and is also sufficient to cover folate requirements in the later stages of pregnancy. An exception should be made for women who have previously given birth to a child with a neural tube defect, in which case a regimen of 4 - 5 mg folic acid per day before conception until 12 weeks of pregnancy is advised.[6]

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