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MTHFR 677 TT genotype and folate requirements for preventing neural tube defects: is there a case for personalised nutrition?

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Given the known protective effect of folic acid (FA) in preventing neural tube defects (NTD), women of reproductive age in most countries worldwide are recommended to take 400 µg/d FA from before conception up to the 12th gestational week; however compliance with this recommendation is typically poor[1]. There is a well-established inverse relationship between maternal red cell folate (RCF) concentrations and NTD risk, with a maternal RCF concentration of ≥ 907 nmol/l associated with the lowest risk of an NTD affected pregnancy[2]. The 677C→T polymorphism in the gene encoding methylenetetrahydrofolate reductase (MTHFR) produces a variant enzyme which results in impaired folate metabolism; women with this genotype are reported to be at increased risk of adverse pregnancy outcomes including NTD. The aim of this investigation was to examine folate status by MTHFR 677C→T genotype in relation to FA usage reported by pregnant women. In particular we considered the timing of commencing FA supplementation.

Data from a previous investigation of women's compliance with current FA recommendations (*n* 226)[1] were analysed for the purpose of this study.

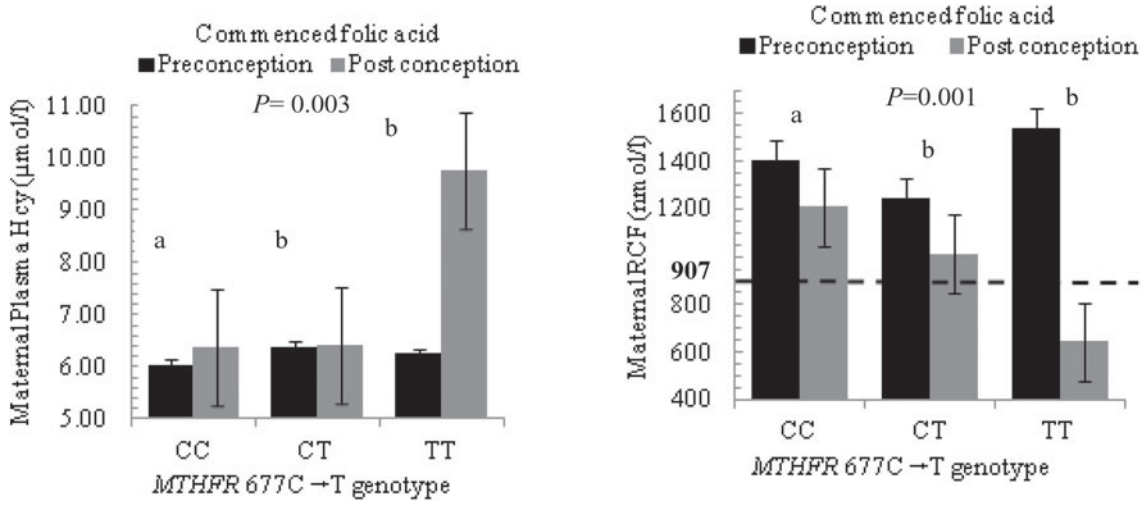

Figure 1: Mean (±SEM) Hcy (Left) and RCF (Right) at 14 weeks gestation by MTHFR 677C→T genotype. Probability values refer to interaction obtained from a Two-way Between-group ANOVA ($P<0.05$); different lowercase letters indicate significant differences between genotype groups by Tukey's post hoc test.

By the 14th gestational week, women with the TT genotype had significantly higher Hcy ($P = 0.002$) and lower RCF ($P = 0.006$) if they had not commenced FA before conception, compared to those that had, whereas these differences were not evident in the other genotype groups. Higher Hcy is linked to a number of adverse pregnancy outcomes[3] and RCF at this time reflects maternal folate status over the previous 12 weeks including the critical period of when the neural tube is closing. The majority of women (83%) with the TT genotype who started FA post conception failed to achieve a RCF concentration associated with the lowest risk of having an NTD affected pregnancy[2]. In conclusion, this study indicates the much greater need for women with the *MTHFR* 677TT genotype to adhere to the specific recommendation of commencing FA prior to conception for the prevention of NTD. These findings have important public health implications given that the frequency of the TT genotype is 10% worldwide but much higher in some populations.

1. McNulty B, Pentieva K, Marshall B *et al.* (2011) *Hum Reprod* **26**, 1530–1536.
2. Daly LE, Kirke PN, Molloy A *et al.* (1995) *JAMA* **274**, 1698–1702.
3. Vollset SE, Refsum H, Irgens LM *et al.* (2000) *Am J Clin Nutr* **71**, 962–8.