

The 13th European Nutrition Conference, FENS 2019, was held at the Dublin Convention Centre, 15–18 October 2019

Investigation of Blood Pressure during the First Trimester of Pregnancy in relation to the *MTHFR* C677T Polymorphism

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Abstract

The common C677T polymorphism in the *MTHFR* gene encoding the folate-metabolising enzyme methylenetetrahydrofolate reductase is implicated in hypertension and hypertension in pregnancy. Hypertension affects up to 15% of all pregnancies and has been identified as a leading cause of maternal and neonatal morbidity and mortality worldwide. We previously reported higher systolic and diastolic blood pressure (BP) in non-pregnant women with the variant *MTHFR* 677TT genotype compared to CT/CC genotypes. In addition, randomised controlled trials (RCTs) in non-pregnant hypertensive adults from our Centre demonstrated that supplemental riboflavin (co-factor for *MTHFR*) lowers BP specifically in those with the TT genotype. However, the role of this common folate polymorphism and its interaction with riboflavin during pregnancy remains unclear. The aim of this study was to investigate the impact of *MTHFR* genotype and riboflavin status on BP in pregnancy. Data were generated from the ongoing Optimal Nutrition for the Prevention of Hypertension (OptiPREG) project. Pregnant women were recruited at the end of the first trimester from antenatal clinics in Northern Ireland and in the Republic of Ireland. Participants were screened for *MTHFR* genotype and BP was measured according to current clinical guidelines. Biomarker status of riboflavin was determined using the erythrocyte glutathione reductase activation coefficient (EGRac), a functional assay with higher EGRac values representing a lower status. Overall, 117 (11.6%) participants were identified with the variant *MTHFR* 677TT genotype. Both systolic and diastolic BP decreased from 8th to 16th gestational week (GW), however, this typical BP pattern was not observed in the TT genotype group. After adjusting for maternal age, GW and body mass index, women with the TT genotype at 12th GW had higher mean systolic (P 0.035) and diastolic (P 0.034) BP. When the results at the 12th GW were stratified by riboflavin status, the BP phenotype owing to this polymorphism was evident only among women with lower status (i.e. EGRac > 1.30), with mean (SEM) systolic BP of 120.4 (3.1) mmHg compared to 112.6 (2.5) mmHg in those with higher status (EGRac ≤ 1.30) within the TT genotype group; in contrast, low versus high riboflavin status had no impact on BP in CT/CC genotype groups. These results suggest that *MTHFR* genotype influences BP during pregnancy and that riboflavin can exert an important modulating effect on BP in women with TT genotype. An RCT is required to fully investigate the role of *MTHFR* genotype and its interactive effect with riboflavin in BP during pregnancy.

Conflict of Interest

There is no conflict of interest.