

Abstract

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MTHFR 677C->T genotype is associated with folate and homocysteine concentrations in a large, population-based, double-blind trial of folic acid supplementation.

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BACKGROUND: The methylenetetrahydrofolate reductase (MTHFR) genotype is associated with modification of disease and risk of neural tube defects. Plasma and red blood cell (RBC) folate and plasma homocysteine concentrations change in response to daily intakes of folic acid supplements, but no large-scale or population-based randomized trials have examined whether the MTHFR genotype modifies the observed response.

OBJECTIVE: We sought to determine whether the MTHFR 677C→T genotype modifies the response to folic acid supplementation during and 3 mo after discontinuation of supplementation.

DESIGN: Northern Chinese women of childbearing age were enrolled in a 6-mo supplementation trial of different folic acid doses: 100, 400, and 4000 µg/d and 4000 µg/wk. Plasma and RBC folate and plasma homocysteine concentrations were measured at baseline; after 1, 3, and 6 mo of supplementation; and 3 mo after discontinuation of supplementation. MTHFR genotyping was performed to identify a C→T mutation at position 677 (n = 932).

RESULTS: Plasma and RBC folate and homocysteine concentrations were associated with MTHFR genotype throughout the supplementation trial, regardless of folic acid dose. MTHFR TT was associated with lower folate concentrations, and the trend of TT < CC was maintained at even the highest doses. Folic acid doses of 100 µg/d or 4000 µg/wk did not reduce high homocysteine concentrations in those with the MTHFR TT genotype.

CONCLUSION: MTHFR genotype was an independent predictor of plasma and RBC folate and plasma homocysteine concentrations and did not have a significant interaction with folic acid dose during supplementation. This trial was registered at clinicaltrials.gov as NCT00207558.

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