

Impact of Daily Folate Intake on Plasma Homocysteine and Folate Levels in Patients With Different Methylenetetrahydrofolate Reductase Genotypes

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Elevated plasma homocysteine level is associated with coronary artery disease (CAD). Homozygosity for the C677T mutation in the methylenetetrahydrofolate reductase (MTHFR) gene is typically associated with hyperhomocysteinemia. However, this association is inconsistent and may depend at least in part on the intake and plasma levels of folate, a co-factor in homocysteine metabolism. We examined the impact of daily intake of folate on plasma homocysteine and folate levels in CAD patients with different MTHFR genotypes.

Methods: Daily folate intake was assessed from 3-day food records in 99 patients with CAD: 35 with the T/T (homozygous mutant) genotype and 64 with the C/C or C/T (non-T/T) genotypes.

Results: Patients with the T/T genotype had higher fasting plasma homocysteine levels (18.4±1.9 vs 12.6±0.6 µmol/L, p=0.01) and lower plasma folate levels (17.8±1.7 vs. 20.8±1.0 nmol/L, p=0.02). There were no differences between the genotype groups in energy-adjusted folate intake. In patients with non-T/T genotypes, higher folate intake was associated with higher plasma folate levels and lower plasma homocysteine levels. In T/T homozygotes there was an upper limit to the impact of folate intake on plasma folate and a lower limit to its impact on plasma homocysteine levels. Linear regression analysis showed that folate intake, the MTHFR genotype, plasma vitamin B12 levels, and the interaction between plasma folate level and MTHFR genotype, predicted elevated homocysteine levels (folate intake, p=0.04, MTHFR genotype, p=0.03, plasma folate, p=0.02, and plasma B12 level, p=0.004). The model explained only 29% of the variance in log-transformed plasma homocysteine levels.

Conclusions: In T/T homozygotes, fasting plasma homocysteine is more sensitive to the combination of low folate intake, low plasma folate and B12 level, than in non-T/T genotypes. The variability in plasma homocysteine among T/T homozygotes is only partly explained by folate intake.