

Abstract

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Genetic and lifestyle factors related to the periconception vitamin B12 status and congenital heart defects: A Dutch case-control study.

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BACKGROUND: Maternal hyperhomocysteinemia is associated with congenital heart defects (CHDs) in the offspring. A low periconception vitamin B12 status is determined by genetic and lifestyle factors and causes hyperhomocysteinemia.

METHODS: We investigated methionine synthase reductase (MTRR) and transcobalamin II (TC) genes and maternal intake and serum concentrations of vitamin B12 in association with CHD risk. Seventeen months after the index-pregnancy, we studied 230 children with a CHD and 251 non-malformed children and their parents. Data were collected on current and periconception maternal vitamin supplement use and maternal dietary vitamin B12 intake of the month before the study moment. Blood samples were taken for the determination of MTRR A66G and TC C776G genotypes in families and maternal serum vitamin B12 concentrations. Transmission disequilibrium tests and univariate and multivariate analyses were applied.

RESULTS: Allele transmissions were not significantly distorted. The MTRR and TC genotypes did not significantly affect CHD risk. Neither polymorphisms in mothers and/or children revealed significant interactions nor in combination with low vitamin B12 intake. Low maternal serum vitamin B12 combined with the maternal or child's MTRR 66 GG genotype resulted in odds ratios of 1.4 (95% confidence interval 0.6-3.5) and 1.3 (0.5-3.4), respectively. The TC 776 GG genotype in mothers and children revealed risk estimates of 2.2 (0.7-7.1) and 1.9 (0.5-7.4), respectively.

CONCLUSIONS: MTRR 66 GG and TC 776 GG genotypes in mothers and children may contribute to the risk of CHDs, particularly when the maternal vitamin B12 status is low. The future enlargement of our sample size might demonstrate significant associations.

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