Genetic variation in folate metabolism may be linked to inherited heart defects

Summary

Congenital heart defects are frequent, occurring in about 1 of every 100 live births. They represent one of the most frequent causes of infant death. Prior evidence suggests that heart defects may be related to the body's ability to metabolize folate, or convert it as needed for essential processes. Several genetic variations at different points of the folate metabolism pathway have previously been identified. This study examines the association between four of these variations, called polymorphisms, and the risk for congenital heart defects in 156 children with congenital heart defects and 181 mothers of children with congenital heart defects. The frequency of different polymorphisms among these children and women were compared to 69 children without heart defects and 65 mothers of children without defects. All affected children were born in 1997, before Canada mandated folic acid supplementation in grains. DNA was analyzed from all subjects using restriction fragment length polymorphism (RFLP) analysis. Single nucleotide polymorphisms (SNP) were examined in four genes in each subject: methionine synthase reductase (MTRR), reduced folate carrier (SLC19A1), and two SNPs in methylenetetrahydrofolate reductase (MTHFR). Congenital heart defects were identified using echocardiography. It was found that a maternal MTHFR SNP was associated with a greater risk for congenital heart defects in the child, while the MTRR SNP in children protected them from congenital heart defects.

What families should know

Folate is an essential ingredient for healthy embryonic development. It is a vitamin that naturally exists in many foods, however, not all new mothers have access to it. In 1998, Canada mandated that all grain products should incorporate Folic acid, the synthetic form of folate. After ingesting folate or folic acid, the mother's body converts this vitamin into an active form that is crucial for embryonic development. It helps cells divide and helps build and maintain DNA.

What practitioners should know

This study suggests that a maternal MTHFR SNP is associated with an increased risk for aortic valve stenosis in children. This conflicts with prior findings that suggest no association between this SNP and a child's risk for a congenital heart defect. This study also demonstrates an association between a MTRR SNP in children and lower risk for congenital heart defects, particularly aortic valve stenosis and ventricular septal defect. These findings are only preliminary, and should be further investigated, since they do not completely agree with previous findings. Nonetheless, the use of a cohort of individuals predominantly un-supplemented with folic acid offers strength to this study, since it allows for a more precise analysis of the link between folate metabolism and congenital heart defects.

Reference

Christensen, K., Zada, Yassamin., Rohlicek, C., Andelfinger, G., Michaud, J, et al. (2012). Risk of congenital heart defects is influenced by genetic variation in folate metabolism. Cardiology in the Young. Advance online publication. doi:10.1017/S1047951112000431.