

Abstract

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Protective effect of periconceptional folic acid supplements on the risk of congenital heart defects: a registry-based case-control study in the northern Netherlands.

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AIMS: To investigate the potentially protective of periconceptional folic acid use on the risk of congenital heart defects (CHDs) relative to other non-folate related malformations.

METHODS AND RESULTS: We analysed data from a large regional register of birth defects (EUROCAT-Northern Netherlands), over a 10 year period (1996-2005) for a case-control study. The cases were mothers who had delivered infants with isolated or complex heart defects, without any related syndrome or genetic abnormality (n = 611). We used two control groups; one from the EUROCAT database and another from the general population. The registry controls consisted of mothers of children with a known chromosomal or genetic defect, and with infants with other non-folate related congenital malformations (n = 2401). Additional folic acid was taken as a single supplement or as a multivitamin containing folic acid in a dose of ≥ 400 microg daily. Mothers who had used folate antagonists or who had diabetes, and mothers of children with oral clefts, hypospadias, limb reduction- or neural tube defects, were excluded from both groups. Potentially confounding factors of periconceptional folic acid use in relation to CHD were explored, including baby's birth year, maternal body mass index, education, maternal age at delivery of index baby, smoking behaviour, and alcohol use during pregnancy. Periconceptional folic acid use revealed an odds ratio (OR) of 0.82 (95% CI 0.68-0.98) for all types of CHD relative to other malformations. The estimated relative risk for CHDs of additional folic acid use compared with the general population was comparable [OR 0.74 (95%CI 0.62-0.88)]. Subgroup analysis showed an OR of 0.62 (95% CI 0.47-0.82) for isolated septal defects. The proportions of the potential confounders between mothers of case and control infants did not differ significantly.

CONCLUSIONS: Our results support the hypothesis that additional periconceptional folic acid use reduces CHD risk in infants. Use of periconceptional folic acid supplements was related to approximately 20% reduction in the prevalence of any CHD. Given the relatively high prevalence of CHD worldwide, our findings are important for public health.

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