



ABSTRACT

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Introduction: One recent report has suggested an increased risk of major malformations after in utero exposure to topiramate.¹

Objective: To test the hypothesis that prenatal exposure to topiramate increases the risk of adverse pregnancy outcomes.

Methods: Since 1997, the North American AED (antiepileptic drug) Pregnancy Registry has enrolled 6,456 pregnant women taking AED, as well as a reference group of 372 friends and family members not taking AED. Data on drug use, dosage, demographic characteristics, vitamin use and the presence of malformations was determined in three telephone interviews and confirmed by medical records. We compared the frequency of adverse pregnancy outcomes in users of topiramate in monotherapy with controls and estimated the relative risk (RR) and 95% confidence interval (CI).

Results: The prevalence of major malformations in women exposed to topiramate during the first trimester was 3.8% (11/289). Compared to the prevalence of 1.3% (5/372) in the unexposed reference group; the RR for topiramate was 2.8 (95%CI: 1.0-8.1). The corresponding RRs for lamotrigine and carbamazepine, the most commonly reported AED, were 1.3 (95 CI 0.52 to 3.5) and 2.1 (95 CI 0.82 to 5.4), respectively. Four infants exposed to topiramate had cleft lip, 2 (0.69%) of them were isolated; the expected prevalence of isolated cleft lip is around 0.07%. The prevalence of low birth weight (<2,500 grams) in liveborn singletons without major malformations was 9.8% for topiramate and 3.6% for controls (RR 2.7, 95%CI: 1.4-5.1). Prenatal exposure to topiramate was associated with a mean lesser birth weight of 307 grams (P<0.001) compared to controls. For lamotrigine and carbamazepine, the mean lesser birth weights were 74 and 94 grams, respectively (not significant).

Discussion: Topiramate monotherapy was associated with a higher risk of major malformations and low birth weight. Whether these associations are causal or due to unbalanced risk factors among users of specific AED deserves further exploration.

¹ Hunt S et al. Topiramate in pregnancy: Preliminary experience from the UK Epilepsy and Pregnancy Register. *Neurology* 2008;71;272-276

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