

Artama M et al. Antiepileptic drug use of women with epilepsy and congenital malformations in offspring. *Neurology* 64, 1874-1878, 2005

Type of study	Population-based retrospective cohort
Where	Finland
When	1991-2000
Characteristics of the cohort	Newborns whose mothers with epilepsy were treated with antiepileptic drugs (AEDs) during pregnancy or discontinued AEDs before pregnancy, identified in the National Medical Birth Registry and the Social Insurance Institution of Finland
Characteristics of the treated diseases	Not indicated
Exposure definition	Intake in the first trimester of pregnancy
Ascertainment of drug exposure	Medical records of the mothers with epilepsy from 45 hospitals. Information included use, type and dose of AEDs (carbamazepine (919), valproate (361), oxcarbazepine, phenytoin, lamotrigine, clonazepam, other medication group)
Size of the studied cohort	Exposed to the studied drugs: 857 women, 1411 newborns Unexposed reference group: 561 women, 939 newborns
Exposed cohort	Newborns exposed to the studied drugs
Control cohort	Infants not exposed to the studied drugs. Mothers with epilepsy untreated during the first trimester of pregnancy
Malformations definition	Anomalies classified according to the International Classification of Diseases, ninth revision (ICD-9). No distinction between minor/major malformations. Only main categories of malformations, as defined by ICD-9, included in the analyses. If a child had more than one congenital anomaly of one organ system, those anomalies were considered as a single outcome of the organ system
Malformations ascertainment	As documented at discharge from the maternity unit. Information on congenital malformations was missing for 36 births (25 not on medication, 9 on monotherapy, 2 on polytherapy), excluded from the analyses
Prevalence of malformations among control offspring	2.8%
Analysis	Adjusted OR and 95% CI were estimated (logistic regression to control for potential confounders: maternal age at delivery, number of previous births)
Strengths	Exposed/unexposed infants selected from a defined population (nonvolunteer sample) - Reference group of untreated patients with epilepsy - Exposure data not dependent on patient recall, information based on recorded data - Detailed information on AEDs use - The largest study on oxcarbazepine
Weaknesses	- Medical records indicate drug dispensing rather than actual use - Incomplete information on congenital anomalies (not escludible minor malformations) - Some birth defects may not be included because they appear later after birth - Possibility of confounding by indication - No information regarding different types of epilepsy, spontaneous abortions, elective terminations, supplementation of folic acid, socioeconomic status - Not indicated if information on maternal drug use was available at the time of paediatrician's examination

Main results	<p>- Small number of other AEDs unlike carbamazepine and valproate</p> <p>Congenital malformations were more common among offspring of women on AEDs (4.6%) than of untreated patients (2.8%) (p=0.02). The risk of malformations was higher in the offspring of patients using valproate as monotherapy (OR 4.18, 95% CI 2.3-7.6) or valproate as polytherapy (OR 3.54, 95% CI 1.4-8.1) than of untreated patients. Polytherapy without valproate was not associated with increased risk of malformations</p>
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