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Risks during pregnancy in women with epilepsy

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Since 2000, a great deal of new information has become available about pregnancy outcomes in women with epilepsy. Most of this information has been related to the risks of major congenital malformations and cognitive behavioural deficits in children of women with epilepsy who had fetal antiepileptic drug exposure.^{1–3} These studies have emphasised the risks of major congenital malformations, cognitive impairment, and autistic spectrum disorder for children exposed in utero to valproate (9.3% at 1 year of age).^{1–7} Intermediate risks for major congenital malformations have been associated with fetal phenobarbital (5.5%) and topiramate (4.2%) exposures.^{1,2,4} Low risks for major congenital malformations have been associated with exposure to carbamazepine (2.9%), lamotrigine (2.0%), levetiracetam (2.4%), and oxcarbazepine (2.2%).^{1,2,4} Low risks for cognitive problems have been reported for carbamazepine, lamotrigine, and levetiracetam, which do not differ statistically from the unexposed population.^{6,8} The risks for most antiepileptic drugs and polytherapies are uncertain.

Even less information is available for other pregnancy risks in women with epilepsy, and individual studies have resulted in varied and imprecise estimates of risks. The American Academy of Neurology (AAN) reviewed the scientific literature and published practice parameters in 2009, which stated that probably no substantially increased risk exists of caesarean delivery, late pregnancy bleeding, or premature labour and delivery in women with epilepsy who are taking antiepileptic drugs.² Women with epilepsy who were seizure-free during the 9 months before conception are likely to stay seizure-free during pregnancy.² The AAN review group concluded that strong evidence is needed to establish if there are increased risks for a variety of obstetrical and seizure events during pregnancy in women with epilepsy.

In *The Lancet*, Luz Viale and colleagues present the results of their systematic review and meta-analysis⁹ of observational studies to assess risks of maternal and fetal complications (excluding malformations and cognitive-behavioural deficits). Viale and colleagues' analyses included 38 studies with 2837325 pregnancies. Women with epilepsy versus those without epilepsy had increased risks for spontaneous miscarriage (odds ratio [OR] 1.54, 95% CI 1.02–2.32), antepartum haemorrhage (1.49, 1.01–2.20), postpartum haemorrhage (1.29, 1.13–1.49), hypertensive disorders (1.37, 1.21–1.55), induction of labour (1.67, 1.31–2.11), caesarean section (1.40, 1.23–1.58), any preterm birth (1.16, 1.01–1.34), and fetal growth restriction (1.26, 1.20–1.33). Women with epilepsy taking antiepileptic drugs versus women with epilepsy not taking antiepileptic drugs had increased risk for post-partum haemorrhage (1.33, 1.16–1.54), induction of labour (1.40, 1.05–1.85), fetal growth restriction (3.51, 1.23–10.01), and admission to a neonatal intensive care unit (1.42, 1.13–

1.78). Women with epilepsy on polytherapy versus monotherapy had increased risk of caesarean section (1.47, 1.07–2.02). No increased risk was noted for fetal or neonatal mortality. The investigators conclude that epilepsy and exposure to antiepileptic drugs are associated with a small but significant risk for several adverse outcomes during pregnancy.

Viale and colleagues' study⁹ is well conducted and adds to existing published work by providing improved estimates for several risks during pregnancy in women with epilepsy. This information can be used to counsel women with epilepsy and manage care during their pregnancies. Limitations to the study include a shortage of information about seizures, parity, smoking, underlying medical conditions, specific antiepileptic drugs, dosing, and blood concentrations. The differences in statistical findings for women with epilepsy versus women without epilepsy, women with epilepsy on antiepileptic drugs versus those not on antiepileptic drugs, and women with epilepsy on polytherapy versus those on monotherapy might be due to differences in sample sizes across these comparisons.

Although most women with epilepsy have normal pregnancy outcomes, they and their children are at increased risk of adverse outcomes. Knowledge of these risks has grown since 2000, but many issues are uncertain. Future prospective investigations are needed to address risks of seizures, specific antiepileptic drugs, effects of antiepileptic drug dose, congenital malformations, long-term cognitive-behavioural outcomes, and other pregnancy outcomes. Furthermore, these studies need to address the risks of antiepileptic drug treatment during pregnancy in women without epilepsy, because more than half of antiepileptic drug prescriptions are for disorders other than epilepsy (eg, pain and psychiatric symptoms).¹⁰

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