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Maternal Serotonergic Antidepressant Use in Pregnancy and Risk of Seizures in Children

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Study Question

Do children born to women who use serotonergic antidepressants (i.e., selective serotonin reuptake inhibitors [SSRIs] and serotonin–norepinephrine reuptake inhibitors [SNRIs]) during pregnancy have higher risk of neonatal seizures and epilepsy?

What Is Known and What This Paper Adds

Several studies have documented an association between serotonergic antidepressant use in pregnancy and neonatal seizures in children, but few studies have examined whether these medications are associated with recurrent seizures (i.e., epilepsy). The current study aimed to expand the understanding of the potential effect of prenatal serotonergic antidepressant exposure on seizure outcomes using a nationwide sample of children by considering many confounders not incorporated in prior studies. This study provides Class II evidence that exposure to SSRIs/SNRIs in the first trimester of pregnancy is not associated with an increased incidence of neonatal seizures or epilepsy.

Methods

We used Swedish register-based data to examine associations between maternal reported use of SSRIs/SNRIs in pregnancy and neonatal seizures and epilepsy (using diagnosis codes) in a cohort of >1.2 million children. To examine the influence of confounding, we adjusted for a range of factors in a stepwise fashion: (1) maternal indication for SSRI/SNRI use (i.e., depression and anxiety), (2) parental epilepsy, and (3) parental background factors and pregnancy-specific characteristics. We used log-binomial regression to estimate the risk of neonatal seizures and Cox proportional hazard regression to estimate the risk of epilepsy.

Results and Study Limitations

Compared with unexposed children, children of women who reported SSRI/SNRI use in pregnancy had an elevated risk of neonatal seizures (risk ratio [RR] 1.41, 95% CI 1.03–1.94) and epilepsy (hazard ratio [HR] 1.21, 95% CI 1.03–1.43).

Table Associations Between Maternal Reported SSRI and SNRI Use During Pregnancy and Seizures in Children

	Unadjusted	Adjusted for maternal indications	Additionally adjusted for parental epilepsy	Additionally adjusted for all other covariates
Neonatal seizures (n = 1,551,906), RR (95% CI)	1.41 (1.03, 1.94)	1.30 (0.94, 1.80)	1.30 (0.94, 1.79)	1.10 (0.79, 1.53)
Epilepsy (n = 1,367,087), HR (95% CI)	1.21 (1.03, 1.43)	1.13 (0.95, 1.33)	1.11 (0.93, 1.31)	0.96 (0.81, 1.14)

Abbreviations: HR = hazard ratio; RR = risk ratio; SNRI = serotonin–norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

The estimates of association were attenuated by adjustment for maternal indications for SSRI/SNRI use (RR 1.30, 95% CI 0.94–1.80; HR 1.13, 95% CI 0.95–1.33), but not by additional adjustment for parental epilepsy history (RR 1.30, 95% CI 0.94–1.79; HR 1.11, 95% CI 0.93–1.31). Additional adjustment for parental and pregnancy-specific factors substantially attenuated the remaining associations (RR 1.10, 95% CI 0.79–1.53; HR 0.96, 95% CI 0.81–1.14). The findings suggest that associations are due to confounding factors rather than SSRI/SNRI use in pregnancy. Study limitations include possible misclassification of exposure and outcomes.

Study Funding and Competing Interests

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