NEWS

Epilepsy drugs pose risks to developing brains, study suggests

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Some drugs used to treat **epilepsy** harm children who are exposed to them in the womb or through breast milk, a new analysis of the literature suggests[1]. The drug valproate is particularly risky, boosting the likelihood of autism and other developmental problems up to 17-fold.

The study is the first to compare the relative risks of taking various epilepsy drugs during pregnancy. Some of these medications are also used to treat bipolar disorder and migraines.

“We know that these antiepileptic drugs are taken by many women every year,” says lead researcher **Andrea Tricco**, assistant professor of epidemiology at the University of Toronto in Canada.

Still, the absolute risk of autism — even in children exposed to valproate — is low. And in many cases, the benefits outweigh the risks, says **Jacqueline French**, professor of neurology and director of translational research and clinical trials at the Comprehensive Epilepsy Center at NYU Langone Medical Center, who was not involved in the study.

“Sometimes, in order to control some very serious and life-threatening seizures, valproate is necessary,” French says.

Studies have shown that **prenatal exposure to valproate** significantly increases the risk of autism[2,3]. For example, a 2013 population-based study in Denmark found that 4.4 percent of children exposed to valproate have autism, compared with 1.5 percent of unexposed children[3]. Last month, **France banned** doctors from prescribing some forms of the drug — those used to treat bipolar disorder — to pregnant women.

Still, some of the studies in the new analysis were small, and used diverse methods, leading experts to question the statistical strength of the findings.

Ranking risks:

Tricco and her colleagues searched the scientific literature for studies of children exposed to any of 26 epilepsy drugs, or drug combinations, in the womb or through breast milk. They identified 29 studies, which together included 5,100 children, that assessed autism features or developmental delays after exposure to the medications.

They found that the odds of autism are 17 times higher in children exposed to valproate than in those not exposed to any epilepsy medications. The odds of language, cognitive and motor delays are eight-, seven- and fourfold higher, respectively, in children exposed to valproate. The odds of psychomotor delays jump 19-fold in children of women who take valproate along with two other epilepsy medicines, carbamazepine and phenobarbital.

Exposure to another drug in the group, oxcarbazepine, ups the risk of autism 14-fold, whereas the antiepileptic lamotrigine is associated with a 9-fold increase. A combination of valproate and lamotrigine in the womb boosts risk 133-fold. Eight other drug treatment regimens show no association with autism. The results appeared 20 July in *BMJ Open*.

The findings are surprising, French says. In particular, lamotrigine has been considered safe for pregnant women. “If lamotrigine indeed was associated with an increased risk of autism, that would be big news,” she says.

Suspect statistics:

French is not convinced of the risk, however. Some other factor may underlie the use of certain medications and an increased risk having a child with autism, she says. For instance, women who take valproate or lamotrigine during pregnancy may have particularly severe forms of epilepsy.

Tricco points out that the data her team used to draw their conclusions are imperfect. Only 5 of the 29 studies included in the analysis provided information about a child’s autism status. (The other studies measured other types of developmental delays or issues.) She also notes that because some of the epilepsy drugs were used by relatively few women, the estimates of their risk are preliminary.

In addition, the studies used different methods for assessing children’s cognitive, linguistic and motor abilities. “My primary concern is that they have grouped together data which do not actually measure the same skill,” says **Rebecca Bromley**, research fellow at the University of Manchester in the United Kingdom, who was not involved in the new research.

The researchers did not know whether any of the children have a family history of autism, which could be another confounding factor, Tricco says.

Women should discuss the possible risks and benefits of these drugs in consultation with their doctors, the experts say.

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