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New Studies Show Mixed Results on Epilepsy Drugs and Birth Defects

St. Paul, Minn. – New studies show mixed results on the effects of epilepsy drugs taken during pregnancy. With a newer drug, lamotrigine, the risk of birth defects was similar to that in women without epilepsy. But long-time epilepsy drug valproic acid, or sodium valproate, does increase the risk of birth defects. Both studies were published in the March 22 issue of *Neurology*, the scientific journal of the American Academy of Neurology.

Another study in the same issue found that children ages 6 to 16 who had been exposed to valproic acid during pregnancy had lower verbal IQ scores than children exposed to other epilepsy drugs or no epilepsy drugs during pregnancy.

The good news comes from the study of lamotrigine, which is one of several newer epilepsy drugs introduced after 1990. Few studies have been done on these drugs' effects on human fetuses. This study monitored birth defects in lamotrigine-exposed pregnancies reported over more than 11 years in the International Lamotrigine Pregnancy Registry.

Among 414 pregnancies where the fetus was exposed during the first trimester to lamotrigine as the only epilepsy drug used, there were 12 cases of major birth defects. That translates to a 2.9 percent risk of having a birth defect, which is similar to the 2 to 3 percent risk in the general population. That risk jumped to 12.5 percent for women who were taking lamotrigine along with valproic acid during the first trimester.

“Even though the number of women enrolled in this study was large, the number of pregnancies is still too small to give us absolute answers,” said neurologist Patricia Penovich, MD, of the Minnesota Epilepsy Group PA, who wrote an editorial accompanying the studies. “But the results can be somewhat reassuring to women. They also emphasize the importance of trying to control seizures with only one epilepsy drug if possible and the importance of planning carefully how epilepsy drugs will be used during pregnancy before the pregnancy occurs.”

The bad news is about the drug valproic acid. One study monitored the rate of birth defects in infants whose mothers had taken valproic acid as their only epilepsy drug during the first trimester of pregnancy and were enrolled in the North American Antiepileptic Drug (AED) Pregnancy Registry. Of the 149 women in the study, there were 16 infants with birth defects, or 10.7 percent. The women taking valproic acid were nearly three times more likely to have an infant with a birth defect than women taking another epilepsy drug. They were more than seven times more likely to have an infant with a birth defect than women in the general population.

For the second study on valproic acid, British researchers recruited 163 mothers with epilepsy and their children and gave them a number of tests. A total of 249 children between the ages of 6 and 16 took the tests. The 41 children who were exposed to valproic acid during pregnancy were more likely to have low verbal IQ scores (average of 84) compared to other groups in the study, such as those exposed only to the drug phenytoin (average score of 99) or those not exposed to any epilepsy drug during pregnancy (average score of 92).

Those exposed to valproic acid were also more likely to have overall IQ scores in the extremely low, or mentally impaired, range. Two to three percent of the population would be expected to fall in this range. In the study, 22 percent of those exposed to valproic acid were in this range.

Penovich noted that maintaining effective epilepsy treatment during pregnancy is crucial. "Seizures can cause fetal distress, and the severe epilepsy state called status epilepticus where attacks occur in rapid succession may cause catastrophic damage to the brain of the fetus," she said. More studies must be done to understand how valproic acid works to affect fetal development. "Without good animal models, the mechanism for the abnormalities remains unknown," Penovich said.

"It's very important that physicians and women have as much information as possible about these medications," said Diego Wyszynski, MD, PhD, of Boston University School of Medicine and senior epidemiologist with the Antiepileptic Drug Pregnancy Registry. "Pregnancy registries are really the only way at present to collect data on what medications women are taking and what effects they may be having on their babies."

Women can sign up for the Antiepileptic Drug Pregnancy Registry, which is based at Massachusetts General Hospital, by calling toll-free (888) 233-2334. Women can talk to their doctors about enrolling in the International Lamotrigine Pregnancy Registry.

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The American Academy of Neurology, an association of more than 18,000 neurologists and neuroscience professionals, is dedicated to improving patient care through education and research. A neurologist is a doctor with specialized training in diagnosing, treating and managing disorders of the brain and nervous system such as stroke, Alzheimer's disease, epilepsy, Parkinson's disease, autism and multiple sclerosis.

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