
Anti-Seizure Drug Valproate Linked to Birth Defects

(22 Mar, 2005) - Contributed by Jai A. Dennison

A drug that has been a common choice to treat epilepsy for years, valproic acid, or sodium valproate, has been found to increase the risk of birth defects in a new study published in the March 22 issue of the journal of the American Academy of Neurology.

The 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.

Lower Verbal IQ Scores

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.

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 also were 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.

Cautious Optimism: Lamotrigine

a third study in the same publication focused on a newer epilepsy drug, lamotrigine, which was found to have no effect on the risk of birth defects, with the rate among pregnant women taking it similar to that of women without epilepsy.

Lamotrigine 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, says 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," she adds. "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.

Pregnancy Registries Gather Valuable Data

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, says 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.

The International Lamotrigine Pregnancy Registry is funded by GlaxoSmithKline, the manufacturer of lamotrigine.