

## Seizure Drug May Be Harmful During Pregnancy

Mon Mar 21, 2005 06:44 PM ET

By Karla Gale

NEW YORK (Reuters Health) - Women who take the epilepsy drug valproate during pregnancy may be raising their baby's risk of severe birth defects, according to reports in the medical journal *Neurology*. In contrast, another drug, lamotrigine, appears to be safe.

The research is just the latest study to suggest that valproate may be harmful to the developing fetus. "These results alongside 12 previous studies highlight the growing body of evidence that raises concern about the use of valproate in women of childbearing age," the authors note.

Dr. Gus A. Baker, at the Walton Center for Neurology and Neurosurgery in Liverpool, UK, and colleagues performed neurologic testing on 256 children of 163 mothers with epilepsy.

Verbal IQ score was lower in children exposed to valproate compared those exposed to carbamazepine, phenytoin, and those whose mothers were not taking any anti-epileptic drug during pregnancy. Children exposed to valproate were also more likely to score within the extremely low range of IQ.

In a second study, Dr. D. F. Wyszynski, at Boston University School of Medicine, and colleagues evaluated infants of mothers enrolled in the North American Anti-Epileptic Drug Pregnancy Registry. The study included children of 149 women who took valproate during their first trimester and 1048 children whose mothers took other antiepileptic drugs.

The rate of major birth defects in the valproate group was 11 percent, while the rate in the comparison group was just 3 percent. In the general population, the rate is only 1.6 percent.

In a related editorial, Dr. Patricia Penovich, at the University of Minnesota in St. Paul, and Dr. Eija Gaily at Helsinki University in Finland, note that the link between valproate and birth defects may relate to characteristics of the mother with epilepsy that predispose the child to problems.

The emerging evidence, however, should make the physicians consider an alternative to valproate therapy in women with epilepsy prior to conception, the editorialists advise.

In an interview with Reuters Health, Penovich pointed out that for some women, valproate may be necessary during pregnancy because "it may be the only thing controlling a patient's seizures, and the risk of a seizure on the fetus is very marked."

According to a third study, evidence from the International Lamotrigine Pregnancy Registry suggests that lamotrigine is not associated with increased risk of major malformations.

Dr. Marianne Cunnington, with GlaxoSmithKline in Harlow, UK, and colleagues followed women enrolled in the worldwide registry between 1992 and 2004. More than 700 pregnancies involving a lamotrigine-treated mother were included in the analysis. Once again, birth defect rates were about 3 percent, except when the drug regimen included valproate and then it climbed to 13 percent.

After reviewing the three reports, Penovich and Gaily conclude: "The risks for mother and child can be most effectively minimized by careful planning of anti-epileptic drug therapy before pregnancy, by supplementing with folate, and by using only the most effective drug at the lowest dose possible."

SOURCE: *Neurology*, March 22, 2005.