



PIC QUESTION OF THE WEEK: 5/11/09

Q: What are the recommendations for using antiepileptic drugs, especially valproic acid, during pregnancy?

A: Nearly one-half million American women of childbearing age suffer from epilepsy. It is estimated that 3 to 5 births per thousand will be to women with epilepsy (WWE). The American Academy of Neurology (AAN) has just distributed a *practice parameter* that addresses many of the issues related to the teratogenicity of antiepileptic drugs (AEDs). The report was based on an evaluation of 52 published studies related to the use of AEDs during pregnancy. Some of the major findings included an increased risk of major congenital malformations (MCMs) such as facial clefts, neural tube defects, and hypospadias as well as evidence of reduced Apgar scores and newborn size that was small for gestational age. Decreased IQ and cognition were also associated with specific AEDs. The following are some of the major recommendations offered by the AAN:

- *If possible*, avoid AED polytherapy during the first trimester and throughout pregnancy as polytherapy increases the risk for MCMs.
- *If possible*, avoid valproic acid (VPA) during the first trimester and throughout pregnancy as this drug is associated with a greater risk of MCMs than other AEDs.
- VPA may have a significant effect on cognitive function. A recent report cited below evaluated the effect of in-utero exposure to VPA, CBZ, phenytoin (PHT), and lamotrigine (LTG) on IQ score at 3 years of age. Those exposed to VPA had an average 9 point lower IQ score than the highest scoring group exposed to LTG. CBZ and PHT appeared to provide an intermediate risk of cognitive impairment.
- Monotherapy with AEDs other than VPA during the first trimester has produced mixed results regarding the risk for MCMs relative to WWE not exposed to AEDs. The report suggests that CBZ, PHT, or LTG are clearly better alternatives to VPA.

VPA is currently labeled as pregnancy category D by the FDA and contains a specific Black Box Warning regarding teratogenic effects. PHT, CBZ, and phenobarbital are also labeled category D, while LTG, gabapentin, and topiramate maintain a designation of category C. For more specific recommendations on this topic and others relating to pregnancy and epilepsy, the reader should refer to the April 27, 2009 E-pub section of the AAN website.

References:

- Harden CL, Sethi NK. Epileptic disorders in pregnancy: an overview. *Curr Opin Obstet Gynecol* 2008;20:557-62.
- Meador KJ, Baker GA, Browning N, et al. Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs. *N Engl J Med* 2009;360:1597-605.
- Practice parameter update: Management issues for women with epilepsy—focus on pregnancy (an evidence-based review): Teratogenesis and perinatal outcomes. Report of the Quality Standards Subcommittee and Therapeutics and Technology Subcommittee of the American Academy of Neurology and American Epilepsy Society
Neurology <http://www.neurology.org/cgi/rapidpdf/WNL.0b013e3181a6b312v1.pdf> Accessed May 6, 2009.

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