Anticonvulsants May Not Affect Child’s IQ

BY DOUG BRUNK
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TUCSON, ARIZ. — The use of carbamazepine, phenytoin, or phenobarbital as monotherapy by pregnant women was associated with significant deficits in full-scale IQ in their offspring, a small study showed.

However, these data counter previous reports of lowered intellectual ability in children born to mothers who took anticonvulsant medications during pregnancy. Dr. Kenneth Lyons Jones said at the annual meeting of the Teratology Society that “substantial controversy” exists regarding their impact on neurobehavioral outcomes.

“Compounding these concerns is the fact that in the United States, between 7.6 million and 12.7 million women have epilepsy, and 95% of them are being treated with anticonvulsant drugs,” Dr. Jones said. “In addition, 1 in every 200 pregnant women have epilepsy, and 95% of the exposed children differ from those exposed to phenobarbital and only 3% of those exposed to carbamazepine. No one in the control group was considered affected.

In terms of the FSIIQ, there were no statistically significant differences in scores between exposed children and controls, nor did any of the exposed children differ from each other, even after controlling for age and socioeconomic status. Dr. Jones acknowledged certain limitations of the study, including the fact that the population studied was homogenous, the sample size was small, and there was potential for selection bias.

First- and Second-Generation Anticonvulsants

Although it has been known for years that some first-generation antiepileptic drugs (AEDs) cause birth defects, in utero teratog enicity during her pregnancy .”

The first-generation AEDs known to cause birth defects and other developmental toxicities include the hydantoins (ethotoin [Peganone], fosphenytoin [Cerebyx], mephenytoin [Mesantoin], and phenytoin [Dilantin]), phenobarbital, primidone (Mysoline), carbamazepine (Tegelet), and valproic acid derivatives (Depakene, Depakote). In a 2001 study, the incidence of embryopathy (major and minor anomalies, microcephaly, and IUGR) after first-trimester monotherapy was 21% (Phenytoin), 27% (phenobarbital), 14% (carbamazepine), 21% (any monotherapy), and 28% (polysyndrome) (N. Engl. J. Med. 2001;344:1132-8).

Phenytoin also causes a pattern of defects collectively called the fetal hydantoin syndrome (FHS), characterized by variable degrees of hypoplasia and ossification of the distal phalanges and craniofacial abnormalities [Trileptal].

Other defects, such as those involving heart and growth, are commonly observed. A syndrome with carbamazepine consisting of minor craniofacial defects, finger-nail dysplasia, and developmental delay has been observed; this drug may also cause neural-tube defects (NTDs).

The defects observed with primidone are similar to those in FHS. Phenobarbital has been associated with an increase in congenital defects when used for epilepsy, but not for use in other indications. The use of valproic acid derivatives between the 17th and 30th day after fertilization is associated with a 1%-2% risk of NTDs. Other defects are those of the head and face, digits, urogenital tract, and mental and physical growth. Carbamazepine, phenytoin, primidone, and phenobarbital affect folate metabolism or absorption, and this may increase the risk of birth defects, including NTDs. Women taking these agents should take folic acid 4.5 mg/day, preferably starting before conception. Moreover, anticonvulsants, particularly the hydantoins and barbiturates, are related to hematopoietic disease of the newborn. In a review of a large database of phenobarbital K should be given to the newborns exposed to AEDs in utero.

In contrast, first-generation AEDs that do not appear to be associated with a significant risk of birth defects include the benzodiazepines (clonazepam [Klonopin], clobazepam [Tranzene], diazepam [Valium], and lorazepam [Ativan]) and succinimides (ethosuximide [Zonegran], carbamazepine, phenobarbital, primidone, and phenobarbital affect folate metabolism or absorption, and this may increase the risk of birth defects, including NTDs. Women taking these agents should take folic acid 4.5 mg/day, preferably starting before conception. Moreover, anticonvulsants, particularly the hydantoins and barbiturates, are related to hematopoietic disease of the newborn.

Carbamazepine and phenytoin are known to cause toxicity in the nursing infant and should not be given during breast-feeding. There are no data for the remaining AEDs, but they have the potential to cause toxicity and, if used during breast-feeding, the infants should be closely monitored.

Catheter Use in Hyperemetic Patients Tied to Complications

WASHINGTON — Complications were significantly more likely among pregnant women whose hyperemesis was managed with a peripherally inserted central catheter line than with either a Dobhoff tube or medication, Dr. Calla M. Holmgren reported in a paper presented at the annual meeting of the American College of Obstetricians and Gynecologists.

Dr. Holmgren and her colleagues at the University of Utah, Salt Lake City, compared the three interventions in a prospective cohort study of 70 hyperemetic patients. Two of 24 patients whose mother’s hyperemesis was managed with a PICC line developed sepsis and were admitted to the neonatal intensive care unit, and one fetus died as a direct result of PICC line use. Also, 7 of the 24 patients had thrombosis, 3 had skin infections, and 2 had bacteremia. One patient with bacteremia was admitted to the NICU.

By comparison, 1 of 13 women managed with a Dobhoff tube had sepsis, and 1 of 2 had bacteremia. Women managed with medication had adverse reactions.

Heidi Splete

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One in every 200 pregnant women requires antiepileptic medication during her pregnancy.

DR. JONES

A small study showed that “substantial controversy” exists regarding the impact of antiepileptic medications during pregnancy. Dr. Kenneth Lyons Jones said at the annual meeting of the Teratology Society that “substantial controversy” exists regarding their impact on neurobehavioral outcomes.

In terms of the FSIIQ, there were no statistically significant differences in scores between exposed children and controls, nor did any of the exposed children differ from each other, even after controlling for age and socioeconomic status. Dr. Jones acknowledged certain limitations of the study, including the fact that the population studied was homogenous, the sample size was small, and there was potential for selection bias.

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