When to Discontinue Anticonvulsants in Pregnancy

Lack of neurologic abnormalities, normal EEG, onset of epilepsy in childhood bode well for stopping the drugs.

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Anticonvulsants are known to cause birth defects when taken during pregnancy, but physicians should weigh the benefits and risks before discontinuing anticonvulsant therapy, Jennifer R. Niebyl, M.D., said at the annual meeting of the American College of Obstetricians and Gynecologists.

The risks are not all that large, said Dr. Niebyl of the University of Iowa, Iowa City. Only 5%-10% of women taking anticonvulsants during pregnancy develop fetal hydantoin syndrome.

Women taking a single anticonvulsant medication have about 2.5 times the risk of having this embryopathy as do epileptic women not taking anticonvulsants. Those taking at least two anticonvulsants have a significantly higher risk: 3.7 times as high as epileptics not taking anticonvulsants. This suggests it is the drug, not the epilepsy itself, that causes the syndrome.

Children with fetal hydantoin syndrome typically show multiple symptoms, including disorders of growth and of mental development, dysmorphic craniofacial features, and hypoplasia of the nails and distal phalanges.

Dr. Niebyl said it's becoming clear that it's desirable to wean women planning a pregnancy from their anticonvulsant medications if possible. This is more likely to be successful in women whose epilepsy is idiopathic, rather than caused by a head injury.

Other factors that bode well for getting women off anticonvulsants include a lack of neurologic abnormalities, a normal EEG, onset of epilepsy in childhood, seizures controlled by a single drug, and being seizure free for at least 2 years.

About 75% of these women will remain seizure free after discontinuing medication. But since 25% will have a seizure—and it's impossible to predict who will fall into that group—these women should be instructed not to drive during the time they're off the drug.

It's desirable to wean a woman planning a pregnancy from anticonvulsant medications, if possible.

DR. NIEBYL

"If you don't see the patient until they're already pregnant, the benefits of continuing therapy usually outweigh the risks," Dr. Niebyl said.

Anticonvulsants can interfere with folate metabolism, so Dr. Niebyl recommended being especially vigilant about folic acid supplementation. And some of these drugs—particularly phenytoin, primidone (Mysoline), and phenobarbital—inhibit the transfer of vitamin K across the placenta. This results in a decrease in fetal clotting factors and an increase in the risk of fetal hemorrhage. For this reason, many physicians will put patients on vitamin K supplementation (20 mg/day) for the final month or two of pregnancy, although there's no definitive evidence that this has a beneficial effect.

Some of the newer anticonvulsant medications, such as lamotrigine (Lamictal), may confer a smaller risk of birth defects than the older drugs, Dr. Niebyl said, but once again definitive evidence is lacking.

Dr. Niebyl said she had no financial conflicts of interest relevant to her presentation. ■

Intrapartum Fever Is Associated With Neonatal Encephalopathy

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — Isolated intrapartum fever and chorioamnionitis are independent risk factors for neonatal encephalopathy, Heidi Blume, M.D., said at the annual meeting of the Pediatric Academic Societies.

"It remains unclear if fever is the cause of injury, exacerbates injury, or is a sign of some other noxious process," said Dr. Blume of the University of Washington, Seattle.

Neonatal encephalopathy, which affects up to 6 in 1,000 term infants annually, is a clinically defined syndrome of disturbed neurologic function during the infant's earliest days of life. Symptoms include difficulty initiating and maintaining respiration; depressed tone and reflexes; subnormal level of consciousness; and, sometimes, seizures.

Dr. Blume undertook a population-based, case-control study of infants born in Washington from 1994 to 2002. She used data from the Washington State Birth Registry; this information is linked to the state's Comprehensive Hospital Abstract Reporting System. The system includes discharge diagnoses, diagnosis and procedure codes, and dates of hospitalization.

The 1,114 cases were singleton term infants whose ICD-9 discharge diagnoses included birth asphyxia, newborn convulsions, central nervous system dysfunction, or other cerebral irritability.

These cases were matched with 6,046 control infants. Exposure to isolated fever was defined as maternal intrapartum fever of 38° C or greater, or ICD-9 diagnosis of maternal intrapartum pyrexia without chorioamnionitis.

Exposure to chorioamnionitis was defined by ICD-9 diagnosis of chorioamnionitis or infection of the amnion.

It remains unclear whether isolated intrapartum fever 'is the cause of injury, exacerbates injury, or is a sign of some other noxious process.'

Mothers of encephalopathy cases were more likely to be of low socioeconomic status, to be nulliparous, and to have had preeclampsia.

Case infants were more likely to have received late prenatal care and to be of low birth weight, and slightly more likely to be male, according to the researcher.

Both isolated maternal fever and chorioamnionitis were more common in encephalopathy cases than in controls. Exposure to maternal fever reportedly occurred in 2.5% of the controls and 8% of cases, for an adjusted odds ratio of 3.2. Chorioamnionitis was present in 1.2% of controls and 6% of cases, for an adjusted odds ratio of 5.7.

"These relationships persisted in subgroups of cases who were diagnosed with seizures and birth asphyxia," Dr. Blume said at the meeting, sponsored by the American Pediatric Society, the Society for Pediatric Research, the Ambulatory Pediactric Association, and the American Academy of Pediatrics.

Infants exposed to intrapartum maternal fever had a threefold increase in the risk of being diagnosed with seizure and a 3.5-fold increased risk of being diagnosed with birth asphyxia.

Infants exposed to chorioamnionitis had a fivefold increased risk of being diagnosed with seizure and almost a sevenfold increased risk of being diagnosed with birth asphyxia.

Dr. Blume noted some limitations in the study. She was not able to review charts, so it was impossible to determine what symptoms led to the diagnosis and discharge codes. However, she felt certain that few of the infants had meningitis, since the cases were limited to infants who were diagnosed during their newborn hospitalization, or who were admitted within 2 days of birth. ■

Study Finds 5-Minute Apgar Highly Predictive of Respiratory Distress Syndrome

BY KATE JOHNSON
Montreal Bureau

SAN FRANCISCO — Newborns with a 5-minute Apgar score of 7 or less have a high risk of developing respiratory distress syndrome, according to Linda R. Chambliss, M.D., associate director of maternal fetal medicine at the Maricopa Integrated Health System in Phoenix, Ariz.

The recent findings should help alert physicians to high-risk infants who should be monitored more intensively or given therapies to reduce the incidence or severity of respiratory distress syndrome (RDS), she reported at the annual meeting of the American College of Obstetricians and Gynecologists.

"What is surprising is that many people, including myself, have felt that as long as the 5-minute Apgar hits 7, the baby will be fine, but this is not necessarily the case," she told this newspaper. "Clinicians who deliver an infant with such a score should counsel the families and the nursery that RDS is very likely. These infants have to be watched very closely."

Her study analyzed more than 26,000 births from a statewide registry and identified 657 admissions to neonatal intensive care with a diagnosis of RDS.

Of these admissions, 540 infants had an Apgar score of 7 or less, compared with 3,803 infants who had the same Apgar score but no RDS.

After controlling for education level, marital status, race, parity, smoking, prenatal care, diabetes, hypertension, preeclampsia, induction/augmentation of labor, intrapartum fever, prolonged rupture of membranes, abruption, nonreassuring fetal heart rate, delivery by cesarean, infant's gender and gestational age, the 5-minute Apgar score of 7 or less was an independent risk factor for RDS, with an adjusted odds ratio of 25, Dr. Chambliss said.

When the infant's birth weight was substituted for gestational age, the risk remained similar (odds ratio 22).

Low birth weight and prematurity are well-recognized risk factors for the development of RDS, even when Apgar scores are normal, Dr. Chambliss said.

But her findings suggest that regardless of birth weight or prematurity, or any of the other variables that the researcher measured, the 5-minute Apgar score of 7 or less remains a high risk factor for RDS.

"People may not have realized how strongly this predicts future problems with RDS. While the Apgar score may not be the best way to predict some complications, such as neurological injury, we feel it has a great deal of utility to predict the risk RDS even when controlled for a number of other variables," she said. ■

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