Breast-Fed Babies Unhurt By Moms' Antiepileptics

BY DENISE NAPOLI
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CHICAGO — The infants of mothers taking antiepileptic drugs showed no adverse cognitive effects as a result of breast-feeding, judging from the findings of a small, preliminary study.

"Concerns have been raised, but there are no prior formal studies examining the effect of breast-feeding in women taking antiepileptic drugs," the study's lead author, Dr. Kimford Meador, the Melvin Greer Professor of Neurology at the University of Florida, Gainesville, where he serves as director of the epilepsy program and of the clinical Alzheimer program, said in an interview. Findings from "our study suggest that it is safe."

Dr. Meador and his colleagues looked at 187 children of mothers enrolled in the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study. The NEAD study is a multicenter, prospective, parallel-group, observational study that is ongoing at 25 centers in the United States and the United Kingdom. Pregnant mothers with partial or primary generalized epilepsy taking pharmacologic monotherapy (including valproate, carbamazepine, phenytoin, or lamotrigine) were eligible to enroll. In this study, a blinded cognitive assessment of the children was conducted at 2 years old; follow-up assessments will be conducted at years 3, 4.5, and 6.

Compared with their non–breast-fed counterparts, the breast-fed children in this cohort (41%) actually had higher cognition, 98.1 vs. 89.5 on the Bayley Mental Developmental Index. However, Dr. Meador said that when investigators controlled for the mother's IQ, there was no significant difference between groups.

"The NEAD study is not randomized and was not specifically designed to examine the effects of breast-feeding," he said, listing some of its limitations. Also, "there are only four drugs in the study." However, "breast-feeding during antiepilepsy drug treatment doesn't appear to have a negative impact on a child's cognitive abilities."

Speaking at the annual meeting of the American Academy of Neurology, Dr. Meador added that the 3-year follow-up data analysis is just being completed and that the final child in the study will reach age 6—the last follow-up point—in 2010.

Dr. Meador has received research support from GlaxoSmithKline Inc., UCB SA, Eisai Co., Myriad Genetics Inc., NeuroPace Inc., and SAM Technology Inc. His fellow researchers also disclosed financial or other relationships to drug companies. ■

Severe Lacerations May Harm Postpartum Sexual Function

SAVANNAH, GA. — Women who have received lacerations requiring sutures as a result of childbirth might have poorer sexual function post partum than women who did not, according to data from questionnaires completed by 326 postpartum women.

Dr. Rebecca Rogers of the University of New Mexico, Albuquerque, presented study results in a poster session at the annual meeting of the Society of Gynecologic Surgeons. She and her colleagues followed 576 low-risk pregnant women who were cared for by midwives between 2005 and 2007. The women's cases were classified as minor or major trauma. Minor trauma was defined as no trauma or first-degree perineal, labial, periurethral, or clitoral lacerations. Major trauma was defined as second-, third-, or fourth-degree lacerations or any trauma requiring suturing. Women who had an episiotomy or who required operative delivery were excluded.

At follow-up, the women were asked if they had been sexually active since the birth. The 326 women who answered yes were asked to complete the Intimate Relationship Scale, a 12-item questionnaire designed to measure postpartum sexual function.

Of these women, 273 reported being sexually active at 3 months post partum. The majority of the women sustained some type of trauma, with only 16% delivering intact. Of those with trauma, most had minor trauma (70%). Women in the two groups differed by parity, length of active pushing, and education. Intimate Relationship Scale scores were not significantly different between women with major and minor trauma—36 vs. 33. However, women requiring sutures had significantly lower scores (mean 31) than did women who did not (mean 35.5) after adjusting for parity, length of pushing, and education.

Dr. Rogers disclosed that she is a speaker and investigator for Pfizer Inc. The meeting was jointly sponsored by the American College of Surgeons.

—Kerri Wachter

DRUGS, PREGNANCY, AND LACTATION

Antidepressants and Neonatal Withdrawal Symptoms

Poor adaptation syndrome in newborns exposed in late pregnancy to a selective serotonin reuptake inhibitor (SSRI) or selective norepinephrine reuptake inhibitor (SNRI)—with symptoms such as jitteriness, difficulty feeding, and being inconsolable—were first described several years ago.

The most unusual feature of this syndrome that has not been described in babies experiencing opioid or benzodiazepine withdrawal is respiratory distress, often with need for respiratory support.

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These symptoms were present in about 20% of newborns exposed to an SSRI or SNRI late in pregnancy in a series of cases we studied.

The good news is that those symptoms resolved in these babies, usually within several days; most were treated with sedation, after which they did well.

We systematically reviewed all published reports of neonatal discontinuation syndrome following exposure to antidepressants in late pregnancy and estimated that between 10% and 30% of babies exposed in utero to an SSRI or SNRI in late pregnancy experienced some signs of withdrawal (CMAJ 2005;172:1457-9).

Because adults who stop these drugs abruptly can experience typical withdrawal symptoms—nervousness, unrest, tremors, insomnia, and even seizures—it makes biologic sense that a newborn may develop withdrawal symptoms after exposure in utero.

Although it often has been assumed that these symptoms are manifestations of withdrawal, they could in some cases be the signs of toxicity of these drugs—serotonergic syndrome—which in neonates are indistinguishable from those described in withdrawal.

Considering what we know about the pharmacokinetics of the SSRIs and SNRIs, and what we know from a few studies that measured drug levels in newborns exposed in late pregnancy, it is highly likely that most observed cases represent genuine withdrawal.

However, one published case report from London, Ont., describes a baby with poor adaptation symptoms, whose mother was taking paroxetine during her pregnancy. Toxic levels of paroxetine were detected in the baby, whose symptoms resolved once the levels dropped below toxic levels (Ther. Drug Monit. 2006;28:5-7).

Differentiating between toxicity and withdrawal may therefore be important. Based on the same pharmacologic rationale behind the treatment of newborns in opiate withdrawal with small doses of narcotics, it would make sense to treat the baby with antidepressant withdrawal symptoms with small amounts of the antidepressant.

But if there is a chance that some cases are due to toxic drug levels, one has to be careful with this approach.

The only way to determine if a baby is experiencing withdrawal or toxicity is with therapeutic drug monitoring, which currently is not practiced in newborns anywhere, but may be in the future.

A European report of a baby exposed to the SNRI venlafaxine (Effexor) in late pregnancy, whose symptoms resolved after receiving a small dose of the drug, strengthened the concept that this might be a beneficial approach to treating neonatal withdrawal symptoms.

The Food and Drug Administration and Canadian authorities responded to reports of neonatal withdrawal syndrome with suggestions that physicians may consider tapering these antidepressants during the third trimester, which is included in the U.S. labels of these drugs.

This is unfortunate, because the best predictor of postpartum depression is depression in late pregnancy. Up to 20% of women may be diagnosed with depression during pregnancy and may need treatment with an antidepressant.

There is a wide consensus among psychiatrists and experts in our field that stopping treatment late in pregnancy is not necessarily the ideal approach and that women with depression responsive to SSRIs or SNRIs should be properly treated, especially since the neonatal withdrawal syndrome is self-limited.

Exposure to an SSRI or SNRI late in pregnancy should be considered a possible cause in newborns with symptoms consistent with withdrawal. When symptoms of respiratory distress are present, hyaline membrane disease, aspiration, infections, cardiac malformations, and other possible causes of the symptoms need to be ruled out.

My colleagues and I at Motherisk strongly believe that if a new mother is being treated with an SSRI or SNRI for depression, discharging her and her newborn within the regular 24 hours is not ideal. Motherisk recommends that babies whose mothers were treated with antidepressants be monitored closely for more than 24-48 hours after birth, and we are working toward developing practice guidelines on discharge recommendations for women and for their babies who were exposed in utero to antidepressants.

Currently, there are no official protocols on how to manage babies with these withdrawal symptoms, and neonates are most commonly managed with phenobarbital, which, after many years of use in this age group, has a strong safety record.

In future studies, we hope to define the role of therapeutic drug monitoring in this situation, and whether treatment with low doses of the SSRI or SNRI would be safe and effective in severe cases.

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