Diabetes Boosts Risk Of Atrial Septal Defect

BY MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO — Women with either gestational or established diabetes were much more likely to deliver an infant with an atrial septal defect than were those with normal glucose control, based on the results of a retrospective, case control study that included almost 5,000 women.

Women with established diabetes before they became pregnant were nearly 11-fold more likely to give birth to a child with an atrial septal defect (ASD), compared with women without diabetes, Dr. Creighton W. Don and his associates reported in a poster at the annual scientific sessions of the American Heart Association. Maternal diabetes was previously linked to other types of congenital defects in newborns, but the relationship of ASD with maternal diabetes had not been previously well studied, said Dr. Don, a cardiologist at the University of Washington, Seattle, and his coinvestigators.

They used January 1987–December 2005 birth certificate–hospital discharge data from all nonfederal hospitals in the Comprehensive Hospital Abstract Reporting System in Washington state. Cases were live-born singleton infants diagnosed with ASD. Controls were infants born without ASD in the same year.

The incidence of ASD reports in hospitals from eastern Washington seemed unusually high, so those hospitals were excluded and the analysis was limited to hospitals in western Washington. The analysis also excluded infants born at less than 32 weeks' gestation or less than 2,500 g. This left about 800 cases and 4,000 control infants who were included in a logistic regression analysis. The analysis controlled for several variables, including gestational age, birth weight, maternal age, maternal body mass index, race, and hospital location.

The analysis showed that women with established diabetes were 10.6-fold more likely to give birth to an infant with an ASD than were mothers without diabetes, and that mothers who developed gestational diabetes were 3-fold more likely to have a child with ASD. The differences between the case and control rates for both subgroups were statistically significant.

Other factors linked with significant increases in ASD were non-Hispanic black race, which raised the risk 3.9-fold, and maternal age of 35 years or older, which raised the risk 2.5-fold. ■

Neuraxial Analgesia Superior In External Cephalic Version

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Signs of fetal well-being returned more rapidly after external cephalic version in 47 women given combined spinal-epidural analgesia, compared with 48 women given systemic opioids in a randomized study.

Neuraxial analgesia has been shown in previous studies to reduce pain from external cephalic version and to improve maternal satisfaction, compared with systemic opioids, but the fetal heart rate effects of the two types of analgesia have not been compared before the current study, Dr. John T. Sullivan and associates reported in a poster presentation at the annual meeting of the American Society of Anesthesiologists.

As part of a larger study on the success of external cephalic version using different analgesia techniques, pregnant women with breech presentation were randomized to combined spinal-epidural analgesia using intrathecal bupivacaine 2.5 mg plus 15 mcg of fentanyl, or to intravenous systemic opioid analgesia using 50 mcg fentanyl. A perinatologist blinded to assignments evaluated fetal heart rate patterns for 30 minutes before and for 60 minutes after external cephalic version.

No significant differences were seen between groups in preprocedural and postprocedural baseline fetal heart rates, the degree of heart rate variability, the number of accelerations, or the number and type of decelerations, said Dr. Sullivan, associate professor of anesthesiology, Northwestern University, Chicago.

A reactive fetal heart rate after external cephalic version is a sign of fetal well-being, so investigators assessed the time to reactivity from initiation of analgesia to the development of two 15-beat accelerations (of 15 seconds duration) occurring within 20 minutes of each other.

The median time to reactivity in the combined spinal-epidural group was 13 minutes, significantly shorter than the median 39 minutes in the systemic opioid group.

One patient in each group underwent cesarean delivery immediately after external cephalic version for nonreassuring fetal heart rate patterns.

"Combined spinal-epidural analgesia for external cephalic version has no discernible deleterious impact on fetal heart rate pattern as compared with systemic opioid analgesia," Dr. Sullivan and his associates concluded. "Furthermore, it results in a more rapid return of a reactive fetal heart rate tracing. Therefore, combined spinal epidural may provide more immediate reassurance of fetal well-being following external cephalic version." ■

DRUGS, PREGNANCY, AND LACTATION

Increasing Folic Acid Supplementation

BY GIDEON KOREN, M.D.

The Society of Obstetricians and Gynecologists of Canada has new guidelines on folic acid supplementation in pregnant women, recommending prenatal vitamins that include 5 mg of folate in certain patients. Unless clinicians can ensure excellent daily compliance with the typical prenatal vitamin containing 0.8-1.1 mg of folate, the society recommends this higher folate dose during pregnancy.

The basis of the new recommendation is evidence indicating that compliance with prenatal vitamins is not ideal, and as a result, prevention of neural tube defects with folate supplementation is suboptimal.

The current recommendation in the United States and Canada is that women of reproductive age consume at least 400 mcg of folic acid/day in a prenatal multivitamin, foods fortified with folic acid, or both to reduce their risk of having a baby with a neural tube defect (NTD) such as spina bifida, anencephaly, and others. The amount of folic acid currently recommended for women who have already had a child with an NTD is 4 mg/day.

The recommendation for folic acid supplementation prenatally and during pregnancy was formed in the early 1990s. Subsequent fortification of enriched cereal grain products in 1998 in North America has had a marked impact on the rate of NTDs over the last decade. However, questions have been raised about whether the folic acid dose included in prenatal vitamins is adequate to prevent NTDs.

For example, in a report published in 2001, using data from studies correlating the folic acid supplementation and the associated serum folate concentrations, and a large cohort study of the NTD risk based on serum folate, the authors determined that 5 mg of folic acid per day would prevent almost 90% of women from having a baby with an NTD. Nicholas Wald and his colleagues concluded that the currently recommended dose would protect only part of the population from NTDs, and recommended that women planning to become pregnant should take a 5-mg dose of folic acid per day (Lancet 2001;358:2069-73).

Corroborating this calculation were findings from a study of a large group of reproductive-aged Ontario women aged 15-45 years in 2005 and 2006, whose folic acid intake was unknown. We measured erythrocyte folate levels and determined that 40% of these women did not achieve the 900-nmol level needed to protect against NTDs, despite the fortification of flour and the recommendation that all women of reproductive age consume 400 mcg of folic acid daily. These findings, published in an abstract last year, strengthened our belief that the 5-mg recommendation is probably correct.

One of the two main arguments against an increase in folic acid is that an excess in the diet can mask pernicious anemia, caused by vitamin B_{12} deficiency in older people. However, since flour was fortified, there has been no evidence of an increasing problem with pernicious anemia.

The second major concern is the potential effect of folate in increasing the risk of some cancers, which includes evidence that folic acid supplementation may increase the growth or number of colorectal polyps. However, the bulk of data indicate that an adequate folic acid level decreases the risk of about 10 cancers, including colon cancer. Clearly, if a risk of cancer exists, it would be associated with long-term exposure and would be a potential concern for people who consume a large amount of folic acid in flour-based products, not pregnant women who take an increased amount for a limited period of time.

In a recently completed clinical study of pregnant women at the Motherisk Program, we found that despite the women being under supervision, the compliance rate with prenatal multivitamins was low—an average of 53%-58%, ranging from 0% to 100%. The likelihood that a substantial proportion of women prescribed a prenatal vitamin containing 1 mg of folic acid per tablet will miss a few days every week strengthens the recommendation that the inclusion of a higher dose of folic acid in prenatal vitamins would be beneficial for women who may not be entirely compliant with their daily vitamin intake, and that many more women, with less than ideal compliance, would have protective folate levels if the supplement contained 5 mg/day.

One prenatal vitamin tablet typically contains 1 mg of folic acid. A Canadian manufacturer recently introduced a prenatal vitamin containing 5 mg of folic acid, which was approved by the Canadian authorities in response to our conviction that such a product is necessary, and other companies may follow.

Now is the time, we believe, to move forward with this new guideline, and we hope that the American College of Obstetricians and Gynecologists will join the initiative.

DR. KOREN is a professor of pediatrics, pharmacology, pharmacy, medicine, and medical genetics at the University of Toronto. He heads the Research Leadership in Better Pharmacotherapy During Pregnancy and Lactation at the Hospital for Sick Children, Toronto, where he is director of the Motherisk Program, a teratogen information service (www.motherisk.org). He is also the Ivey Chair in Molecular Toxicology at the University of Western Ontario.