C-Section Ups Placenta Previa, Abruption Risk

BY KATE JOHNSON
Montreal Bureau

TORONTO — Women whose first babies are delivered by cesarean section face an elevated risk of placenta previa and placental abruption in their second pregnancies. And with two previous cesarean deliveries the risk of placenta previa is increased further in the third pregnancy, according to a study by Dr. Darios Getahun of the Robert Wood Johnson Medical School in New Brunswick, N.J., and his colleagues.

The study, which was recently published (Obstet. Gynecol. 2006;107:771-8), was presented as a poster at the annual meeting of the Society for Gynecologic Investigation.

"Although cesarean section has previously been reported as a risk factor for placenta previa, it has not been previously associated with abruption," Dr. Getahun said in an interview at the meeting. "Cesarean section causes scarring of the uterine wall, with the result that placentation may not be optimal. That's why it may be leading to abruption," he explained.

The study included a cohort of women from the Missouri longitudinally linked live birth and fetal death data files. Singleton births were analyzed for 156,475 women whose first two consecutive births occurred within the study period of 1989-1997, and 31,102 women whose first three consecutive births occurred within that period.

Among 40,472 women whose first delivery was by cesarean section, the relative risk of placenta previa was 1.5, and that of placental abruption was 1.3 in the second pregnancy, compared with women whose first delivery was vaginal.

There was a dose response noted for the risk of placenta previa, but not for placental abruption risk. Therefore, when both the first and second deliveries were by cesarean section, the risk of placenta previa doubled in the third pregnancy, but the risk of placental abruption did not increase further, compared with women whose first two deliveries were vaginal.

The interval between pregnancies also was analyzed, and the study found that for cesarean deliveries, but not vaginal ones, an interval of less than 1 year was associated with a relative risk of 1.7 for placenta previa and 1.5 for placental abruption. ■

Ultrasound's Value for Diagnosing Abnormal Placentation Confirmed

BY SHARON WORCESTER
Southeast Bureau

MIAMI BEACH — Pelvic ultrasound is accurate for ruling out placenta accreta, and should be used as the primary screening tool in patients at high risk for this condition, Dr. Carri Warshak said at the annual meeting of the Society for Maternal-Fetal Medicine.

Magnetic resonance imaging also should be considered in the evaluation of all suspected cases, she added.

A historical cohort study of 433 patients with placenta previa who underwent ultrasound showed that this screening modality accurately predicted placenta accreta (which for the purposes of this study also included placenta increta and percreta) in 25 of the 32 women whose diagnosis was confirmed by pathologic examination, for a sensitivity of 0.78. Ultrasound ruled out the condition in 397 of 401 patients, for a specificity of 0.99; MRI ruled out the condition in the remaining 4 patients, said Dr. Warshak of the University of California, San Diego.

Of an additional 58 women who were referred for MRI based on equivocal ultrasound findings, 39 were shown on pathologic examination to have placenta accreta. MRI accurately predicted the condition in 35 of the 39 patients for a sensitivity of 0.90, and ruled out the condition in the remaining 19 patients for a specificity of 1.

Information for the study was obtained from a perinatal database for patients screened by ultrasound between January 2000 and June 2005 and for patients screened by MRI between January 1992 and June 2005.

The 10-fold increase in the incidence of abnormal placentation is largely due to the increased cesarean section rate; about 9% of pregnancies are affected.

The findings are important because they confirm the accuracy of ultrasound and MRI for detecting a condition that requires accurate prenatal diagnosis for optimal management, she said.

Furthermore, the incidence of abnormal placentation has increased 10-fold over the past decade, largely due to the increased cesarean section rate. An estimated 9% of pregnancies are affected, she noted.

The findings confirm those from the three largest studies of ultrasound diagnosis for placenta accreta; pooled data from those studies and the current study show pelvic ultrasound is 81% sensitive and 98% specific for diagnosis, she said.

MRI has been less well studied, and results have been conflicting, but the findings of this study suggest it has an important role in optimizing diagnostic accuracy, particularly in patients with equivocal findings on ultrasound, she concluded. ■

DRUGS, PREGNANCY, AND LACTATION

Gastrointestinal Agents: Part III

BY GERALD G. BRIGGS, B.PHARM.

The final part of this series covers the use of infliximab, anticholinergics/antispasmodics, gastrointestinal stimulants, and anorectal preparations in pregnant and lactating women.

▶ **Infliximab (Remicade):** Infliximab is a monoclonal antibody used to treat severe Crohn's disease and autoimmune diseases such as ankylosing spondylitis, rheumatoid arthritis, and psoriasis. It binds to and inhibits human tumor necrosis factor–α (TNF-α). Animal reproduction studies have not been conducted with the agent because it does not react with animal TNF-α. Human pregnancy exposure consists of about 30 cases, which are limited to case reports and observational studies. The drug does not appear to represent a significant risk for developmental toxicity. Still, if possible, the best course is to avoid its use in pregnancy. If pregnancy exposure does occur, health care providers are encouraged to register these patients in the Organization of Teratology Information Specialists (OTIS) Autoimmune Diseases in Pregnancy study by calling the toll-free number, 877-311-8972.

▶ **Anticholinergics/antispasmodics:** These agents have been used for years for peptic ulcer and functional GI disorders such as diarrhea, hypermotility, neurogenic colon, irritable bowel syndrome, ulcerative colitis, and biliary tract spasm. The agents—available under numerous trade names—include atropine, belladonna, dicyclomine, glycopyrrolate, L-hyoscyamine, mepenzolate, methscopolamine, propantheline, and scopolamine. Only atropine, scopolamine, and dicyclomine have sufficient data in pregnancy. There are no reports suggesting that these agents cause birth defects. However, an excessive dose of scopolamine in labor has been associated with newborn toxicity. The other drugs are also probably low risk, but cannot be classified as such because of the very limited or complete lack of human pregnancy experience. However, anticholinergic combinations formulated with phenobarbital or other sedatives should be avoided in pregnancy and lactation. Although the data are very limited, all anticholinergics, except dicyclomine, appear to be compatible with breast-feeding. Dicyclomine is concentrated in milk and has been associated with apnea in one nursing infant.

▶ **GI stimulants:** Dexpanthenol (Ilopan) is given by intramuscular injection to prevent paralytic ileus after abdominal surgery. Although the drug has been promoted for constipation in pregnant women, there are no reports of its use or studies in pregnant or lactating animals or humans. Thus, the drug should not be given during pregnancy or breast-feeding.

In contrast, another GI stimulant, metoclopramide (Reglan, Maxolon), has substantial human pregnancy experience, primarily as an antiemetic. Although it is considered compatible with pregnancy, its use during breast-feeding is controversial. It has been successfully used as a lactation stimulant at doses of 20-45 mg/day. The drug is excreted into milk, but the estimated dose ingested by a nursing infant from milk is much lower than the therapeutic infant dose. However, mild intestinal discomfort has been observed in two infants. Because of its dopaminergic blocking action, the American Academy of Pediatrics classifies metoclopramide as a drug of potential concern during breast-feeding.

▶ **Anorectal preparations:** These include a large group of agents that are available in various topical formulations such as creams, ointments, foams, lotions, tissues and pads, and suppositories. With the exception of the hydrocortisone products, all are available over the counter, so you might not know that your patient is using them unless a careful history is taken. The OTC preparations are formulated with low concentrations of various drug mixtures, such as local anesthetics, vasoconstrictors, astringents, antiseptics, emollients/protectants, counterirritants, keratolytics, and wound healing agents. Only a few of these products and drugs have been studied in human pregnancy or lactation, but these preparations are used for their local effects and clinically significant systemic levels are not expected.

About 26% of the corticosteroid is absorbed from hydrocortisone suppositories, but the maximum strength of these products is only 30 mg, so the amount reaching the circulation is clinically insignificant. Therefore, at recommended doses, the use of anorectal preparations during pregnancy or breast-feeding can be considered low risk.

Of the drugs covered in this series, misoprostol and tetracycline cause structural defects, castor oil can induce labor, and mesalamine-containing agents and dicyclomine have caused toxicity in nursing infants. Most GI agents are safe in pregnancy and lactation, but many have insufficient data to judge their risk.

MR. BRIGGS *is a pharmacist clinical specialist, Women's Pavilion, Miller Children's Hospital, Long Beach, Calif.; clinical professor of pharmacy, University of California, San Francisco; and adjunct professor of pharmacy, University of Southern California, Los Angeles.*