Postcesarean Oxytocin Boluses of Low Benefit

BY KATE JOHNSON
Montreal Bureau

BANFF, ALTA. — The routine practice of giving oxytocin boluses to reduce the risk of postpartum hemorrhage appears to be of limited benefit even in high-risk patients after cesarean section, as long as an appropriate oxytocin infusion is given, according to the first randomized, placebo-controlled trial of the practice, said Dr. Kylie King from Maitland (Australia) Hospital.

The practice of administering oxytocin boluses has recently come under scrutiny. "Although the adverse hemodynamic effects [of oxytocin boluses] are well documented, one recently reported death associated with a 10-U bolus in the U.K. has prompted a change in dose from 10 to 5 units given slowly," she said at the annual meeting of the Society for Obstetric Anesthesia and Perinatology. "This begs the question: Is a bolus necessary? Is 5 U the right dose? How slowly should it be given? And might an infusion be sufficient?"

Her study, which was conducted at British Columbia Women's Hospital in Vancouver, compared 143 subjects: 70 received an intravenous 5-U bolus of oxytocin, and 73 received normal saline, given over 30 seconds following cesarean section and cord clamping.

Both groups also received an identical infusion of 40 U of oxytocin in 500 mL of normal saline over 30 minutes, followed by 20 U of oxytocin in 1 L of saline over the next 8 hours.

"Our hypothesis was that the bolus, given in addition to the infusion, would reduce the need for additional drugs to contract the uterus," said Dr. King. Because previous studies have suggested that oxytocin may have little or no effect in a low-risk population, study subjects were specifically selected as being high risk for postpartum hemorrhage. "Multiple gestations and macrosomia were the most common risk factors."

Overall, 53% of the cesarean sections were elective, with 47% classified as emergency procedures. The need for additional uterotonics was high—between 30% and 40% overall—confirming that the population was indeed high risk, but need for more uterotonics was similar in both groups as assessed by a surgeon who was blinded to the patients' randomization. In addition, there was no difference between groups in the secondary outcomes of estimated blood loss, need for blood transfusion or hypotension.

"Even in a high-risk group, a 5-U bolus is of limited additional benefit provided that an adequate infusion is given," concluded Dr. King. "Getting a stronger initial contraction at 1 minute doesn't reduce the need for additional uterotonics over the next 24 hours." ■

Ultralight Epidural Works as Both Infusion, Patient-Controlled Bolus

BANFF, ALTA. — Ultralight doses of epidural analgesia given either as a continuous infusion or as patient-controlled boluses appear to result in comparable pain and Apgar scores as well as medication usage, according to the preliminary results of an ongoing study.

"Our numbers are very small right now, but as soon as we get more I am sure we will see a statistical difference between the two in terms of patient satisfaction," predicted Dr. Maya Suresh, chief of obstetric anesthesiology at Baylor College of Medicine, Houston. "I think patient-controlled epidural analgesia [PCEA] is advantageous to the patient because she is in control of her own pain. And, if you are not called frequently to intervene or to trouble-shoot that also adds to the provider's satisfaction," she said in an interview.

The study, presented at the annual meeting of the Society for Obstetric Anesthesia and Perinatology, is the first to compare outcomes using an ultralight epidural solution of 0.0625% bupivacaine plus 2 mcg/mL fentanyl. Fifteen nulliparous parturients requesting epidural were randomized to the continuous-infusion epidural analgesia (CIEA) arm and received the solution at a dose of 14 L/hr. Another 15 women were randomized to PCEA and received an 8-mL/hr background infusion of the same solution with the option for 5-mL boluses on demand at a 5-minute lockout interval, and an hourly limit of 26 mL, reported Dr. LaToya Mason from the same institution, who presented the study.

There was no statistically significant difference between the groups in umbilical artery pH scores, Apgar scores, or pain scores, said Dr. Mason. All patients had spontaneous vaginal deliveries except for four who had cesareans (two in each group).

—Kate Johnson

DRUGS, PREGNANCY, AND LACTATION

Hypnotic Sleep Aids

BY GERALD G. BRIGGS, B.PHARM, FCCP

The physical discomforts of pregnancy that are induced by the surge of progesterone and the expanding uterus will result in nearly universal sleep deprivation in pregnancy. An increased need to urinate, nausea and vomiting, heartburn, difficulty in finding a comfortable sleeping position, and, as the pregnancy progresses, the kicking and movement of the fetus, all conspire against a good night's sleep.

Prescribing sleeping medications in pregnancy may not be the best solution because long-term use can lead to habituation in the woman, as well as in her fetus. However, patients will frequently seek drug therapy to help them sleep, so it is essential to have adequate knowledge of what is relatively safe and what is not.

Hypnotics can be categorized into five subclasses: barbiturates, benzodiazepines, nonbenzodiazepines, over-the-counter antihistamines, and herbal and natural products.

► **Oral barbiturates.** In this group are aprobarbital (pregnancy risk factor C) (Alurate); pentobarbital (D) (Nembutal); and secobarbital (D) (Seconal). Developmental toxicity has not been proven, but more studies are needed regarding the potential for behavioral toxicity after long-term in utero exposure. Their long elimination half-lives (24, 22-50, and 28 hours, respectively) can cause prolonged sedation, or hangover. They are controlled substances with potential for abuse, which makes them more difficult to prescribe. Although they are excreted into milk in low amounts, they can be classified as compatible with breast-feeding.

► **Benzodiazepines.** Estazolam (ProSom), flurazepam (Dalmane), quazepam (Doral), and temazepam (Restoril) are in this category. Data on the use of these agents in pregnancy are very limited. Although there has been no proven association between any of these agents and birth defects, they probably have effects on the embryo or fetus similar to diazepam (Valium), including neonatal motor depression (floppy infant syndrome) and/or withdrawal when used in the third trimester. Moreover, all four agents are categorized as contraindicated (risk factor X) by their manufacturers, so they should not be prescribed. Small amounts of quazepam and temazepam are excreted into milk, and the other two agents are most likely in milk as well. Occasional dosing during breast-feeding is probably safe, but the long-term effects on a nursing infant are unknown.

► **Nonbenzodiazepines.** The five drugs in this category are chloral hydrate (for example, Somnote), ramelteon (Rozerem), zaleplon (Sonata), and low-dose (25-75 mg) trazodone (Desyrel), all risk factor C, and zolpidem (Ambien), which is risk factor B. The use for sleep of the antidepressant trazodone is off label, but the drug is sometimes combined with other antidepressants for this purpose. As with the benzodiazepines, the human pregnancy data are very limited or nonexistent. There are no animal data for chloral hydrate, an old product that is now rarely used, but animal data on the other nonbenzodiazepines suggest low risk in pregnancy. Nevertheless, as with most drugs, the best course is to avoid them in the first trimester. Occasional use during the second and third trimesters probably is low risk, but long-term use (more than 4 weeks) should be avoided. Although small amounts of these drugs are excreted into milk, occasional, short-term use probably is compatible with breast-feeding.

► **OTC antihistamines.** There are two in this category, diphenhydramine (for example, Benadryl) and doxylamine (Unisom Nighttime Sleep Aid). Diphenhydramine (risk factor B) is safe throughout gestation, as is doxylamine (risk factor A). A major advantage of these antihistamines is that both have antiemetic properties that can reduce pregnancy-induced nausea and vomiting. If pyridoxine (vitamin B_6) is taken with doxylamine, the combination is the antiemetic most frequently studied in pregnancy. There is little or no experience with these agents during lactation. Although some manufacturers consider them contraindicated during breast-feeding, the lack of toxicity reports suggests that these antihistamines probably are low risk for full-term nursing infants.

► **Natural products.** Although about 50 natural products are or have been advocated for sleep, few have enough data to recommend their use in pregnancy or lactation. Moreover, the content and purity of natural products are generally unregulated.

Low risk: With these qualifications, the agents that appear to be low risk are ginseng (not Siberian), honey, nutmeg, oats, and St. John's wort. It should be noted, though, that ginseng potentially can cause hypertension and hypoglycemia.

Avoid: Natural products that should be avoided in pregnancy and lactation are American hellebore, butterbur or other petasites, kava, marijuana, melatonin (available only as an orphan drug in the United States), mugwort, passion flower, quassia, rauwolfia, Siberian ginseng, taumelloolch, tulip tree, and valerian.

A nonpharmacologic approach is the best and safest course for pregnant patients with insomnia. If medications are required, occasional, short-term use is recommended; one of the OTC antihistamines is probably the best choice. A nonbenzodiazepine agent, such as zolpidem would be my second choice. For more information, clinicians can visit www.babycenter.com, a Web site frequently visited by women to obtain information about their pregnancies, including tips on sleeping well.

MR. BRIGGS *is 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. He is also a fellow of the American College of Clinical Pharmacy and coauthor of the reference book "Drugs in Pregnancy and Lactation."*