Pregnancy Appears to Be Safe After Recent Bariatric Surgery

BY JEFF EVANS
Senior Writer

San Francisco — Pregnancy soon after bariatric surgery does not appear to pose safety concerns for the mother or newborn, Dr. Tuoc N. Dao reported at the annual meeting of the American Society for Bariatric Surgery.

Surgeons have generally recommended that bariatric surgery patients should not become pregnant until 12-18 months after the procedure because of a perceived risk to the fetus or the woman during the period of large weight loss and limited calorie and nutrient intake following the surgery, said Dr. Dao, a surgical resident at Baylor University Medical Center at Dallas.

Although her review of 24 patients indicated that "the desire for pregnancy should not be a deterrent for Roux-en-Y gastric bypass as a weight-loss procedure," Dr. Dao and her colleagues continue to recommend that most bariatric surgery patients wait 12-18 months before becoming pregnant "due to the psychological component of trying to undergo all of these changes at one time. Trying to lose weight and deal with a pregnancy at the same time, I think, would be too much for people."

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Several previous studies have not reported any major adverse events or outcomes in women who became pregnant after bariatric surgery.

In a study of 298 deliveries, no adverse perinatal outcomes were reported in women who had restrictive or malabsorptive surgery, although Roux-en-Y gastric bypass (RYGB) was associated with an increased risk of premature rupture of membranes, labor induction, and fetal macrosomia (Am. J. Obstet. Gynecol. 2004;190:1335-40).

A separate review of 18 pregnancies after gastric bypass showed few metabolic problems or deficiencies in vitamin B_{12} or iron (South. Med. J. 1989;82:1319-20).

In another group of 46 deliveries, four of seven preterm infants were born to mothers who became pregnant within 16 months of their surgery. Pregnancy was safe outside of that time period (Am. Surg. 1982;48:363-5).

Pregnancy during the period of rapid weight loss immediately after surgery can cause deficiencies in iron, folate, calcium, and vitamin B_{12}.

It also has been questioned whether women will be able to lose additional weight post partum during the early postoperative phase.

Fetal and maternal deaths have been reported in a few cases of postoperative small bowel herniations and ischemia, but other reports have recorded good outcomes with early detection and treatment of this complication, Dr. Dao said.

In her review of 2,532 patients who underwent RYGB at Baylor during 2001-2005, 24 became pregnant within 1 year after the surgery.

These patients were 32 years old with a body mass index of 49 kg/m^2 at the time of surgery.

At the time of delivery, the women were 34 years old and had gained a mean of 0.3 pounds during pregnancy, although this varied widely from losing 70 pounds to gaining 45 pounds.

The patients' mean body mass index dropped from 34 kg/m^2 when they became pregnant to 32 kg/m^2 at a mean follow-up of 13 months after delivery. At follow-up after delivery, they had lost an average of 76% of their excess weight.

Only one patient failed to sustain their excess weight loss.

The 24 women had 26 pregnancies, 2 of which were early miscarriages in women who soon became pregnant again and carried to term. Of three other miscarriages, two occurred in the first trimester and one at a gestational age of 20 weeks.

Another patient had an ectopic pregnancy.

One patient had mild iron deficiency during pregnancy that resolved with iron supplementation.

One patient had symptomatic cholelithiasis and underwent laparoscopic cholecystectomy after the delivery of her baby.

An internal hernia in one patient was detected early and repaired without any incident.

Another patient with a gastrogastric fistula was treated conservatively until her delivery.

Two patients had preterm labor. One patient had preeclampsia and one had mild hypertension that was much improved since her last pregnancy before bariatric surgery.

The 21 babies (including one set of twins) had an average birth weight of 2,874 g. Three neonates, including the twins, had a low birth weight (less than 2,500 g). One infant had intrauterine growth restriction (born to the mother with an internal hernia).

Another infant had intrauterine growth restriction plus a low birth weight (born to the mother with a gastrogastric fistula).

No infants had any congenital or developmental defects.

In five of the women who had pregnancies before their RYGB surgery, there were fewer instances of diabetes, hypertension, and complications during postsurgery pregnancies than in those that occurred before the operation.

Dr. Dao did not know how many of the other patients who received RYGB in the cohort were lost to follow-up, but she said that patients who report pregnancy at clinical visits or on follow-up surveys are interviewed to gather information. ■

Drugs, Pregnancy, and Lactation

Morphine Poisoning in Infants

BY GIDEON KOREN, M.D.

Last month, my associates and I published a case report of an apparently healthy full-term newborn who died at 13 days from morphine poisoning. The cause was determined to be a genetic polymorphism in the mother, which made her an ultrarapid metabolizer of codeine to morphine, via cytochrome P450 2D6 (CYP2D6), increasing the formation of morphine from codeine.

The coroner investigating the death contacted us after detecting an extremely high blood morphine concentration in the baby because the mother had been taking codeine for episiotomy pain and had been breast-feeding. We suspected the mother might have the polymorphism, identified over the last few years in a subgroup in the general population. Genetic testing of the mother, father, baby, and extended family members identified the mother (and maternal grandmother) as ultrarapid CYP2D6 metabolizers, but not the baby. An analysis of frozen breast milk detected a morphine level that was far higher than described in the literature: 87 ng/mL vs. the typical concentration of 1.9-20.5 ng/mL associated with maternal doses of 60 mg of codeine every 6 hours (Lancet 2006;368:704).

This is a case report, but potentially an important one because, overall, there has been the perception that codeine is safe for the baby during breast-feeding. The few studies that have evaluated breast milk in women taking codeine have not found high morphine levels, and the American Academy of Pediatrics and other authorities list codeine as compatible with breast-feeding. In most cases, this remains true. But considering the number of cesarean births in North America, and the common practice of prescribing codeine for pain after childbirth with episiotomy or by cesarean section, a large number of babies are at potential risk. The prevalence of the ultrarapid metabolizer status ranges from 1% in Denmark and Finland to 10% in Greece and Portugal to 29% in Ethiopia, the highest known prevalence.

Can we genotype all women before we prescribe codeine? Not at the present time because pharmacogenetic tests are not widely available. A genetic test is commercially available, but it is expensive and is currently not routinely performed. There are other options, each with pros and cons. Some people would recommend against giving women codeine in the postpartum period, but codeine is sometimes clearly needed for pain. For example, using a nonsteroidal anti-inflammatory drug and avoiding codeine when breast-feeding eliminates the risk of toxicity in the baby, but may not adequately control pain. Using a lower dose of codeine minimizes the potential toxicity to the baby, but may not provide sufficient pain control for the mother and the dose could still be too high if she is an ultrarapid metabolizer. Another option is to avoid breast-feeding while taking codeine, but then the baby would lose the benefits of breast-feeding.

In our case the mother took codeine until the child died at 13 days, which is longer than usual. This suggests that use for no more than 2-3 days is advisable. In retrospect, there were clinical signs hinting that the mother was an ultrarapid metabolizer: Despite being on a low dose of codeine, in combination with paracetamol, she was somnolent and constipated, and the dose had to be reduced on the second day of treatment. This raises a critical point for identifying such cases: Be alert for signs and symptoms in a patient that may indicate she is reacting to the drug more than would be expected based on the dose, including somnolence, sleepiness, dizziness, and constipation. These symptoms indicate that she may be an ultrarapid metabolizer. The metabolism to morphine by CYP2D6 is responsible for most of the analgesic and CNS depressant effects of codeine.

We have been asked why cases like this one have not been previously reported. I suspect such cases may not be as rare as we thought, but it is likely that not all the cases are as tragic because the mothers do not take codeine for as long a time. For example, in a paper we published more than a decade ago on outcomes in babies exposed to drugs in breast milk, 25 women reported taking codeine while breast-feeding, and in 5 cases their babies were described as being sleepy.

Eventually, this is the type of pharmacogenetic information everyone will be aware of and will have available when presenting for medical care. For now, we are conducting a large case-control pharmacogenetic study funded by Genome Canada on babies who were breast-fed while the mother was using codeine to better define the scope of this issue.

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