Prepregnancy Obesity Linked to Birth Defects

BY MARY ANN MOON
Contributing Writer

Maternal obesity before pregnancy significantly increased the risk for offspring with anorectal atresia, hypospadias, limb reduction defects, diaphragmatic hernia, and omphalocele in a large study.

D. Kim Waller, Ph.D., of the University of Texas School of Public Health, Houston, and her associates used data from the National Birth Defects Prevention Study to assess whether maternal weight affected risk for several categories of structural birth defects. This is the first study to report a link between maternal obesity and these five types of defects using sufficient sample sizes of 150 or more cases.

More than half of American women aged 20-39 years are estimated to be overweight (with a body mass index [kg/m^2] in a range greater than or equal to 25 up to less than 30), or obese (BMI greater than or equal to 30). A strong association between these conditions and higher fetal risk for spina bifida and heart defects has already been reported. However, "the potential relation between obesity and other birth defects remains less certain, as those studies that have examined a range of different birth defects did not have sufficient numbers of cases to generate precise odds ratios," Dr. Waller and her associates said.

The investigators analyzed data on 10,249 babies born with structural birth defects in eight states between 1997 and 2002, as well as 4,065 control subjects representative of the general population.

Maternal obesity was found to raise the risk for spina bifida and heart defects, confirming the findings of previous studies. It also significantly increased the risk for anorectal atresia, hypospadias, limb reduction defects, diaphragmatic hernia, and omphalocele, with odds ratios ranging from 1.3 to 1.6. Maternal obesity also carried a borderline increase in risk for cleft palate, the researchers said (Arch. Pediatr. Adolesc. Med. 2007;161:745-50).

Maternal overweight significantly increased the risk for heart defects, hypospadias, and omphalocele, and slightly raised the risk for craniosynostosis.

Unlike previous studies, this analysis failed to demonstrate an association between maternal obesity and anencephaly, hydrocephaly, or cleft lip. However, this finding may have been the result of chance, because the number of cases of these three birth defects was relatively low. ■

Routine Enema in First Stage of Labor May Prolong Delivery

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — Routine use of an enema during the first stage of labor significantly prolonged the time to delivery in a randomized trial conducted at the Carolinas Medical Center in Charlotte, N.C.

Although routine enemas have been abandoned in many hospitals, anecdotal beliefs persist that the procedure enhances uterine stimulation, makes for a "cleaner delivery," and reduces neonatal wound infections, Dr. Noellee T. Clarke said.

Labor and delivery nurses in some regions hold to the notion that enemas for this purpose are best administered "high and hot and a hell of a lot," she noted following the oral presentation of her study.

To see if enemas do reduce labor time, Dr. Clarke and coinvestigator Dr. Todd R. Jenkins conducted a trial that randomized 152 women in uncomplicated early labor at their institution either to undergo an enema or to have no enema on admission. At baseline, women in the two groups were similar in terms of parity, age, and other relevant variables.

Enemas were performed using a standard protocol (1 L water plus two packets of castile soap at a mean cervical dilatation of 3.6 cm). Mean time to delivery was 505 minutes in 75 women who received enemas, vs. 393 minutes in 77 women who did not receive an enema, for a highly statistically significant difference of 112 minutes.

Intrapartum infection rates were 12.3% among patients receiving enemas and 2.7% for those receiving no enema; however, this difference lost its significance when investigators controlled for differences in duration of membrane rupture.

No differences were seen between groups in epidural use, delivery mode, or presence of meconium, she said at the annual meeting of the American College of Obstetricians and Gynecologists.

Women who underwent a routine enema had less fecal soiling at delivery, observed in 8 of 75 (11%) in the enema group vs. 23 of 77 (30%) in the group that received no enema.

Dr. Clarke said the study results were accepted by some, but not all, labor and delivery nurses on her service. "I was unpopular a little bit," she said in response to a question following her presentation. ■

DRUGS, PREGNANCY, AND LACTATION

Yet More Reproductive Safety Data on SSRIs

BY LEE COHEN, M.D.

Over the last 5 years, several studies analyzing the reproductive safety of the selective serotonin reuptake inhibitors (SSRIs), individually and as a group, have been published in the United States and elsewhere. Earlier studies that failed to show an association between first-trimester exposure to SSRIs and an overall increased risk of major congenital malformations were typically small cohort studies; subsequent meta-analyses of the available cohort studies have also failed to show an increased risk, which has been reassuring.

The cohort study, which prospectively follows both exposed and unexposed people longitudinally, is the gold standard for evaluating the teratogenic potential of drugs. However, such a study is limited by the difficulty in enrolling enough exposed subjects to demonstrate a statistically significant difference between the two groups (which is particularly true for relatively rare outcomes that can easily be missed).

Recently, several large case-control studies have been published that questioned the safety of SSRIs with respect to teratogenic risk. Case-control studies identify cases of an outcome of interest, such as a certain birth defect, and analyze case and control groups of patients to determine if an association exists between various exposures and the outcome.

Such studies have included an analysis of records from a large managed care organization, which found an increased risk of heart defects in the babies of women who were prescribed paroxetine (Paxil) during pregnancy, compared with the babies of women prescribed other antidepressants during pregnancy. Another study, using data from the Swedish Medical Birth Registry, also found an increased risk of cardiac defects among infants with first-trimester exposure to paroxetine.

Two large case-control studies published in June represent the latest efforts to use large multicenter birth defect surveillance programs to refine our understanding of the reproductive safety of SSRIs. Based on their size, these studies might be expected to refine the risk estimate for congenital malformations following fetal exposure to SSRIs, but these investigations produced some divergent results.

The National Birth Defects Prevention Study compared 9,622 infants with birth defects with 4,092 control infants born in the United States from 1997 to 2003 and found no significant association between use of any SSRI from 1 month before to 3 months after conception and congenital heart defects or most other birth defects analyzed.

There was, however, a significantly increased risk for anencephaly (odds ratio 2.4), craniosynostosis (OR 2.5), and omphalocele (OR 2.8) associated with SSRI use in early pregnancy; these are birth defects that have not been associated with in utero exposure to SSRIs in previous studies. The relationship was particularly strong with paroxetine (N. Engl. J. Med. 2007;356:2684-92).

But no associations were identified between maternal SSRI use in early pregnancy and these three anomalies or congenital heart defects overall in the accompanying case-control study of 9,849 infants with birth defects and 5,860 infants with no birth defects enrolled in the Slone Epidemiology Center Birth Defects Study, at Boston University (N. Engl. J. Med. 2007;356:2675-83). However, there was a significant association between the use of sertraline (Zoloft) specifically and both omphalocele (odds ratio 5.7) and septal defects (2.0).There was also a significant association between paroxetine exposure and right-ventricular outflow tract obstruction defects (odds ratio of 3.3). It should be noted that the number of actual exposures in these studies to a specific SSRI was particularly small, fewer than 10 actual reported exposures.

Where do these two important studies leave the patient and the clinician? Despite the divergent findings, both studies suggest that the absolute risk of overall major congenital malformations or even particularly rare malformations is extremely small, as pointed out by the respective authors and the accompanying editorial (N. Engl. J. Med. 2007;356:2732-3). For example, the Slone study authors point out that the estimated prevalence of right-ventricular outflow tract obstruction defects is about 5.5 cases per 10,000 live births, so the risk of this defect would be only 0.2% if an SSRI increased the risk fourfold. It also has been noted that in such studies the search for numerous outcomes associated with potentially numerous exposures may result in a finding by chance.

Clinicians and patients deciding about treatment during pregnancy will need to continue to make decisions on a case by case basis, weighing the risks and benefits using the available, incomplete data on the relative risks of exposure to the medicine or to depression, and the patient's wishes.

In addition, clinicians and patients should consider that, while we have not yet absolutely quantified the risk of prenatal exposure of SSRIs (which might not be achievable), a critical finding influencing treatment decisions is that untreated depression during pregnancy dramatically increases risk for postpartum psychiatric relapse. In fact, perhaps nothing trumps the importance of sustaining maternal emotional well-being during pregnancy, even given the small absolute risks that may be associated with an individual SSRI during pregnancy.

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