ACOG Advises Against Paroxetine in Pregnancy

BY MARY ELLEN SCHNEIDER
New York Bureau

The American College of Obstetricians and Gynecologists is advising physicians to avoid prescribing the antidepressant paroxetine (Paxil) to pregnant women and women planning to become pregnant, because of a possible increased risk of congenital cardiac malformations.

The use of other selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors during pregnancy should be "individualized," ACOG recommended in a new opinion from its Committee on Obstetric Practice (Obstet. Gynecol. 2006;108:1601-4).

A number of studies on SSRI use in pregnancy have not shown an increased risk of major congenital malformations, ACOG reported, but data from two recent unpublished studies have signaled an increased risk of atrial and ventricular septal defects with first-trimester exposure to the SSRI paroxetine.

Last year, the Food and Drug Administration issued a public health advisory on paroxetine use in pregnancy, cautioning that the use of the drug during the first trimester could increase the risk for congenital malformations, particularly cardiac malformations. At the request of the FDA, the drug's manufacturer changed its pregnancy category from C to D, indicating that the drug has been found to have a harmful effect on human fetuses.

ACOG is also recommending that physicians consider fetal echocardiography for women who were exposed to paroxetine early in pregnancy.

But decisions about continuing treatment with other SSRIs and selective norepinephrine reuptake inhibitors may be more complicated. The ACOG committee opinion cited one study showing that women who discontinued antidepressants during pregnancy had a greater risk of depression relapse than those who continued on the drugs, whereas another study cited by the committee showed an increase in the risk of persistent pulmonary hypertension for newborns whose mothers took SSRIs after 20 weeks' gestation.

"The potential risk of SSRI use throughout pregnancy must be considered in the context of the risk of relapse of depression if maintenance treatment is discontinued," the ACOG committee wrote. "Untreated depression may increase the risk of low weight gain, sexually transmitted diseases, and alcohol and substance abuse, all of which have maternal and fetal health implications." ■

Graves' Warrants Lower-Dose Thyroid Rx During Pregnancy

PHOENIX — Infants of women with Graves' disease are rarely born with suppressed thyroid function, but their mothers should continue taking lower doses of thyroid medication during pregnancy, according to data presented at the annual meeting of the American Thyroid Association.

Maternal free thyroxine (FT_4) levels just above normal (at least 1.9 ng/dL) were associated with normal FT_4 levels in the newborn, Dr. Naoko Momotani of the Tokyo Health Service Association in Tokyo.

This study of 249 pregnant Graves' disease patients is the first to show that a mother's thyroid hormone level is linked to her newborn's health, Dr. Momotani said.

Graves' disease can cause underactivity of the thyroid in the developing fetus. When a pregnant woman with Graves' disease takes antithyroid medication, the TSH receptor antibodies are transferred to the fetus. "But the drug doses that are ideal for the mother might be too much for the fetus," she said.

The women in the study took antithyroid drugs throughout pregnancy. The highest reported maternal FT_4 level was 4.1 ng/dL. Overall, 41 fetuses had elevated TSH, but none had a visible goiter at birth.

There were no cases of below-normal fetal FT_4 levels and only one case of elevated TSH in a fetus among women whose FT_4 levels were greater than 1.9 ng/dL (that is, higher than the upper normal range of 1.2-1.9 ng/dL).

By contrast, 102 mothers had normal free T_4 levels (0.6-1.2 ng/dL) at the time of delivery, and 23 of their infants had low FT_4 and/or high TSH levels at birth. Only 1 of these 23 infants had an elevated TSH level when the infants were screened for congenital hypothyroidism.

One infant had both suppressed TSH and normal free T_4 levels at birth, which suggested central hypothyroidism, and the mother's FT_4 in this case was 2.1 ng/dL.

—Heidi Splete

DRUGS, PREGNANCY, AND LACTATION

Emerging Data on Prenatal Exposure to SSRIs

Over the last year, several studies on possible neonatal effects of prenatal exposure to SSRIs have been reviewed in this column. These studies have raised concerns about potential risks, including congenital malformations—as may be the case with paroxetine (associated with a putative increased risk for cardiovascular malformations, prompting a change in the pregnancy risk category label from C to D)—and perinatal distress and pulmonary complications, as noted in two recent studies. Other studies discussed here have highlighted the high risk of depressive relapse associated with discontinuation of antidepressants during pregnancy.

BY LEE COHEN, M.D.

These and further studies reported in recent years reflect the heightened interest in perinatal psychopharmacology and have provided a more refined scientific focus on the relative risks of prenatal SSRI exposure vs. the potential risks of untreated mood disorder during pregnancy. Physicians need to discuss these relative risks with patients, making the best clinical decision possible based on the individual clinical situation.

Until recently, few studies have tried to parse out the neonatal effects of untreated depression and prenatal SSRI exposure. Most of the available data have been in women treated with an SSRI for underlying depression, and have not included a comparison group of unmedicated women with depression.

But a study published in August by researchers at the University of British Columbia, Vancouver, using population-based health data and linking records of neonatal birth outcomes with hospital records of psychiatric diagnoses at maternal discharge and prenatal SSRI prescriptions, provides an opportunity to tease apart these two potentially important predictors of neonatal outcomes (Arch. Gen. Psychiatry 2006;63:898-906).

The study compared outcomes of babies born to women diagnosed with depression and treated with an SSRI to outcomes of babies born to women diagnosed with depression who were not treated with medication, and to a control group of babies whose mothers were neither depressed nor on antidepressant medication, between 1998 and 2001.

Among babies exposed to SSRIs, birth weights were lower, hospital stays were longer, and gestational ages were shorter, compared with babies in the control group. A similar pattern was seen when the SSRI-exposed babies were compared with those of depressed mothers who were not treated, except for birth weight for gestational age. In addition, significantly more of the infants of medicated women had respiratory distress and jaundice, compared with babies in the other two groups. Feeding problems were significantly more common among SSRI-exposed infants than among infants of unmedicated women with depression. The rate of convulsions was not significantly different between the groups.

Using propensity scores to match severity of depression in untreated and treated women, the researchers sought to match women by degree of depression in the year before and during pregnancy, essentially controlling for illness severity while looking at neonatal outcomes. When they compared birth outcomes in these two groups, the associations between prenatal SSRI exposure and feeding problems and jaundice were no longer present. What remained significant was a greater rate of respiratory distress in infants of SSRI-treated mothers and the incidence of birth weight below the 10th percentile. The findings suggest that the effect on respiratory distress may be due to SSRI exposure, not maternal depression.

The authors appropriately acknowledge the limitations of using claims data and discharge diagnoses as proxies for real diagnostic assessments. They also note that alcohol or illicit drug use, smoking, or socioeconomic conditions beyond income—all of which can affect neonatal well-being—could not be ascertained. Not factored into the study is another critical issue, the risk of postpartum depression, which is strongly associated with depression during pregnancy. In many respects, postpartum depression may have more enduring long-term outcome than other types of fetal exposures. Also unknown is the nature of respiratory distress, and whether it persisted. In one recent study, for example, symptoms of a "neonatal abstinence syndrome" were transient and did not require clinical intervention (Arch. Pediatr. Adolesc. Med. 2006;16:173-6).

The conclusion from the Canadian study, considering its limitations, is that there may be an independent effect of maternal depression on neonatal outcome and an independent effect of medication exposure, and these effects may be additive. Confirming this finding may be possible only with a prospective study that more accurately assesses maternal diagnosis and severity over time, and where medication exposure is confirmed prospectively.

In considering the increasing amount of data on both sides of this relative risk equation, it is critical for clinicians to discuss with patients the range of issues, from the potential neonatal effects of these medicines, to the high risk for relapse when antidepressants are discontinued, to the impact of untreated illness on the baby and mother.

Our own research and clinical experience suggest that patients presented with the same information, including women with extremely similar clinical illness histories, will make very different decisions about medication use during pregnancy. So, there is our task: to present this information and to let patients make decisions consistent with their wishes. With the backdrop of continually evolving data, patient decisions will also evolve, decisions not driven by the clinician, but by collaboration between the clinician and patient.

DR. COHEN *directs the perinatal psychiatry program at Massachusetts General Hospital, Boston, which provides information about pregnancy and mental health at www.womensmentalhealth.org. He serves as a consultant to manufacturers of several antidepressants, including SSRIs.*