Drugs, Pregnancy And Lactation

Atypical Antipsychotics

The reproductive safety of the older typical antipsychotics, such as haloperidol, is supported by extensive data that have accumulated over the past 40 years, at least with respect to teratogenic risk. Much of the data come from their use in treating nausea, particularly with prochlorperazine (Compazine). Long-term neurobehavioral data have been somewhat sparse, but no particular indications of risk have been raised in more than 4 decades of use.

BY LEE COHEN, M.D.

We have far less reproductive safety data on the newer "atypical" class of antipsychotics that have become widely used over the past decade because they lack some of the long-term side effects associated with the typical antipsychotics. These drugs—olanzapine (Zyprexa), risperidone (Risperdal), quetiapine (Seroquel), aripiprazole (Abilify), ziprasidone (Geodon), and clozapine (Clozaril)—are approved for schizophrenia; several are approved for acute mania indications as well. They are also being used widely across psychiatric disease states, including anxiety, generalized anxiety disorder, and obsessive-compulsive disorder, and as adjunctive treatment of depression.

Because reproductive safety data on the atypicals have been sparse, clinicians are again faced with the difficult situation where a relatively new class of medicine is being used frequently. What data are available have been largely limited to manufacturers' accumulated case series or spontaneous reports, which have inherent biases with respect to overreporting of adverse outcomes.

To date, such information has not suggested any "signals" with respect to specific concerns regarding their use during pregnancy, but we can make only limited conclusions based on such information. Clinicians have been in a bind with respect to use of the atypicals during pregnancy.

A study published last April, the first prospective study of the reproductive safety of the atypicals in the literature, provides some reassuring data regarding the risk of malformations, albeit in a relatively small sample of 151 patients. Investigators from the Motherisk Program in Toronto prospectively followed these women who took olanzapine, risperidone, quetiapine, or clozapine during pregnancy. All of the women had taken one of these agents during the first trimester, and 48 were exposed throughout pregnancy. A total of 151 pregnant women who had taken a nonteratogenic drug also were followed.

In the atypical-exposed group, one child was born with a major malformation (0.9%), a rate lower than the 1%-3% background rate in the general population; compared with two (1.5%) babies in the control group, an insignificant difference.

Differences between groups in rates of spontaneous abortions, stillbirths, or gestational age at birth were not statistically significant. Women taking atypical antipsychotics did have significantly higher rates of low-birth-weight babies (10% vs. 2%) and therapeutic abortions (10% vs. 1%) (J. Clin. Psychiatry 2005;66:444-9). This is the first prospective study that complements spontaneous reports from the manufacturers.

Among the 242 reports of olanzapine-exposed pregnancies, there was no increase of major malformations or other abnormal outcomes above baseline. Of the 523 clozapine exposed pregnancies reported, there were 22 "unspecified malformations."

Of the 446 quetiapine-exposed pregnancies, 151 outcomes were reported, of which 8 were different congenital anomalies. Eight malformations were reported among the approximately 250 reports of pregnancies and lactation exposed to risperidone, but no pattern of abnormalities was noted.

Obviously, if a patient can do without the medication, then it would be appropriate to discontinue it, but this is frequently not the case and decisions have to be made on a case-by-case basis weighing relative risks versus benefits.

For a patient planning a pregnancy who has a severe psychiatric illness and who is maintained on an atypical antipsychotic to sustain functioning, switching to a typical antipsychotic may be prudent. However, we often see women who present when they are already pregnant and on an atypical agent. At this point a switch may not be the wisest decision, if she is at a risk of relapse. For those women, the Motherisk data are not a guarantee of safety but do provide information that is at least moderately reassuring.

Although this small study is encouraging, given the prevalence of reproductive-age women on these agents, it would be ideal if the industry performed postmarketing surveillance studies that would rapidly provide the amount of cases we need to reliably estimate reproductive risks. Such studies may soon be mandated by the Food and Drug Administration in this post-Vioxx era, with increased emphasis on the safety of marketed drugs.

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Pregnancy Outcomes Seem Unchanged After Transplant

BY DOUG BRUNK
San Diego Bureau

Pregnancy outcomes in women who have an organ transplant are no worse after they undergo the procedure than before they have the surgery, results from a large Swedish population study have found.

"The outcome data in the present study agree well with what is known in the literature: a very high rate of preterm birth, of low birth weight, and of small for gestational age," reported the investigators, led by Bengt Källén, M.D., of the Tornblad Institute, University of Lund, Sweden.

"The advantage of the present study is that it represents a total population and that the outcome data were obtained from a medical birth register, based on original medical record data," they said (Br. J. Obstet. Gynaecol. 2005;112:904-9).

Using Sweden's hospital discharge register, the investigators identified women who had an organ transplant during 1973-2002. Their deliveries before and after transplantation were identified from the country's medical birth register over that same period.

A total of 976 deliveries occurred before organ transplantation and 149 after the procedure, which represented only about half the expected number of deliveries, after the researchers adjusted for year of delivery and maternal age.

No statistically significant differences in the odds of having a miscarriage before transplantation vs. after transplantation were seen (odds ratios of 2.2 vs. 3.2, respectively). High rates of preeclampsia (22% following kidney transplantation and 33% for liver transplantation), preterm birth (46%), low-birth-weight (41%), and small for gestational age babies (17%) were found for deliveries after transplantation, but similar frequencies were found among deliveries that occurred a few years before transplantation.

A congenital malformation was identified in 5.8% of infants born before organ transplantation and in 6.7% of those born after organ transplantation, but the two rates did not differ.

The authors pointed out that "among the 15 infants born after maternal liver transplantation, there were two with a congenital malformation, one of which was complex and serious: esophageal atresia with a heart defect and an iris malformation. This woman was the only one who had been treated with MMF [mycophenolate mofetil]. This may be a coincidence. Only few pregnancies exposed for MMF are published in the literature."

The authors reported that the major reason for the overall pregnancy outcomes observed in the study stems from disease morbidity, not from the transplantation itself or from medications associated with the procedure. ■

Discuss Wine Consumption With Pregnant Patients

BY SHARON WORCESTER
Southeast Bureau

ST. PETE BEACH, FLA. — It is important to take the time to focus specifically on the issue of wine consumption when routinely questioning pregnant patients about their use of alcohol.

That was the message conveyed in a poster on a study of alcohol consumption during pregnancy presented at the annual meeting of the Teratology Society.

The prospective, clinic-based cohort study presented involved a total of 4,494 women interviewed at their first prenatal visit.

Of these, 16% reported signs that were consistent with alcohol abuse and dependence, and half of those reported steady or binge drinking during pregnancy, according to William Rayburn, M.D., of the University of New Mexico, Albuquerque, and his colleagues.

Two hundred eight of the women with signs of alcohol abuse or dependence completed the study, including a 1-month postpartum interview.

Wine turned out to be the beverage of choice for about 25% of the participants. Those patients who drank wine tended to consume lower quantities of alcohol, but a high percentage (43%) of these wine drinkers continued their wine drinking after becoming aware of their pregnancy, the investigators found.

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DR. RAYBURN

This was particularly true among the group of older white women, who were significantly more likely than younger women and minorities to continue drinking after pregnancy awareness.

Wine is one of the most widely consumed alcoholic beverages among women of reproductive age, including those who are problem drinkers both before and after becoming aware of their pregnancy.

Specifically discussing the matter of wine consumption with pregnant patients is worthwhile, according to Dr. Rayburn and his associates. ■