BY LEE COHEN, M.D.

Drugs, Pregnancy, and Lactation

Atypical Antipsychotics

Data on the reproductive safety of certain psychotropics, such as selective serotonin reuptake inhibitors and anti-epileptic drugs, have increased in recent years, but information on the attendant risks of fetal exposure to antipsychotics remains sparse.

This is particularly true for the newer atypical antipsychotics, which are increasingly being used in women of reproductive age for a range of psychiatric disorders.

It is therefore critical that providers and women have solid information on which to base decisions about continuing treatment during pregnancy. Data from large studies support the reproductive safety of the typical antipsychotics such as haloperidol or thiothixene, but reproductive safety data for the atypical antipsychotics are sparse.

To date, few prospective studies on atypicals in pregnant women have been published. In a study comparing pregnancy outcomes in 151 subjects exposed to different atypicals—60 to olanzapine, 49 to risperidone, 36 to quetiapine, and 6 to clozapine—with nonexposed controls, major malformation rates were not significantly different between the two groups (J. Clin. Psychiatry 2005;66:444-9). However, that sample was relatively small.

Other available safety data on atypical antipsychotics in pregnant women are derived mainly from case reports or small case series, which have not identified an increased risk for major malformations.

Most of the prospectively identified cases of exposure are to olanzapine (133), risperidone (over 500), and quetiapine (42), with very few to aripiprazole and clozapine, and possibly none to ziprasidone. At a meeting in March, some of the first registry data on atypicals were reported from the Australian Pregnancy Registry: There were no major malformations in 38 pregnancies exposed to atypical antipsychotics.

Association of the atypicals with weight gain, diabetes, and hypertension raises another safety issue about their use in pregnancy as weight gain and adiposity in pregnancy have been linked to higher risk of neural-tube defects, independent of folate status (Am. J. Psychiatry 2002;159:136-7).

As is often the case when considering the use of psychotropics during pregnancy, the specific clinical approach depends on when the patient sees the clinician.

For a patient who presents for evaluation before pregnancy on a low dose of an atypical antipsychotic as an adjunct to a mood stabilizer, it may make sense to switch to an antipsychotic for which more reproductive safety data are available. This may not always be feasible because many patients present when they are already pregnant, and if they are well maintained, the provider may be reluctant to make changes.

Because of the absence of indicting data, we tend to maintain patients on atypical antipsychotics if they are already pregnant because of concerns about clinical destabilization. However, we recommend close follow-up for safety issues such as weight gain, diabetes, and hypertension in pregnancy, in collaboration with the obstetrician. In addition, although there are no robust data clearly distinguishing differences in efficacy, some patients seem to derive particular benefit from an atypical antipsychotic.

Based on the limited data available, there does not appear to be a glaring reproductive safety signal for the atypicals. But given the prevalence of use of these medicines in psychiatry, we clearly need more quality data on this drug class, so that that the atypicals can be safely integrated into the treatment algorithms used during pregnancy to treat women across that spectrum of disease states.

We are establishing an atypical antipsychotic pregnancy registry at Massachusetts General Hospital. We hope that data on atypical antipsychotics will be collected in a timely fashion and will make it possible for women and their physicians to make more informed decisions about use of this class of medicines during pregnancy. ■

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 is a consultant to manufacturers of atypical antipsychotics.