Pregnancy Is No Protection Against Depression Relapse

BY MARY ANN MOON
Contributing Writer

Women who discontinue antidepressant medication when they become pregnant have nearly a 70% rate of depression relapse during the course of the pregnancy, reported Dr. Lee S. Cohen of Massachusetts General Hospital, Boston, and his associates.

"Pregnancy has historically been described as a time of emotional well-being, providing general 'protection' against psychiatric disorder.

"However, systematic data to support this impression are sparse," the researchers noted.

They undertook what they described as the first study to examine the risk of depression relapse during pregnancy in women with recurrent depression, noting that there is an almost uniform belief that antidepressants should be discontinued during pregnancy to avert prenatal exposure to the drugs.

The 4-year prospective study involved 201 pregnant women with diverse socioeconomic backgrounds who had histories of recurrent depression and were being treated at one of three medical centers "with specific expertise in the treatment of psychiatric illness during pregnancy," they wrote (JAMA 2006;295:499-507).

The mean age at onset of depression was 18 years, and the mean duration of depression was 15 years. A total of 44% of the women reported five or more prior recurrences. All had been taking antidepressants for at least 3 months before enrolling in the study, and almost all (92%) were taking SSRIs or dual-action antidepressants either alone or in combination with other agents.

Of the 65 women who discontinued their medication, 44 (68%) relapsed during pregnancy. About half of them relapsed during the first trimester and another 40% during the second trimester. This compares with a 26% relapse rate among women who maintained their medication throughout pregnancy.

After the data were adjusted to account for several variables such as type of medication used and number of prior episodes of depression, "women who discontinued their medication had a fivefold increased risk of relapse over the course of their pregnancy, compared with women who maintained their medication," the researchers wrote.

Women who discontinued their medication had a fivefold increased risk of relapse during pregnancy, compared with women who continued their medication.

Of the patients who discontinued (65 women) or decreased (34 women) their antidepressant medications, 61% resumed taking the drugs during pregnancy because of resurgence of depressive symptoms.

These findings have significant implications, "given the prevalence of depression in reproductive-age women, the prevalence of antidepressant use in this population, and the frequency of unplanned pregnancy," according to the investigators.

Women should be made aware of the risk of depressive relapse following discontinuation of antidepressants. More of those who have recurrent depressive illness may well choose to maintain antidepressant therapy during attempts to conceive and during pregnancy, Dr. Cohen and his associates noted.

"These women must weigh concerns about prenatal exposure to these medications … [but] should also consider the risks of depressive relapse during pregnancy and the effects of untreated depression on fetal and maternal well-being," they added. ■

Lamotrigine–Birth Defect Link Seen Only in Valproate Combo

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — There is no evidence that lamotrigine monotherapy increases the risk of major congenital malformations in infants exposed prenatally to the drug, according to updated data from the International Lamotrigine Pregnancy Registry.

However, when the drug was used as adjunctive therapy along with valproate, the rate of major congenital malformations was significantly higher than the rate for the background population, reported Dr. John A. Messenheimer of GlaxoSmithKline, Research Triangle Park, N.C.

Reports also have identified a significantly increased risk of major congenital malformations among women taking valproate as monotherapy.

Since its inception in 1992, the lamotrigine registry has recorded 2,000 pregnancies exposed to the drug during the first trimester. The interim report contains data up to September 2005 and was presented as a poster at the joint annual meeting of the American Epilepsy Society and the American Clinical Neurophysiology Society.

The updated report contained the following outcome data. Most of the women (707) were taking lamotrigine as monotherapy, 256 were on polytherapy with lamotrigine but without valproate, and 119 were on polytherapy with lamotrigine and valproate.

There were 20 major congenital malformations reported. Of those, two were club feet, two were cases of anencephaly, and three were ventricular septal defects. The remaining malformations included midline defects, urogenital defects, cortical dysplasia, hypoplastic left heart syndrome, hypoplasia of the left ventricle, and diaphragmatic hernia with abdominal organ displacement.

The malformation rate among women on lamotrigine monotherapy was 2.8%, and the rate among those on polytherapy without valproate was 2.7%.

The rate among women on polytherapy with valproate was 11.8%—significantly higher than the background population rate of 2%-3%.

There was no significant relationship between lamotrigine dosage and the incidence of malformation, Dr. Messenheimer said. The rate of malformations among women taking more than 400 mg/day was slightly elevated at 4%. But only 100 women were taking such a high dose, and the confidence intervals in the analysis were wide

Published reports have identified a significantly increased risk of major congenital malformations among women taking valproate as monotherapy (10.7%).

These studies prompted the American Epilepsy Society's pregnancy outcomes forum panel to recommend last year that valproate be avoided as a first-line therapy for any indication in women of childbearing age.

However, the lamotrigine registry could not determine whether valproate exposure alone could explain the higher frequency of defects in the lamotrigine/valproate group, said Dr. Messenheimer. The registry determined that because the numbers of antiepileptic drugs used may be inextricably tied to the frequency and severity of seizures, it would be difficult to assess the contribution of each of these factors to the risk of major malformations.

In adults, lamotrigine is approved as adjunctive therapy for the generalized seizures of Lennox-Gastaut syndrome and for conversion to monotherapy in adults with partial seizures who are receiving treatment. It is also approved for maintenance treatment of bipolar disorder, and it is a pregnancy category C drug.

Physicians are asked to report exposed pregnancies to the international registry by calling 800-336-2176 as soon as the pregnancy is identified. The complete interim report of the International Lamotrigine Pregnancy Registry is available by calling the same number. ■

GERD During Pregnancy Is Common—and Often Overlooked

BY JANE SALODOF MACNEIL
Southwest Bureau

SCOTTSDALE, ARIZ. — Gastroesophageal reflux disease may be significantly underreported and undertreated in pregnant women, according to a poster presented at the annual meeting of the Central Association of Obstetricians and Gynecologists.

Dr. Houmam Al-Hakeem and his coinvestigators at Southern Illinois University in Springfield diagnosed the condition in 72 of 111 pregnant women screened with the Gastrointestinal Symptom Rating Scale Questionnaire, a measure validated in published studies.

The poster reported that a 2-week trial of conservative management, described as "the first line of treatment in pregnant women," failed to improve the cumulative scores of the women who had symptoms of gastroesophageal reflux disease (GERD).

GERD "is very common in pregnancy but at the same time it is very overlooked," Dr. Al-Hakeem said in an interview. Indeed, heartburn is so common, the researchers posited, that many patients and physicians think it is normal in pregnancy.

Conservative management, as prescribed in the study, consists of lifestyle changes such as not lying down after meals, not eating certain foods, raising the head of a person's bed, and taking antacids. Physicians know this does not work, and prescribe medication as a first-line treatment in GERD patients who are not pregnant, according to Dr. Al-Hakeem, who now practices in San Antonio. "Why are we waiting during pregnancy?" he asked. "Because we are afraid to give medicine."

He said the investigators have already begun the second phase of the study: a double-blind crossover trial of GERD treatments in a pregnant population. The study will look at fetal outcomes as well as reflux symptoms in patients treated with conservative management, pregnancy category B drugs Zantac and Prevacid, and a placebo. Dr. Al-Hakeem anticipated results would be available in about a year.

The 111 patients in the first phase were described as being in good health in a pregnancy of at least 24 weeks' gestation. Patients with documented history of GERD, esophageal disorders, Zollinger-Ellison syndrome, hiatal hernia, peptic ulcer syndrome, and irritable bowel syndrome were excluded from the study.

Women were defined as GERD positive if they had a score of at least 4 on Gastrointestinal Symptom Rating Scale questions specific to reflux. The investigators found no significant differences in ethnicity, education, tobacco use, or alcohol and drug use between the 72 women deemed to be GERD positive and the 39 women who were not. ■