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Pregnant Women at Risk of Bipolar Recurrence with Interruption of Medication

AJP Study Underscores the Value of Mood-Stabilizer Medications in Risk/Benefit Equation

Arlington, Va. (Dec. 1, 2007) — Women with bipolar disorder who stop taking their medication — such as lithium, antipsychotics and anticonvulsants prescribed as mood stabilizers — before or shortly after becoming pregnant appear to be much more likely to suffer a recurrence of the disorder, according to a study reported in the December issue of *The American Journal of Psychiatry (AJP)*, the official journal of the American Psychiatric Association (APA).

In the prospective study of 89 pregnant women with bipolar disorder, Adele C. Viguera, M.D., and colleagues at Harvard Medical School and Emory University found that 85 percent of the 62 women they studied who stopped their mood stabilizer medication—up to six months prior to becoming pregnant or in the first 12 weeks of pregnancy—experienced a recurrence of the disorder. In comparison, only 37 percent of the 27 women who continued taking their medication through at least week 12 of pregnancy experienced a recurrence. In addition, Viguera and her colleagues report in “Recurrence Risk in Women With Bipolar Disorder During Pregnancy: Prospective Study of Mood-Stabilizer Discontinuation” that abrupt discontinuation of medication greatly increased and hastened the recurrence, confirming earlier observations by the same researchers.

The majority of the women studied were taking lithium as a mood stabilizer (55 of the 89, or 62 percent) followed in frequency of use by an anticonvulsant mood stabilizer (32/89; 36 percent) or an antipsychotic mood stabilizer (24/89; 27 percent). About half of the women in this study were also taking an antidepressant medication.

Recurrences most often took the form of a depressive or mixed episode (experiencing both symptoms of depression and mania), and most of the recurrences began within the first trimester of pregnancy. Of note, in this study it appears that antidepressant treatment did not affect the risk of recurrence.

“Women and their doctors face difficult decisions in pregnancy, because both the illness and the treatment can potentially harm the fetus,” said Robert Freedman, M.D., *AJP* editor in chief. “Accurate data on the risk of discontinuing treatment for bipolar disorder during pregnancy is part of the evidence that is needed to make the best possible decision for each woman and her baby.”

The episodes of recurring illness spanned on average more than 40 percent of the duration of pregnancy for those women who discontinued mood stabilizer medication, but only 9 percent of the duration of pregnancy for women who continued to take medication. Those whose mood stabilizer was discontinued abruptly (over a period of two weeks or less) had a median time to recurrence of two weeks, compared to 22 weeks for women whose medication was more gradually tapered and stopped.

In designing this study, Dr. Viguera and her colleagues incorporated several improvements over methods used in earlier studies. Previous studies were limited by small size, restricted subject pools and/or the use of retrospective assessments. The current findings are consistent with many previous reports that indicated pregnancy is a period of substantial risk for recurrence of bipolar disorder. The current findings do not support suggestions in previous studies that pregnancy exerts a favorable effect on the illness and therefore limits the risk of recurrence during pregnancy.

Recently the public's focus has been on the possible adverse effects mood stabilizing medications may have on fetal development. As a result, many women (including 70 percent of those in this study) stop taking mood stabilizers before trying to become pregnant. The authors propose that treatment planning for pregnant women with bipolar disorder include consideration of the high recurrence risk associated with discontinuation of mood stabilizer medication.

“These findings have important clinical implications for the overall risk/benefit assessment in managing bipolar disorder during pregnancy,” said lead author Adele Viguera, M.D., now at the Cleveland Clinic. “Patients should be informed not only that there is a significant risk for recurrence associated with stopping treatment, but also that this risk appears to be greatest early on in pregnancy and especially, following abrupt discontinuation. Moreover, stopping treatment is associated with a longer duration of maternal illness during pregnancy compared to remaining on treatment. Therefore, it is critical for patients with bipolar disorder who are pregnant or planning pregnancy to be informed of the magnitude of these risks in order for them to weigh these risks along with risks associated with fetal exposure to medications.”

The study was supported in part by the National Institute of Mental Health, NARSAD, the Stanley Medical Research Institute, the Bruce J. Anderson Foundation, and the McLean Private Donors Psychopharmacology Research Fund. Additional financial disclosures appear at the end of the article.

Note to Editors: Contact Jim Rosack at 703-907-7862 / jrosack@psych.org or the APA Office of Communications and Public Affairs at 703-907-8640 / press@psych.org for copies of the article and an accompanying editorial.

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