Antidepressant Medication Treatment During Pregnancy: Prevalence of Use, Clinical Implications, and Alternatives

In this issue, we have 4 articles addressing antenatal depression, or depression during pregnancy. As all authors note, depression is common during pregnancy, and this is supported by the observation of Petersen and colleagues that a substantial number of women who take antidepressants during pregnancy did not take them prior to pregnancy, indicating either an index episode or relapse and representing 14% of the women who used antidepressants during pregnancy. Also, Petersen and colleagues found that the majority of women taking antidepressants stopped using them prior to conception or early in the first trimester, underscoring the intent of women to avoid antidepressant use during pregnancy, which is observed often in clinical practice.

For many women of reproductive age, their course of depression has established a pattern of either chronicity or recurrence, warranting treatment or exposing the woman and fetus to potential harms of untreated depression during pregnancy.[1] Not surprisingly, Petersen et al found that women who stopped antidepressant drugs while trying to conceive or after discovering they were pregnant did so at a significantly higher rate than women in the control group who were not pregnant. The strengths of the study by Petersen and colleagues include a large sample size and linked data regarding medication use, pregnancy, diagnosis, and socioeconomic factors. Also, the authors selected careful markers of antidepressant use (ie, the filling of a second prescription rather than a single one) to attempt to capture actual use rather than prescribing practices only. This is an example of a study (conducted in the United Kingdom) that would be near impossible to implement in the United States due to the lack of a universal health care system. Follow-up studies are needed to demonstrate outcomes of antidepressant discontinuation or continuation at this population level, as naturalistic, prospective data underscore a high risk of depressive relapse with medication discontinuation.[2] Future studies with samples of this size would also provide essential information if they included not only antidepressant continuation or discontinuation status and obstetric and neonatal outcomes, but also burden of depressive or anxiety symptoms experienced during pregnancy.

In another article in this issue, Sit et al seek to answer questions around the dilemmas related to antidepressant use during pregnancy. They carefully followed 21 women through the second half of pregnancy, monitoring depressive symptoms and antidepressant use. They used assessments of cord blood to quantify end-of-pregnancy medication exposure and used the Peripartum Events Scale to quantify obstetric and neonatal symptoms. All of the mothers took antidepressants during pregnancy, although some women experienced third trimester major depressive episodes, while some were remitted, allowing for comparisons between those on medication and depressed and those on medication and nondepressed. Although numbers of women on each antidepressant were small, the authors were also able to compare exposure to different serotonin reuptake inhibitors, and they compared fluoxetine, with a distinctively long half-life, with shorter half-life antidepressants.

Considerable strengths of the study by Sit et al included the use of raters blinded to the study hypotheses to ascertain neonatal data from hospital records and the prospective longitudinal design, including assessment of both antidepressant use and maternal depressive symptoms. Use of cord blood was also included to quantify late pregnancy exposure. One limitation was the absence of a control group that was neither taking medications nor depressed, to elucidate the rates of neonatal symptoms and obstetric complications in a healthy group from the same community who were not taking antidepressants. Therefore, although rates of perinatal events did not differ between women who were depressed or nondepressed, it is unclear whether the rate

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of perinatal events was higher than that of a more general population from the community wherein the sample was derived. Interestingly, use of fluoxetine was not more likely to lead to perinatal events compared with shorter half-life agents. In fact, the trend for perinatal events was lower with fluoxetine than shorter half-life agents.

In the third article, Suri and colleagues conducted a prospective, naturalistic follow-up assessment of neurobehavioral outcomes in infants of women with major depressive disorder who were followed throughout pregnancy. In the original study, women were selected to continue or discontinue their antidepressant medication for pregnancy, and medication use and depressive symptoms were rigorously tracked. Suri and colleagues then assessed neurobehavioral outcomes of the subjects' infants following antidepressant exposure and compared that group of infants to those of mothers who had major depressive disorder but were not taking antidepressants during pregnancy and to the group of infants born to nondepressed controls. The Brazelton Neonatal Behavioral Assessment Scale (BNBAS) was completed by raters blinded to the mothers' antidepressant use or major depressive disorder history. BNBAS assessments were completed within 1 week of delivery and again between 6 and 8 weeks of age. Infants exposed to antidepressants during pregnancy were born significantly earlier than those in the other 2 groups, although the mean gestational age was still full term. There were no differences between groups regarding preterm birth, birth weight, Apgar scores, and special nursery admissions. There were no significant differences on the BNBAS among the 3 groups. Maternal depressive symptoms, as assessed by the Hamilton Rating Scale for Depression, also did not contribute to a significant difference on the BNBAS.

The fourth article addressing antenatal depression in this issue by Wirz-Justice et al is a treatment study of bright light therapy for antenatal depression. Women were randomly assigned to bright light therapy or a dim light placebo. The response to active treatment was significantly greater than that to placebo, notable after 5 weeks. Twenty-seven women were evaluable in this study, after the investigators excluded 6 women who started antidepressant medication treatment outside of the protocol during the study (underscoring the challenge of clinical research). Most of the participants used light therapy or placebo as monotherapy, while a small number (n = 4) were taking antidepressants at the time of enrollment for at least 3 months without improvement and continued antidepressant medication throughout the trial. Interestingly, all of these participants received active treatment and were responders. Considering the high rates of medication discontinuation observed by Petersen et al among pregnant women, and the experience of many women similar to those characterized by Sit et al who take antidepressants and continue to experience depressive episodes during pregnancy, a nonmedication treatment that is efficacious and safe and that can be used as either a monotherapy or adjunctive therapy is likely to have a major impact on perinatal depression treatment.

We hope that you enjoy the Focus on Women's Mental Health section of *The Journal of Clinical Psychiatry*. For feedback regarding this section, please e-mail me at mfreeman@psychiatrist.com.

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