No Decision Is Without Risk

Rita Suri, MD, and Lori L. Altshuler, MD

Depressive symptoms occur in up to 20% of pregnant women,[1–3] with major depressive disorder affecting 10% of pregnancies.[4] For women with major depressive disorder who discontinue antidepressant treatment close to conception, the risk of relapse is high.[5] Fetal exposure to antidepressant treatment in some, but not all,[6–8] studies has been shown to have adverse effects on pregnancy outcome, including lower birth weight,[9] preterm birth,[10,11] neonatal syndrome,[12] and a small increase in the risk of congenital malformations or persistent pulmonary hypertension of the newborn.[13–15] However, fetal exposure to active symptoms of depression has also been associated with lower birth weight,[16] preterm birth,[10] sleep disturbances in the newborn,[17] potential developmental delay,[18] and behavioral difficulties in children.[19] Untreated depression in pregnancy can result in ambivalence toward the pregnancy and, at its worst, the decision to abort.[20]

Given that treatment with antidepressants and active symptoms of depression both have unintended consequences, women and clinicians face the difficult decision of how to manage major depressive disorder during pregnancy. Recommendations cannot be made as if "one size fits all." In many cases, psychotherapy can be an effective modality. When treatment decisions are made, strong consideration is given to the impact of a woman's depression on her ability to care for herself, as well as its impact on her family, care for other children, marriage, occupation, and other aspects of her life that are of importance to her. Treatment recommendations also may be based on the severity of a woman's prior depression including number of prior episodes, length of time since last episode, history of episodes related to pregnancy and/or the postpartum, and severity of symptoms during an episode. Although there is very little data-driven evidence in the pregnancy literature to support recommendations based on these variables, a prior study by our group and others[5] found that duration of depressive illness and history of more recurrent depressive illness were associated with a significant increase in the risk of relapse during pregnancy.

No decision is risk-free. The field of perinatal psychiatry faces the challenge of trying to understand whether more adverse outcomes occur in women who take antidepressants but remain euthymic or in women who do not take medications but remain depressed in pregnancy. Further, the field needs to better understand the mechanisms by which problematic outcomes occur, be they due to exposure to antidepressants or exposure to depression.[10] For example, are antidepressant effects related to alterations of serotonin 5-HT signaling or vascular and hemostatic processes? Are depression effects related to dysregulation of the hypothalamic-pituitary-adrenal (HPA) system or altered behavior and prenatal care? A better understanding of mechanisms may further elucidate other more subtle but equally significant effects on reproductive and long-term outcome. Further research is necessary to enable women and clinicians to make informed decisions, taking into account the unique clinical circumstances of our individual patients.

References

1. Evans J, Heron J, Francomb H, et al. Cohort study of depressed mood during pregnancy and after childbirth. *BMJ.* 2001;323(7307):257–260.
2. Marcus SM, Flynn HA, Blow FC, et al. Depressive symptoms among pregnant women screened in obstetrics settings. *J Womens Health (Larchmt).* 2003;12(4):373–380.
3. De Tychey C, Spitz E, Briancon S, et al. Pre- and postnatal

depression and coping: a comparative approach. *J Affect Disord.* 2005;85(3):323–326.
4. O'Hara MW, Schlechte JA, Lewis DA, et al. Controlled prospective study of postpartum mood disorders: psychological, environmental, and hormonal variables. *J Abnorm Psychol.* 1991;100(1):63–73.
5. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA.* 2006;295(5):499–507.
6. Einarson A, Choi J, Einarson TR, et al. Incidence of major malformations in infants following antidepressant exposure in pregnancy: results of a large prospective cohort study. *Can J Psychiatry.* 2009;54(4):242–246.
7. Chambers CD, Johnson KA, Dick LM, et al. Birth outcomes in pregnant women taking fluoxetine. *N Engl J Med.* 1996;335(14):1010–1015.
8. Ericson A, Kallen B, Wiholm B. Delivery outcome after the use of antidepressants in early pregnancy. *Eur J Clin Pharmacol.* 1999;55(7):503–508.
9. Oberlander TF, Warburton W, Misri S, et al. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. *Arch Gen Psychiatry.* 2006;63(8):898–906.
10. Wisner KL, Sit DKY, Hanusa BH, et al. Major depression and antidepressant treatment: impact on pregnancy and neonatal outcomes. *Am J Psychiatry.* 2009;166(5):557–566.
11. Suri R, Altshuler L, Hellemann G, et al. Effects of antenatal depression and antidepressant treatment on gestational age at birth and risk of preterm birth. *Am J Psychiatry.* 2007;164(8):1206–1213.
12. Moses-Kolko EL, Bogen D, Perel J, et al. Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications. *JAMA.* 2005;293(19):2372–2383.
13. Louik C, Lin AE, Werler MM, et al. First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *N Engl J Med.* 2007;356(26):2675–2683.
14. Alwan S, Reefhuis J, Rasmussen SA, et al. National birth defects prevention study: use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med.* 2007;356(26):2684–2692.
15. Chambers CD, Hernandex-Diaz S, Ban Marter LJ, et al. Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. *N Engl J Med.* 2006;354(6):579–587.
16. Steer RA, Scholl TO, Hediger ML, et al. Self-reported depression and negative pregnancy outcomes. *J Clin Epidemiol.* 1992;45(10):1093–1099.
17. Field T, Diego M, Hernandez-Reif M, et al. Sleep disturbances in depressed pregnant women and their newborns. *Infant Behav Dev.* 2007;30(1):127–133.
18. Deave T, Heron J, Evans J, et al. The impact of maternal depression in pregnancy on early child development. *BJOG.* 2008;115(8):1043–1051.
19. Luoma I, Tamminen T, Kaukonen P, et al. Longitudinal study of maternal depressive symptoms and child well-being. *J Am Acad Child Adolesc Psychiatry.* 2001;40(12):1367–1374.
20. Suri R, Altshuler LA, Mintz J. Depression and the decision to abort. *Am J Psychiatry.* 2004;161(8):1502.

Author affiliations: Mood Disorders Research Program (Dr Suri) and Department of Psychiatry and Biobehavioral Sciences (Dr Altshuler), University of California, Los Angeles. ***Financial disclosure:*** **Dr Altshuler** has received grant/research support from Abbott and has received honoraria from and is a member of the speakers/advisory boards for Abbott, Forest, and GlaxoSmithKline. **Dr Suri** reports no financial or other relationships relevant to the subject of this commentary. ***Funding/support:*** None reported. ***Corresponding author:*** Rita Suri, MD, Mood Disorders Research Program, 300 UCLA Medical Plaza, Room 1544, Los Angeles, CA 90095 (rsuri@mednet.ucla.edu).
doi:10.4088/JCP.09com05529