To Medicate or Not to Medicate?
Antidepressant Use in Pregnancy

Ladan Sadrehashemi, MD, FRCPC; and Nicolas Misri

Sarah is a typical patient seen in a reproductive psychiatrist's practice. Firstly, it is encouraging to see that Sarah is seeking preconception counselling, thus allowing time for evaluation and psychoeducation rather than deciding after the fact.

The general public and most physicians are apprehensive about using any medications during pregnancy. The current research for the use of psychotropic medications in the antenatal period is, at best, controversial.

In Sarah's case, ultimately what one must decide between is the risk of continuing citalopram during pregnancy vs. the risk of relapse of depression if citalopram is discontinued. What is clear in this situation is neither decision is risk-free.

Sarah's case

Sarah, 34, comes to you for a pre-pregnancy assessment.

History

Sarah has a history of recurrent major depression. She takes 30 mg of citalopram q.d. She has been in remission for one year. In the past, when she has discontinued medications, she has relapsed.

Sarah also has a family history of both anxiety and depression. She and her husband are planning to start a family. While she is reluctant to be on antidepressants during her pregnancy, she is also concerned about stopping the citalopram.

Sarah wants to know if you would recommend that she stop citalopram given that she wants to get pregnant, or at least advise her to continue on it to avoid relapse in pregnancy.

Questions

1. How do you proceed to be able to answer her questions?
2. What must be taken into consideration when deciding whether to use antidepressants in pregnancy?

For the conclusion to Sarah's case, turn to page 76.

Depression in pregnancy

Depressive disorders occur more frequently in women during the childbearing age. The prevalence of depressive symptoms can range from 6.9% to 20% during pregnancy.[1] If a woman has had a depressive episode then she is at increased risk of developing depressive symptoms during her pregnancy and in the postpartum period. Women who stop taking their antidepressant while pregnant are five times more likely to relapse.[2] When seeing a patient for a pre-pregnancy assessment, there are a number of factors to be considered with respect to the patient's depression history:

- Number of previous episodes
- History of relapse following the discontinuation of an antidepressant

- Severity of previous episodes:
  - Did the patient have to stop working?
  - Did they require hospitalization?
  - Did they develop psychotic symptoms?
  - Did they make a suicidal gesture?
- Family history of mood disorders

Maternal depression has been associated with:

- preterm birth,
- lower birth weight,
- smaller head circumference and
- lower activity, pulse, grimace, appearance and respiration (APGAR) scores.[3]

Mothers who have depression during pregnancy have been found to exhibit poor self-care that can lead to compromised antenatal care. They are at higher risk to self medicate and abuse substances. There is an increased risk of obstetrical complications. There may be postpartum exacerbation which may lead to impaired bonding between the mother and infant. Diego, *et al* found that maternal psychological distress, during pregnancy, led to increased cortisol levels, which led to lower fetal weight.[4] Field, *et al* reported that babies of depressed mothers had decreased levels of serotonin and dopamine and increased levels of cortisol and norepinephrine.[5]

Antidepressants in pregnancy

When thinking about using antidepressants in pregnancy, we worry about the following factors:

- risk of teratogenicity,
- adverse neonatal effects at birth and
- potential negative infant development in the short and long-term.

Sarah's case cont'd...

It is highly likely that Sarah's depression will return if she discontinues citalopram, given that she:

- has recurrent episodes of depression,
- has relapsed upon discontinuation of her medication and
- has a family history of depression.

Thus, the recommendation would be that she continue taking citalopram during her pregnancy. However, in case she may still decide to stop the medication despite this clinical opinion, it would be best if she were to taper off it slowly, likely over the period of one month. Close, frequent monitoring of her mood throughout this period and after she conceives is warranted.

MAOIs

All psychotropic medications are secreted in the amniotic fluid and easily diffuse across the placenta to the developing fetus.[6] Monoamine oxidase inhibitors (MAOI) have been associated with fetal growth restriction in animal studies and are not recommended in the antenatal period.[7]

Tricyclic antidepressants

Of the tricyclic antidepressants, there is some data with clomipramine suggesting association with congenital heart disease and withdrawal seizures in the neonate.[8]

Dr. Sadrehashemi is a practicing Psychiatrist in Emergency Psychiatry at Vancouver General Hospital and Reproductive Psychiatry at St. Paul's Hospital, Vancouver, British Columbia.

Mr. Misri is a Research Student working with the Reproductive Mental Health Program at St. Paul's Hospital and British Columbia Women's Hospital, Vancouver, British Columbia.

If a woman has had a depressive episode then she is at increased risk of developing depressive symptoms during her pregnancy and in the postpartum period.

SSRIs

With respect to selective serotonin reuptake inhibitors (SSRIs), there have been recent Food and Drug Administration (FDA) and Health Canada warnings regarding neonatal withdrawal abstinence syndrome, which has been reported to occur in 30% of neonates exposed to SSRIs.[9] There has also been a recent FDA warning regarding paroxetine, based on a report showing an overall increased risk in congenital malformations (in particular ventricular septal defects) moving the drug to Category D.[10] This means that positive evidence of fetal risk has been demonstrated in humans, according to the FDA. However, the potential benefits of use in pregnant woman may outweigh the potential risks, thus decisions must be made on an individual basis.

The latest warning of SSRI use during pregnancy, which is cause for further concern, is regarding the development of persistent pulmonary hypertension.[11]

In Sarah's case, with respect to citalopram, antenatal exposure has not shown an increase in congenital malformations. There has been one case of infant withdrawal published.[12] Dx

The authors would like to thank Dr. Shaila Misri for her help reviewing the article.

References

1. Mian AI: Depression in pregnancy and postpartum period: Balancing adverse effects of untreated illness with treatment risks. J Psychiatr Pract 2005; 11(6):389-94.
2. Einarson A, Selby P, Koren G: Discontinuing antidepressants and benzodiazepines upon becoming pregnant. Beware of the risks of abrupt discontinuation. Can Fam Physician 2001; 47:489-90.
3. Orr ST, Millar CA: Maternal depressive symptoms and the risk of poor pregnancy outcome: Review of the literature and preliminary findings. Epidemiol Rev 1995; 17(1):165-71.
4. Diego MA, Jones NA, Field T, et al: Maternal psychological distress, prenatal cortisol and fetal weight. Psychosom Med 2006; 68(5):747-53.
5. Field T, Diego M, Hernandez-Reif M, et al: Pregnancy anxiety and comorbid depression and anger: Effects on the fetus and neonate. Depress Anxiety 2003; 17(3):140-51.
6. Kim J, Riggs KW, Misri S, et al: Stereoselective disposition of fluoxetine and norfluoxetine during pregnancy and breastfeeding. Br J Clin Pharmacol 2006; 61(2):155-63.
7. Gjerdingen D: The effectiveness of various postpartum depression treatments and the impact of antidepressant drugs on nursing infants. J Am Board Fam Pract 2003; 16(5):372-82.
8. Schimmell MS, Katz EZ, Shaag Y, et al: Toxic neonatal effects following maternal clomipramine therapy. J Toxicol Clin Toxicol 1991; 29(4):479-84.
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. GlaxoSmithKline: Epidemiology study preliminary report on bupropion in pregnancy and occurrences if cardiovascular and major congenital malformation, 2005.
11. Chambers CD, Hernandez-Diaz S, Van Marter LJ, et al: Selective serotonin-reuptake inhibitors and risk of persistent pulmonary hypertension of the newborn. New Engl J Med 2006; 354(6):579-87.
12. Franssen EJE, Mejis V, Ettaher F, et al: Citalopram in pregnancy and lactation. Clin Pharmacol Ther 2006; 72(2):184-91.