SSRIs in pregnancy: What should you tell your depressed patient?

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Mrs. D is a 28-year-old married woman who became depressed after her first pregnancy. The depression was treated successfully with paroxetine, 20 mg/d. Before beginning treatment, she reported low mood, spent most of the day in bed, was unable to care for herself, and confessed to thoughts of harming her child.

Mrs. D presents to your clinic asking whether she should continue her selective serotonin reuptake inhibitor (SSRI) because she and her husband are thinking about having a second child. Recently, she tells you, she saw a news article suggesting that antidepressants show little benefit, and she is concerned that her baby might have a heart defect if she continues paroxetine.

Mrs. D wants to discontinue her medication, but her husband thought she should discuss doing so with you first. During this visit she takes a pregnancy test, which is positive. She wants to know what to do.

SSRI use is increasing among women during their childbearing years, a period that also carries the highest risk of depression. An estimated 7% to 23% of pregnant women experience depression; 3.8% of pregnant women receive an SSRI.[1] SSRIs are the most commonly prescribed antidepressants during pregnancy, but their use remains controversial. There is disagreement about the maternal and neonatal risks of untreated depression and SSRI exposure.[2-10] Media reports of studies demonstrating adverse effects associated with SSRIs may generate fear among women, possibly prompting them to self-discontinue medication.

Evidence of risks and benefits

Clinicians should be aware of possible adverse effects of SSRI use and untreated depression (***Table, page 42***).[2-10] The available data precludes definitive associations between untreated depression and poor outcomes (***Box, page 42***). Studies of SSRI use during pregnancy have shown conflicting results for all potential outcomes. Absolute risk, with the exception of neonatal adaptation syndrome, is estimated to be small. Neonatal adaptation syndrome—which is characterized by jitteriness, poor muscle tone, weak cries, respiratory dis-

Practice Points

- Make decisions about the **use of SSRIs in pregnancy** case by case.
- **Understand the risks** of both untreated depression and the use of SSRIs during pregnancy.
- Sertraline, paroxetine, citalopram, and fluoxetine are the **most studied SSRIs** in pregnancy.
- Consider **cognitive-behavioral therapy** for mild depression.

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Series Editor

Clinical Point

For pregnant women with mild or moderate depression, CBT might be an appropriate first-line therapy

Table

Potential adverse outcomes during pregnancy

When depression is untreated
Spontaneous abortion
Preterm delivery, low birth weight, small for gestational age
Preeclampsia
Reduced fetal responsiveness in utero
Lack of maternal health maintenance (poor weight gain; use of tobacco, alcohol, or cocaine; less likely to regularly attend appointments)
Maternal suicide
Neonatal neurobehavioral effects (reduced attachment, developmental delays, behavioral problems)
When depression is treated with a selective serotonin reuptake inhibitor
Spontaneous abortion
Preterm delivery, low birth weight, small for gestational age
Preeclampsia
Congenital cardiac septal defects
Persistent pulmonary hypertension of the newborn
Neonatal adaptation syndrome
Poor neurodevelopmental outcomes
Respiratory distress syndrome in newborn
Endocrine and metabolic disturbance in newborn

Source: References 2-10

Box

Evidence on SSRI use in pregnancy is necessarily limited

Because of the ethical problems of conducting prospective, randomized, controlled trials of selective serotonin reuptake inhibitors (SSRIs) in pregnant women, evidence often is inconsistent and methodologically flawed. Much of the current literature is based on retrospective reviews of administrative databases, teratology services, or birth registries. This methodology often does not incorporate confounding variables such as dose, timing of exposure, use of other medications, alcohol, tobacco, or illicit drugs, severity of depression, and other medical conditions in the mother. Many of these studies compared women receiving treatment with non-depressed controls, which makes it difficult to separate effects of SSRIs from those of depression. Studies may have small sample sizes, report relative risk over absolute risk, and vary in measured outcomes—making quantitative systematic reviews challenging.

tress, hypoglycemia, low Apgar scores, and seizures—occurs in 15% to 30% of infants born to mothers taking SSRIs, but it is transient and resolves during the first weeks of life.

Treatment recommendations

Given the conflicting nature of the evidence, treatment plans should be individualized, weighing the risks and benefits of treatment and the patient's beliefs and psychiatric history. Consider severity of symptoms and history, including effective therapy and history of relapse. For women with mild or moderate depression, cognitive-behavioral therapy might be an appropriate first-line therapy. However, non-pharmacotherapeutic interventions might not relieve severe depression or be available to all women. When discontinuing an SSRI before pregnancy, counsel the patient to not discontinue the medication abruptly and provide an appropriate taper schedule. See ***Related Resources*** (***page 44***) for detailed recommendations from the American Psychiatric Association and the American College of Obstetricians and Gynecologists.

Reviewing the SSRI literature regarding pregnancy

Sertraline, paroxetine, citalopram, and fluoxetine are the most studied SSRIs during pregnancy; little information is available on escitalopram and fluvoxamine.[11] Prescribing preference generally is given to the medications with the most evidence; paroxetine may be an exception. In 2005, the FDA requested a change in paroxetine's pregnancy category from C to D, indicating that adequate studies demonstrated a risk of congenital cardiac malformations.[11]

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Related Resources

- Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. Gen Hosp Psychiatry. 2009;31:403-413.
- MGH Center for Women's Mental Health. www.womensmentalhealth.org.

Drug Brand Names

Citalopram • Celexa	Fluvoxamine • Luvox
Escitalopram • Lexapro	Paroxetine • Paxil
Fluoxetine • Prozac	Sertraline • Zoloft

Clinical Point

The American Academy of Pediatrics considers SSRIs to be compatible with breast-feeding

Additional studies have been conducted, and the teratogenicity of paroxetine is debatable. A recent review reports 8 studies that suggest a malformation risk, compared with 15 studies that show no risk.[12]

The American Academy of Pediatrics considers SSRIs to be compatible with breast-feeding.[13] The best-studied drugs include sertraline and paroxetine. Fluoxetine should be avoided when possible because a long elimination half-life can cause the drug to accumulate in the newborn, increasing the risk of irritability, hypertonia, sedation, and poor suckle.[7]

There is no best SSRI for all pregnant women. Risks and benefits, including previous treatment success and failure, should be taken into account before starting or switching therapy. Whenever possible, consider monotherapy to avoid compounding the risk of harm.

References

1. Alwan S, Reefhuis J, Rasmussen SA, et al. Patterns of antidepressant medication use among pregnant women in a United States population. J Clin Pharmacol. 2011;51(2):264-270.
2. Domar AD, Moragianni VA, Ryley DA, et al. The risks of selective serotonin reuptake inhibitor use in infertile women: a review of the impact on fertility, pregnancy, neonatal health and beyond. Hum Reprod. 20113;28(1):160-171.
3. Davalos DB, Yadon CA, Tregellas HC. Untreated prenatal maternal depression and the potential risks to offspring: a review. Arch Womens Ment Health. 2012;15(1):1-14.
4. Spinelli M. Antidepressant treatment during pregnancy. Am J Psychiatry. 2012;169(2):121-124.
5. Oyebode F, Rastogi A, Berrisford G, et al. Psychotropics in pregnancy: safety and other considerations. Pharmacol Ther. 2012;135(1):71-77.
6. Byatt N, Deligiannidis KM, Freeman MP. Antidepressant use in pregnancy: a critical review focused on risks and controversies. Acta Psychiatr Scand. 2013;127(2):94-114.
7. Sie SD, Wennink JM, van Driel JJ, et al. Maternal use of SSRIs, SNRIs and NaSSAs: practical recommendations during pregnancy and lactation. Arch Dis Child Fetal Neonatal Ed. 2012;97(6):F472-476.
8. Jimenez-Solem E, Andersen JT, Petersen M, et al. SSRI use during pregnancy and risk of stillbirth and neonatal mortality. Am J Psychiatry. 2013;170(3):299-304.
9. Nikfar S, Rahimi R, Hendoiee N, et al. Increasing the risk of spontaneous abortion and major malformations in newborns following use of serotonin reuptake inhibitors during pregnancy: a systematic review and updated meta-analysis. Daru. 2012;20(1):75.
10. Stephansson O, Kieler H, Haglund B, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of stillbirth and infant mortality. JAMA. 2013;309(1):48-54.
11. U.S. Food and Drug Administration. Public health advisory: paroxetine. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm051731.htm. Published December 8, 2005. Accessed September 27, 2013.
12. Koren G, Nordeng H. Antidepressant use during pregnancy: the benefit-risk ratio. Am J Obstet Gynecol. 2012;207(3):157-163.
13. American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. Pediatrics. 2001;108:776-789.