

The use of antidepressants in pregnancy and lactation

More information is becoming available on using selective serotonin reuptake inhibitors and related medications to treat pregnant women and new mothers for depression.

ABSTRACT: The perinatal period presents a special problem to health care providers treating psychiatric disorders in women. Many pregnant women and new mothers who need antidepressant medications are hesitant to take such drugs for fear of possible harmful effects on their fetuses and nursing infants. Research on the short-term effects of antidepressant medications, particularly the selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors, suggests they can be used by pregnant and breastfeeding women for the treatment of depression and anxiety disorders. Research also suggests that not treating these disorders can have a negative impact on mother-infant bonding.

Despite the high prevalence and negative consequences associated with depression and anxiety disorders during pregnancy, information to guide women and their physicians about treatment options is limited. Current treatments include psychotherapy (see “Nonpharmacological treatments during pregnancy and lactation,” elsewhere in this issue) and pharmacotherapy. Antidepressant medications—including selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs)—remain the first choice of drugs for treating mood and anxiety disorders during pregnancy and lactation.

Antidepressant use during pregnancy

Of all of the medications used in pregnancy, antidepressants have the largest body of research, the results of which are now being integrated into clinical practice. The short-term effects of fetal exposure to SSRIs have been documented in several case reports and case series (see **Table 1**), while long-term effects are still being explored.

Many women, unless otherwise informed, will discontinue pharma-

cotherapy once pregnancy is confirmed. Health care providers in general are reluctant to prescribe medications for mood and anxiety disorders in pregnancy. However, research shows that relapse rates associated with discontinuing medication are high and have a rapid onset.¹¹ The risks of not treating or of discontinuing treatment during pregnancy must always be weighed against the risk of medication exposure to the fetus, and this should be done on an individual basis for each patient.

Antidepressant use during lactation

All psychotropic medications are found in breast milk in varying amounts, thereby exposing the nursing infant. Thus, when pharmacotherapy is indicated for a postnatal woman, the treating clinician should inform

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Table 1. Effects of exposure to SSRIs, SNRIs, and other antidepressants during pregnancy.

Medication	Effects	References
fluoxetine (Prozac)	Exposure is not associated with increased teratogenic effects in humans, but perinatal effects of third-trimester exposure have been reported. Earlier studies indicated minor malformations in the neonates. However, a study of 55 preschool children exposed to fluoxetine in utero reported no long-term adverse effects with respect to IQ, language, or behavior. A recent follow-up study of 40 children exposed in utero and followed for 15–71 months also reported no effect on cognition, language, or temperament.	1-3
paroxetine (Paxil)	One case series involving 97 exposures to paroxetine in pregnancy did not indicate any increased risk of major malformations. One recent report indicates temporary neonatal respiratory distress associated with late third-trimester paroxetine use in 12 infants, which resolved with no residual effects.	4, 5
fluvoxamine (Luvox)	A case study of 26 infants exposed to fluvoxamine in utero reported that exposure was not associated with increased risk of malformations, lower birth weights, or younger gestational age.	5
sertraline (Zoloft)	A case study of 147 infants exposed to sertraline in utero reported that exposure was not associated with increased risk of malformations, lower birth weights, or younger gestational age.	5
citalopram (Celexa)	A review of 375 cases of citalopram exposure in early pregnancy found that the rate of congenital anomalies was no higher than that for other SSRI exposures or for the general population.	6
venlafaxine (Effexor)	150 women exposed to venlafaxine during the first trimester were monitored. No adverse effects in infants were noted.	7
mirtazapine (Remeron)	Two case studies of pregnancies with early exposure to mirtazapine reported no adverse effects. In another study, seven women exposed to mirtazapine in the first and second trimester delivered healthy babies.	8, 9
bupropion (Wellbutrin)	There are no human data published, although a bupropion registry exists.	10

Establish an accurate diagnosis during pregnancy.

- Take history and perform drug screen.
- Involve partner.
- Consider use of psychotherapy, combination therapy, and psychoeducation.
- Refer and consult as needed.

Watch for recurrent depression leading to relapse during perinatal period.

- If medications are discontinued upon conception and relapse occurs, reinstate.
- Use a single medication rather than multiple medications.
- Do not switch medications if current regimen is effective.
- Make sure communication lines are open between psychiatrist and obstetrician.
- Make sure all health care providers (primary care physician, midwife, nurses, etc.) are aware of diagnosis and treatment plans.

Monitor breast milk and infant serum levels.

Monitor short- and long-term infant neurodevelopment.

Consider maintenance and relapse prevention.

- Follow patient for at least 1 year after remission (longer if breastfeeding, cycling) based on prior episode.
- Discuss future pregnancies and risk of recurrence.
- Ensure adequate follow-up in the community.

Figure. Clinical guidelines for antidepressant use in pregnancy and lactation.

her of this and help her make an informed decision. The medications used most commonly to treat depression in the postpartum period are the SSRIs and SNRIs. The growing body of literature on breast-milk-exposed infants is impressive (see **Table 2**). The short- and long-term developmental effects on infants exposed to these agents are currently being investigated in the BC Reproductive Mental Health program.

Conclusions

Treating pregnant and breastfeeding women for depression and anxiety can be a challenge (see the **Figure**). Most women expect to be emotionally and physically well during pregnancy and postpartum. Therefore, when a woman experiences the onset of depression or anxiety, it comes as a surprise to both her and her caregivers. Because prenatal consultation does not include an assessment of mental health before

and during pregnancy, women at high risk are often not identified. When pregnancy ensues, and depression occurs concomitantly, distinguishing between the signs of pregnancy and the symptoms of depression can be difficult, even for an experienced clinician. Once the diagnosis is made, it is important to involve the woman and her partner in the treatment from the outset. This improves compliance, avoids discontinuation of treatment,

Table 2. Effects of exposure to SSRIs, SNRIs, and other antidepressants during lactation.

Medication	Effects	References
fluoxetine (Prozac)	Low levels of fluoxetine and its main metabolite, norfluoxetine, found in the sera of infants. Some short-term adverse effects have been reported, including colic, seizures, irritability, withdrawal symptoms, and cyanosis.	12-15
paroxetine (Paxil)	Undetected or very low levels of paroxetine found in the sera of infants. No adverse effects have been reported.	16-22
fluvoxamine (Luvox)	Low levels of fluvoxamine found in the sera of all infants exposed through breast milk. No adverse effects have been reported.	20, 23, 24
sertraline (Zoloft)	Low levels of both sertraline and its metabolite found in the sera of infants. One study reported that sertraline was significantly more likely to be detected in an infant if the maternal daily dose was 100 mg or higher. No adverse effects have been reported.	25-27
citalopram (Celexa)	Low levels of citalopram and its metabolite found in all studies. Only one adverse effect, uneasy sleep, has been noted in one study.	28-30
venlafaxine (Effexor)	In 12 documented cases of exposure to venlafaxine, no adverse effects in infants have been reported.	31-33
mirtazapine (Remeron)	No human data published.	none
bupropion (Wellbutrin)	Peak effects found 1–2 hours after dose in three case studies.	34, 35

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and consequently reduces the risk of relapse.

All SSRI and SNRI antidepressants are transferred through the placenta (J. Kim, S. Misri, D. Rurak, et al., unpublished data, 2004). Sertraline and its metabolite, and paroxetine, which has no metabolite, transfer at a lower rate than fluoxetine and its metabolite norfluoxetine. However, the potency of all three medications is high. Clinically, the recommendation at present is to continue the antidepressant medication that the woman has responded to best during pregnancy. The key is *not* to switch medications in pregnancy. Monotherapy is preferred to the use of multiple medications. For best practice guidelines and other information for patients, physicians, and caregivers, refer to www.bcrmh.com and www.wellmother.com.

In the light of current literature on the relative safety of exposure to SSRIs and SNRIs in pregnancy, exposure to SSRIs through breast milk is clearly less of a concern. The impact of untreated maternal depression and anxiety on the developing fetus and the infant is a far more serious concern to reproductive psychiatrists. Studies show that untreated maternal depression has a negative impact on mother-infant bonding and leads to attachment issues thereafter.^{36,37} Health professionals must give careful consideration to prescribing antidepressants for both the pregnant and breastfeeding woman.

Competing interests

None declared.

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