

Breastfeeding and Antidepressants: Clinical Dilemmas and Expert Perspectives

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There is often apprehension about use of antidepressants during breastfeeding. Clinical decision-making regarding breastfeeding and psychotropic use remains an art with some scientific data to guide practice. Clinical experience from experts is invaluable in an area with an incomplete evidence base. To that end, this review will include evidence from the literature infused with comments on important clinical questions from leaders in the field of perinatal psychiatry. In an online forum for perinatal psychiatrists, Teri Pearlstein, M.D., recently posited for discussion questions about antidepressants and breastfeeding. With the permission of those cited, comments from colleagues who are experts in this area are woven into this review.

Postpartum Major Depression

Consideration of medication exposure via breastfeeding is informed by an imperfect literature, and there is often an underappreciation of the consequences of untreated maternal depression on the mother-baby dyad. Postpartum depression affects approximately 10% to 15% of mothers after delivery.¹ It has negative consequences for child development, and a compelling amount of data from animal models supports the negative impact of depression on the young.^{1,2} Mother-infant attachment and interaction are crucial in the postpartum.³ In addition, the impact of a mother's depression on older children must also be considered. The treatment of a mother's depression to remission has been demonstrated to have a positive impact on the mental health of her children.⁴

Therefore, it is not surprising that experts in perinatal psychiatry consider maternal remission as paramount to any discussion of risks and benefits. As described by Lee Cohen, M.D., mood disorder treatment during breastfeeding must focus on "the importance of sustaining maternal euthymia and the potential effects of maternal affective dysregulation on behavioral development in the child." Katherine Wisner, M.D., M.S., states, "I am more intent on managing the mother's mood state to allow her to interact with the developing baby—that is important for brain development in the baby." Jennifer Payne, M.D., concurs, "My approach has always been to emphasize the need for euthymia for mom."

Deciding Whether To Breastfeed

Ideally, breast milk is best for infant feeding.⁵ It is important to consider that breastfeeding is often difficult, such that an entire profession of care providers has emerged to address difficulties, namely lactation consultants. As health care professionals, we can play an important role in putting breastfeeding into context. Although it is ideal, women do not have to breastfeed. If it is causing a mother distress and interfering with her mood, acceptance of treatment, and/or general enjoyment of her baby and new role as mother, we can help allay her guilt and give permission for her to stop breastfeeding.

Zachary Stowe, M.D., states, "Women do not have to breastfeed. . . . In my mind it is not an issue of whether or not to breastfeed, but whether or not the mother needs to be treated—be it pharmacologically, with psychotherapeutic interventions, etc. The data regarding untreated illness on infant well-being are fairly substantial." Laura Miller, M.D., states, "For some depressed women, breastfeeding is highly stressful. For others, it is a relaxing, positive experience that helps them feel competent as mothers." Where formula and clean water are not

readily available, breastfeeding becomes paramount to infant survival. As stated by Dr. Bavanisha Vythilingum, "In the developing world, many women have to breastfeed, as formula is unaffordable. It's really reassuring for me to read about the relative safety of antidepressants in breastfeeding."

Use of Antidepressants During Breastfeeding

Long-term data regarding infant exposures via breast milk are lacking, and there is a fair amount of uncertainty regarding whether exposure via breastfeeding poses long-term risks.^{6,7} However, the long-term risks of untreated maternal depression are well documented and impact many aspects of child development. States Dr. Stowe, "As a class, antidepressants have more detailed data in breastfeeding than any other class of medication. There are very limited data on long-term effects, if any, but the same is true for virtually all medications in breastfeeding."

Safety Data

Two types of publications inform the "safety" of psychotropics during breastfeeding. The first type serves us fairly well. These are studies that focus on quantifying the amount of exposure to babies by measuring medication levels in breast milk and infant serum. The second type, in my opinion, often distracts us from our mission of evidence-based medicine. These are case reports of suspected adverse events, and in many cases are reports of just a single baby, with observations that are difficult to interpret.

Excellent reviews have been done on this topic by Burt et al.⁸ and Weissman et al.,⁹ among others. Study methodology in this area involves enrollment of maternal-baby dyads and quantification of drug and metabolite levels in breast milk and infant blood. Due to the long half-life of fluoxetine and the immature metabolic systems of newborns, we might suspect that newborns would potentially have higher relative levels of fluoxetine compared with other antidepressants. The literature is mixed in this area, with detectable newborn levels more likely at higher doses¹⁰ and studies generally showing low levels of exposure and a lack of adverse events.¹⁰⁻¹³ High levels have been reported with colicky symptoms, and infant monitoring for clinical symptoms appears warranted, particularly with higher doses.^{10,14} In terms of other antidepressants, sertraline and paroxetine have received the most study with the greatest number of mother-infant pairs studied, with both drugs' exposure via breastfeeding appearing relatively low in breast milk and infant blood samples. In smaller numbers, reassuring data regarding low levels in breast milk and infant blood levels have been documented for venlafaxine, citalopram, mirtazapine, and bupropion.^{8,9}

Can Women Breastfeed While Using Antidepressant Medications?

There is no contraindication to breastfeeding posed by antidepressant use. Although we lack long-term data, the alternative of untreated maternal depression has broad and devastating effects. The risks and benefits should be considered carefully with the woman and her partner, and whenever possible the baby's pediatrician should be included in the discussion and informed of the treatment plan. There is little consensus on what antidepressant to start in a breastfeeding woman, but most experts say that if a woman has had a good response in the past to a particular antidepressant, then it is among the top choices. Dr.

Miller reminds us to consider future pregnancies when selecting an antidepressant in postpartum women. Kimberly Yonkers, M.D., also considers bupropion for mothers who smoke, as maternal smoking poses risks for the infant and bupropion is approved for smoking cessation.

States Adrienne Einarson, "Any of the antidepressants are OK to use and breastfeed, as so little gets in the breast milk. The woman should take whichever one is effective for her." Regarding infant safety, a woman should be advised to alert her psychiatrist and the baby's pediatrician if she notes any changes in her baby's behavior after she starts taking an antidepressant while breastfeeding. Additionally, the use of concomitant medications (prescribed and over-the-counter) and substances should be documented, from both a clinical and a medical-legal perspective of exposures.

Switching Medications

Does it make sense to employ a switch strategy of changing medication from one used during pregnancy to a different one during breastfeeding on the basis of published data regarding infant safety and exposure? For example, should women be switched from a different medication to sertraline or paroxetine or another medication if there are more data on that drug versus the one she is currently taking?

The question is often raised regarding whether a woman who wants to breastfeed should be switched from a medication to which she is known to respond to another antidepressant with more data in breastfeeding. Some psychiatrists wonder if women should be switched from the antidepressant used during the pregnancy to another with more data for breastfeeding. Most experts express that maternal wellness must be considered most important, and the postpartum is not a good time for multiple medication trials. If an individual patient has had a good response to a particular antidepressant, continuing treatment with it is a reasonable and prudent option.

Margaret Spinelli, M.D., states that it makes sense to stick with a drug that worked well during pregnancy, stating that "therefore we decrease double drug exposure to the infant." Dr. Stowe concurs, "Arguably, you can not apply the available data to support switching agents from pregnancy to breastfeeding." Dr. Wisner adds, "The issue of breastfeeding must also be cast in light of the minimal exposure received compared to that during pregnancy." Dr. Cohen warns against seemingly arbitrary switches in medication and urges, "Do not jeopardize maternal euthymia by switching antidepressants when a woman is well." Dr. Miller emphasizes a collaborative approach based on patient preference. She states, "Whether to risk switching to a better-studied medication for perinatal use is ultimately up to the woman."

Medication Selection in Breastfeeding Women Who Have Not Previously Used an Antidepressant

When selecting an antidepressant in a woman who has not had previous trials, sertraline and paroxetine are often preferred based on availability of reassuring data. States Vivien Burt, M.D., Ph.D., "My first choices are paroxetine or sertraline." States Dr. Stowe, "If you rank the antidepressants by nursing infant concentration, paroxetine is the lowest, followed by sertraline . . . venlafaxine and bupropion are the highest. But these are not corrected for affinity at the target CNS sites."

Considering the Long Half-Life of Fluoxetine, Should Women Breastfeed While Using It?

C. Neill Epperson, M.D., points out, "We do not have all of the facts regarding pharmacogenetics and how this is likely to contribute to the impact of antidepressants on brain chemistry

and function. . . . I allow women to breastfeed on fluoxetine if this has been helpful to them. I'm unlikely to start it de novo in the postpartum period, but I don't shy away from using it when necessary." Agrees Margaret Chisolm, M.D., "Unless fluoxetine has been of benefit, I tend to avoid it given its long half-life."

Conclusion

In summary, the use of antidepressants during breastfeeding involves careful consideration of the mother's mental health and assessment of the possible risks of exposure to her baby. While the literature is lacking regarding long-term effects for infant antidepressant exposure during breastfeeding, a compelling evidence base cautions against the risks of untreated or under-treated maternal depression for the mother and baby. A collaborative approach involving the woman, her significant other, her psychiatrist, and the baby's pediatrician is ideal.

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REFERENCES

- Altshuler LL, Hendrick V, Cohen LS. Course of mood and anxiety disorders during pregnancy and the postpartum period. *J Clin Psychiatry* 1998;59(suppl 2):29-33
- Newport DJ, Stowe ZN, Nemeroff CB. Parental depression: animal models of an adverse life event. *Am J Psychiatry* 2002;159(8):1265-1283
- Nonacs R, Cohen LS. Postpartum mood disorders: diagnosis and treatment guidelines. *J Clin Psychiatry* 1998;59(suppl 2):34-40
- Weissman MM, Pilowsky DJ, Wickramaratne PJ, et al. STAR*D-Child Team. Remissions in maternal depression and child psychopathology: a STAR*D-Child report. *JAMA* 2006;295(12):1389-1398
- Lawrence RA. Breastfeeding: benefits, risks and alternatives. *Curr Opin Obstet Gynecol* 2000;12(6):519-524
- Pearlstein T. Perinatal depression: treatment options and dilemmas. *J Psychiatry Neurosci* 2008;33(4):302-318
- Newport DJ, Hostetter A, Arnold A, et al. The treatment of postpartum depression: minimizing infant exposures. *J Clin Psychiatry* 2002; 63(suppl 7):31-44
- Burt VK, Suri R, Altshuler L, et al. The use of psychotropic medications during breast-feeding. *Am J Psychiatry* 2001;158(7):1001-1009
- Weissman AM, Levy BT, Hartz AJ, et al. Pooled analysis of antidepressant levels in lactating mothers, breast milk, and nursing infants. *Am J Psychiatry* 2004;161(6):1066-1078
- Hendrick V, Stowe ZN, Altshuler LL, et al. Fluoxetine and norfluoxetine concentrations in nursing infants and breast milk. *Biol Psychiatry* 2001;50(10):775-782
- Taddio A, Ito S, Koren G. Excretion of fluoxetine and its metabolite, norfluoxetine, in human breast milk. *J Clin Pharmacol* 1996;36(1):42-47
- Yoshida K, Smith B, Craggs M, et al. Fluoxetine in breast-milk and developmental outcome of breast-fed infants. *Br J Psychiatry* 1998;172: 175-178
- Kristensen JH, Ilett KF, Hackett LP, et al. Distribution and excretion of fluoxetine and norfluoxetine in human milk. *Br J Clin Pharmacol* 1999; 48(4):521-527
- Lester BM, Cucca J, Andreozzi L, et al. Possible association between fluoxetine hydrochloride and colic in an infant. *J Am Acad Child Adolesc Psychiatry* 1993;32(6):1253-1255

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