Evolving practice in perinatal psychopharmacology: Lessons learned

The following post was first published in OB/GYN News. Please see our OB/GYN News archives here.

Publish date: July 3, 2017

Over the last 2 decades, there has been a growing interest in establishing a rich evidence base for treatment of psychiatric illness in pregnancy and the postpartum period. It seems as if a week does not go by when we don’t find multiple publications in the scientific literature describing a new finding or confirmation or inconsistency with existing data – whether it is a small prospective cohort study or an elegant analysis of a large administrative database. The goals of these reports center on refining our knowledge of safe treatments for perinatal psychiatric disorders.

Despite these strides, my colleagues and I frequently see a divergence between recommendations in the literature and what is done clinically by those who treat women around reproductive associated psychiatric disturbance – premenstrual dysphoric disorder or psychiatric disorder during pregnancy and the postpartum period. In some cases, scientific evidence has not filtered into day to day practice and some physicians continue to follow practices that, while outdated, make intuitive sense. In other clinical situations, limited evidence is being applied too broadly or data are too sparse to clearly inform practice. Regardless of the reason, we frequently see patients in clinical situations in which we are forced to rethink the clinical rationale for advice they have received or the clinical path taken.

Here is a sample of the clinical scenarios in which we have seen inconsistencies between current practice and the best evidence in perinatal psychiatry or situations in which data are too sparse to inform the clearest clinical path.

1. Discontinuation of antidepressants proximate to conception

Despite multiple studies supporting the high risk for relapse of major depression in women on maintenance antidepressant therapy with a history of recurrent depressive illness, it is still quite common for clinicians to routinely advise women to stop antidepressants while planning a pregnancy or after documentation of a pregnancy, regardless of the severity of the underlying illness. This runs counter to data showing high rates of relapse in women who stop antidepressants proximate to conception, the safety of antidepressants in pregnancy, and the harm to the mother and fetus when depression during pregnancy is untreated.

2. Use of a lower dose of antidepressants during pregnancy

It makes intuitive sense to use the smallest dose of medicine like antidepressant during pregnancy. However, multiple studies show that, at least in nonpregnant patients, the dose that gets patients well is typically the dose that keeps them well. One of the quickest paths to relapse in depression is a reduction in the antidepressant dose after someone has gotten well. This is even more relevant in pregnant patients because pregnancy itself dilutes the plasma level of the antidepressant given the rapidly expanding plasma volume seen in pregnancy. One can debate whether clinicians should empirically increase the dose of antidepressant during pregnancy to sustain plasma level of medication, but lowering the dose of this medication proximate or during pregnancy makes little sense.
3. A switch to sertraline in pregnancy/post partum

Another scenario that my colleagues and I often see is a pregnant patient whose depression was previously well controlled with a particular antidepressant, but whose physician, once she decides to conceive or becomes pregnant, switched her to sertraline.

The idea, which has been around for a long time, is that sertraline is the safest antidepressant for pregnant women because it has robust reproductive safety data and has particularly modest amounts of medication (if detected at all) in the plasma of infants of mothers who breastfeed while using the medicine. While we certainly have more safety data on SSRIs that were manufactured earlier, as compared with antidepressants that became available later, we have now accumulated data that fails to demonstrate a clear signal for teratogenicity across many antidepressants manufactured over the last 2 decades. Identifying an antidepressant for a given patient to which she will respond can be a challenging course for the patient. Achieving euthymia and subsequently switching to sertraline or another medication may only put her at risk for recurrence of depression and its attendant morbidity.

4. A change to a Category B label drug

This is another example of switching a patient to a potentially less effective drug in a somewhat misguided effort at finding a treatment that is safer in pregnancy. While the Food and Drug Administration’s drug category label system was a step forward, or at least a well intentioned effort to give women and their clinicians clearer insight into the reproductive safety of a medication, ultimately, the incomplete nature of the information caused the agency to transition to a new system (see the Pregnancy Labeling and Lactation Rule). Switching a woman to a category B medicine with sparse reproductive safety data instead of a category C medicine, which may not be unsafe but has raised some concerns in animal models, is not a better choice. The new labeling system is a step forward.

5. Discontinuation of lithium during pregnancy

Like discontinuation of antidepressants, the discontinuation of lithium during attempts to conceive in a woman whose illness has been well controlled, is associated with a high risk of relapse. In earlier work, it was sometimes recommended that discontinuation of lithium be considered after a long period of wellness. We have learned over time that this can be a risky move. Even women with a remote history of bipolar disorder appear to be at high risk of relapse when a mood stabilizer is stopped. Exquisite response to medicine does not imply less severe illness. Women who have bipolar disorder who have sustained euthymia on lithium should consider maintaining the safest possible regimen before, during, and after pregnancy despite the known small teratogenic risk associated with fetal exposure to this agent.

6. Try supplements or alternative therapies

Out of a desire to avoid any medication with incomplete reproductive safety data, some women and clinicians make the intuitive leap that “alternative treatments” can mitigate relapse in pregnancy, and they stop pharmacological treatments and switch to supplements or alternative therapies, including acupuncture, massage, or light therapy. Unfortunately, data supporting this clinical maneuver are sparse. Frequently, we see women with past histories of severe depression who have stopped antidepressants and who have started supplements as a substitute and who then relapse. Then, they try to restore euthymia with antidepressants and psychotherapy, and the road to restoration of well-being can be long.

Data on efficacy of alternative therapies continues to evolve and is an exciting and important area of research. However, where these treatments are best employed in the algorithm for treating depression in pregnancy, or at other times, has yet to be adequately defined.
7. Stop breastfeeding or defer antidepressant treatment

Many women continue to be counseled to either stop breastfeeding while using antidepressants or to defer treatment with antidepressants if they wish to breastfeed. Not uncommonly, we see women who are suffering from postpartum depression and who are engaged in psychotherapy but who have deferred treatment with antidepressants despite residual depressive symptoms that impair functioning. Clinicians should keep in mind that data supporting evidence of toxicity in newborns of women using antidepressants while breastfeeding are extremely sparse. Unfortunately, some women with postpartum depression are deferring treatment because they were counseled that it is not compatible with their desire to breastfeed.

8. Use of non-benzodiazepine sedative-hypnotics

Insomnia is a common problem in pregnancy, especially when coupled with comorbid anxiety, and, increasingly, it is being treated with non-benzodiazepine sedative-hypnotics. Clinicians should keep in mind that a known small risk may be better than an unknown risk. If a pregnant woman has severe insomnia, she may benefit from a low dose of a benzodiazepine, such as lorazepam or clonazepam, as opposed to a medication such as zolpidem for which reproductive safety data are particularly limited.

9. Pumping and dumping breast milk

Many women are advised to set an alarm to “pump and dump” their breast milk to minimize their baby’s exposure to antidepressants during breastfeeding. Early literature to pump and dump breast milk at peak antidepressant concentration was of great analytic and theoretical interest but has scant clinical application. As an author of many of those early publications, I can say that we never intended for women to sacrifice precious sleep to dump breast milk with the idea that limiting exposure to trace amounts of antidepressants would have beneficial effects over the long term.

10. Failure to bring up contraception use

We continue to see a 50% unplanned pregnancy rate across sociodemographic groups in the United States. This is a critical statistic because it may affect how treatment is managed. Bringing up the topic of reliable contraception prior to pregnancy allows for planned pregnancy and affords us the time to discuss treatment options and the ability to plot a more thoughtful and safe clinical course. However, often, contraception is not discussed.

One of our goals as clinicians is to, first, do no harm and that continues to be a challenge because the data in perinatal psychiatry is still inconsistent in some areas and there are evidence gaps in others. Nevertheless, our task is to take the best available data along with the patient’s wishes and knowledge of her past clinical history and to then translate that into the best care for the individual.

Dr. Cohen is the director of the Ammon-Pinizzotto Center for Women’s Mental Health at Massachusetts General Hospital in Boston, which provides information resources and conducts clinical care and research in reproductive mental health. He has been a consultant to manufacturers of psychiatric medications.