Perinatal Psychiatry: Risk Factors, Treatment Data, and Specific Challenges for Clinical Researchers

Perinatal psychiatric conditions that require intervention are common, and treatment decisions are complex. The psychosocial, psychodynamic, and medical aspects of pregnancy and new motherhood pose challenges and opportunities for our field. The interface between obstetrics and mental health is an area clouded by clinical dilemmas, as care is too often practiced without a net of an evidence base. Ideally, in consideration of the unique issues of fetal and infant exposure, we would be able to offer pregnant and breastfeeding women a wide range of treatment options with strong efficacy and safety data. Instead, we have emerging evidence that is rarely definitive and that often conflicts with other data, making the integration and comprehension of reports in this area a daunting task for psychiatrists and their patients.

In psychiatry, the topic of pregnancy often is discussed amid controversy, conflicting information, and treatment dilemmas pertaining to fetal psychotropic medication exposure and effects upon infants. The psychosocial aspects of pregnancy are compelling in their own right, as demonstrated in this issue by Brandon et al., who found that measures indicative of strong mother-fetal attachment and healthy partner relationships are associated with a protective effect on maternal mood in this understudied population. While it is known that pregnancy does not protect against major depressive episodes,[1–3] high-risk pregnancy has received little focused attention. Brandon et al. report that among women hospitalized during pregnancy for obstetric complications, a large proportion (44.2%) had scores consistent with high likelihood of major depressive disorder (MDD) on the Edinburgh Postnatal Depression Scale (EPDS) (with validated diagnoses of MDD in a subgroup). High attachment to the fetus was associated with lower EPDS scores, while partner relationship dissatisfaction was associated with higher scores. These findings suggest that maternal depression may exact a toll on the entire family even before the birth of the baby. The authors identify the woman's relationship with her significant other as an area in which targeted interventions might be developed.

When a pregnant woman with MDD presents for treatment, the risks and benefits of antidepressant medication are considered as impacting both mother and baby. Many women and their health care providers prefer the use of nonmedication treatments, and omega-3 fatty acids have received study for MDD and more recently perinatal depression. Omega-3 fatty acids are particularly attractive as a potential treatment for perinatal depression, as they are required for optimal central nervous system growth and development in utero and in infants. In this issue, Su et al. present double-blind, placebo-controlled data from a small trial in which omega-3 fatty acids (3.4 g/day of eicosapentaenoic acid and docosahexaenoic acid) were provided to 36 pregnant women with MDD. The omega-3 fatty acid group had significantly lower Hamilton Rating Scale for Depression scores than the placebo group at the end of the study and a significantly higher response rate. However, these promising results conflict with 2 recently published studies by Rees et al.[4] and Freeman et al.,[5] both of which failed to find a benefit of omega-3 fatty acids over placebo in small studies of women with perinatal depression. The study by Rees and colleagues[4] had only 26 subjects, and in the study by Freeman et al. (N = 59),[5] 1 major limitation was that omega-3 fatty acids and placebo were adjunctive to supportive psychotherapy that was provided to both groups and appeared highly efficacious. Therefore, small studies completed independently have delivered conflicting findings, and only larger studies can adequately determine the antidepressant efficacy of omega-3 fatty acids.

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When antidepressant medications are started or continued in pregnancy, there are few data to guide their use and dosing. In this issue, Sit et al. provide much needed data that will inform future research in this area. Physiologic changes of pregnancy may influence antidepressant levels in pregnant women, and since we do not routinely assess levels of newer antidepressants, little is known about medication levels across pregnancy. Pharmacokinetic studies may help to inform dosing guidelines and suggest that in late pregnancy, particular vigilance is required to make sure that therapeutic gains are maintained.

Yonkers et al. contribute an important article in this issue, representing one of the largest studies of antidepressants for postpartum depression published to date and only the second placebo-controlled study of an antidepressant. As the investigators demonstrated, among 70 women with postpartum-onset MDD, paroxetine did not appear to have a significant benefit over placebo in terms of the primary measures of depressive symptoms, such as the Clinical Global Impressions scale. Although mean improvement was found on secondary measures, this study demonstrates some of the difficulties in the assessment of treatments for perinatal depression.

The studies by Su et al. and Yonkers et al. in this issue demonstrate that women with perinatal depression are difficult to enroll and retain in treatment studies, as Su et al. had a small study sample with only two thirds of women completing the entire study, and Yonkers et al. enrolled fewer patients than planned, with 31 of 70 completing the trial. It may be that perinatal women are particularly overwhelmed and find study participation to be a great challenge, possibly due to the physical demands of pregnancy and the postpartum, frequency of prenatal obstetrical visits, and care of a new baby.

An inherent problem with small studies designed to treat MDD is that it is often difficult to demonstrate a separation from placebo, even with treatments with the most evidence to support their efficacy. In fact, this problem has been recently highlighted by a major study that found little difference in large-scale placebo-controlled trials of antidepressants with U.S. Food and Drug Administration indications for MDD.[6] This is indeed the case as treatments are studied in perinatal depression, and many studies include small numbers of participants.

The safety of antipsychotics in the context of breastfeeding is the topic of a systematic review in this issue by Gentile. The safety of antipsychotics is a topic of little formal study and great clinical significance. Women with schizophrenia and bipolar disorder often require ongoing treatment with antipsychotic medication, and the postpartum is a particularly high-risk time for relapse in women with bipolar disorder.[7] Postpartum psychosis, which may represent a new-onset psychotic or affective disorder or recurrence of a chronic disorder, is a serious and usually emergent condition that poses risks, including suicide and infanticide. Many women with psychiatric disorders require antipsychotic treatment in the postpartum, and few data inform questions about safety of use in breastfeeding. A small number of case reports in a context of few safety data lead Dr. Gentile to urge caution with clozapine and olanzapine in breastfeeding women who require commencement of an antipsychotic medication. Due to the serious risks of psychosis in the postpartum, he generally suggests use of continuation of a regimen of an antipsychotic that is effective for the individual. Dr. Gentile emphasizes the importance of nonmedication interventions as well, such as mother-baby hospital units, support of maternal-infant attachment, and psychoeducational programs.

We are grateful to the authors of the articles in this Focus on Women's Mental Health section for their contributions and efforts in the area of perinatal psychiatry.

Please contact me with any feedback or suggestions for this section at mfreeman@psychiatrist.com.

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