Section Contents

Introduction

The articles selected for this month's Focus on Women's Mental Health section all pertain to perinatal psychiatry—considerations pertaining to psychiatric illness during pregnancy and the postpartum.

Dr Gideon Koren, an international leader in the assessment of prenatal exposures to medications, provides us with a comprehensive context for understanding such exposures. His commentary was written at our invitation specifically in regard to an article in this section by Sutter-Dallay and colleagues, but his thoughtful comments are relevant to our other selections, as well as most articles on the topic of psychotropic medication use during pregnancy. Dr Koren draws attention to a critical point in the assessment of the risk of medications, which is the lack of ability to clearly attribute adverse effects to medication or to the underlying illness for which they are used, as well as the severity to which they are experienced during pregnancy. He states, "In counseling women with serious psychiatric conditions, we commonly find . . . that patients are ready to avoid drug therapy even in grave clinical situations, not recognizing the dangers of remaining untreated." Indeed, it is plausible that women who do take psychotropic medications during pregnancy are more ill than their counterparts who do not, and many may be undertreated due to fear about medication exposure. Additionally, optimal control groups are not possible in studies that are not randomized, although many investigators seek to use control groups to understand exposure to both medication and illness during pregnancy. Koren points out, correctly, that one cannot infer direct effects of medication exposure during pregnancy from this study or others, but rather associations between medication use and particular outcomes.

Sutter-Dallay and colleagues' article provides data on several classes of psychotropics and neonatal outcomes after in utero exposure. This research was driven by the limitations of the current data showing an increased risk of obstetrical and neonatal complications with psychotropic medication exposures, generally not controlling for concomitant medication exposures or maternal diagnosis. Participants were women with their babies on specialized inpatient hospital units in France, mother-baby units (MBUs), a model of postpartum psychiatric care delivery that is rarely available in the United States. The primary outcomes were low birth weight, preterm birth, and neonatal hospitalization. Women were recruited postpartum from the MBUs, and exposures to medications during pregnancy were determined retrospectively, by maternal report and medical records. Medications were divided into classes, including mood stabilizers (lithium and anticonvulsants), antidepressants, antipsychotics, and anxiolytics/hypnotics. Timing of exposures by trimesters was also collected.

Forty percent of women on the MBUs used at least 1 psychotropic medication during pregnancy. Compared with those who had not used medication, those with psychotropic drug use had a higher education level, presented more often with psychotic disorders, were more likely to smoke, and had more frequent psychiatric hospitalizations. The researchers found that low birth weight was associated with mood stabilizer use, but not with use of the other classes of medications; there were no associations with any of the medication classes and preterm birth. Neonatal hospitalizations were significantly more likely among infants who had been exposed during pregnancy to antipsychotics, antidepressants, and anxiolytics/hypnotics. As discussed in the article, the reasons for neonatal hospitalizations were not assessed and may have included poor neonatal adaptation, but not necessarily so. As the authors point out, a major limitation of the study is that the sample consisted of subjects who were hospitalized on MBUs during the first year postpartum, and they may not be representative of all women who used psychotropics during pregnancy. In fact, they note that since

inpatient hospitalization represents intensive treatment, it is likely that these patients represent those with psychiatric illness that is more severe than in patients who are treated on an outpatient basis and not hospitalized. The authors also discuss that while many women do indeed require treatment with medication for psychiatric disorders during pregnancy, their findings underscore the need for close follow-up of infants.

While Sutter-Dallay and colleagues focused on outcomes in the immediate neonatal period, Dr Irena Nulman and coworkers present data regarding longer term outcomes after exposure to serotonin reuptake inhibitors (SRIs). As the authors discuss in their introduction, longer term outcomes in behavioral teratology are difficult to ascertain, requiring much investment of time and resources to provide meaningful data. In this article, the authors sought to assess the impact of SRI antidepressants on neurodevelopment. To do so, they enrolled sibling pairs whose mothers had verified histories of major depressive disorder; in each pair, 1 sibling was exposed and 1 was not exposed in utero to SRIs. Child assessments included Full Scale IQ, as well as Verbal and Performance IQ measures, and behavioral problem scales completed by the mothers. They found no significant differences between exposed and nonexposed siblings on the Full Scale, Verbal, or Performance IQ measures, nor were there any differences between children with exposure for 1 trimester only versus 2 trimesters or throughout pregnancy. They also found no significant differences between behavioral measures and SRI exposure. However, maternal depression severity was a predictor of behavioral problems.

In another article, Drs Worly and Gur present an extensive and sophisticated review of the available literature on mental illness, psychotropics, gametes, and fertility. They reviewed preclinical and clinical studies as related to males and females. They provide a thorough review of in vitro studies conducted to date on the effect of direct exposure to psychotropics on gametes, animal studies on the effects of psychotropics on reproductive function, and human studies composed of individuals with and without psychiatric disorders. While much attention is paid to psychotropic use in pregnant women, this review comprehensively targets the less frequently highlighted research on prepregnancy considerations among both men and women and among male and female animals. One intriguing finding is that, on the basis of a small number of studies with few participants, there is a question of a negative impact of antidepressants on sperm quality and a risk of DNA fragmentation, the clinical significance of which remains unknown. The authors also provide a detailed review of fertility and psychological factors, acknowledging that this area of research is limited for the most part by the selection of participants who seek treatment for infertility. They examine aspects of psychological distress/stress and fertility, as well as the more limited data regarding psychotropic use and outcomes of assisted reproductive technologies. The authors call for more research into the impact of psychiatric disorders and psychotropic medications on gametes and reproductive outcomes.

In another study, Dr Mary Chong and coinvestigators sought to identify a biomarker of perinatal anxiety and depression, specifically long-chain polyunsaturated fatty acids (PUFAs). This study was derived from the Growing Up in Singapore Toward Healthy Outcomes (GUSTO) study, a prospective mother-child cohort study that enrolled women during pregnancy. PUFAs include eicosapentaenoic acid and docosahexaenoic acid, 2 long-chain omega-3 PUFAs found in fish and fish oil. To date, studies have been inconclusive with regard to the treatment role of omega-3 fatty acids in depression and the use of omega-3 assays as a biomarker for psychiatric illness.

The State-Trait Anxiety Inventory and Edinburgh Postnatal Depression Scale were administered at 26–28 weeks of pregnancy and at 3 months postpartum. Plasma levels of PUFAs were assessed. Seventy percent of participants completed the scales at both time points. Lower omega-3 levels were associated with higher antenatal anxiety scores, although there were no associations between PUFA levels and antenatal depression or postpartum depression or anxiety. As noted by the authors, women with preexisting psychiatric disorders were excluded from the study, leaving out those at greatest risk of psychopathology from inclusion. From this study, there was a limited finding in regard to PUFA status and perinatal depression and anxiety.

We are grateful for these authors' contributions to the field of Perinatal and Reproductive Psychiatry.

Marlene P. Freeman, MD
mfreeman@psychiatrist.com
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