Psychopharmacology in Pregnancy and Breastfeeding

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KEYWORDS

• Pregnancy • Breastfeeding • Antidepressants • Mood stabilizers
• Postpartum depression

KEY POINTS

- Many psychiatric medications can be taken safely during pregnancy and breastfeeding.
- There are significant risks associated with untreated psychiatric illness during pregnancy and postpartum.
- Many studies examining infant outcomes with exposure to psychotropic medications during pregnancy are confounded by illnesses, behaviors, and other risk factors associated with psychiatric illness.

WHY USE PSYCHIATRIC MEDICATIONS DURING PREGNANCY AND BREASTFEEDING?

Antepartum depression has been associated with low maternal weight gain,[1] increased rates of preterm birth,[1,2] low birth weight,[1] increased rates of cigarette, alcohol, and other substance use,[3] increased ambivalence about the pregnancy, and overall worse health status.[4] Children exposed to peripartum depression have higher cortisol levels than those of mothers not depressed,[5–8] and this continues through adolescence.[8] Importantly, maternal treatment of depression during pregnancy may help normalize infant cortisol levels.[9] Although the long-term effects of elevated cortisol are unclear, these findings may partially explain the mechanism for an increased vulnerability to psychopathology in children of antepartum depressed mothers.[10]

In turn, untreated antepartum depression is one of the strongest risk factors for postpartum depression (PPD),[11] and PPD has potentially devastating consequences, including suicide and infanticide. Suicides account for up to 20% of all postpartum deaths and represent one of the leading causes of peripartum mortality.[12] PPD has

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been associated with increased rates of infantile colic and impaired maternal-infant bonding.[13] PPD also interferes with parenting behavior, including less adequate infant safety and healthy child development practices,[14] such as the increased use of harsh discipline.[15] Finally, PPD has significant negative effects on infant development, including IQ, language, and behavior.[16]

Discontinuation of psychiatric medications for pregnancy is also associated with a high relapse rate of both major depression (MDD) and bipolar disorder (BD). Discontinuation of antidepressants in pregnant women with a history of MDD has been linked to relapse in 60% to 70% of women.[17,18] In women with BD, studies demonstrated a recurrence risk of 80% to 100% in pregnant women who discontinue mood stabilizers, whereas women who continued mood stabilizer treatment had a much lower risk of 29% to 37%.[19–21] Many women with psychiatric disorders experience relapse during pregnancy, both on and off medication. In one study, approximately 50% of women with a mood disorder reported significant mood symptoms during and/or after pregnancy.[22] Relapse then exposes the developing infant to the effects of untreated depression, which leads to adverse consequences for the woman, infant, and family.[1,23,24]

CONTROVERSIES AND LIMITATIONS OF THE LITERATURE

The treatment of psychiatric disorders during pregnancy is complicated by the fact that few studies have been conducted to determine which medications are efficacious, how changes in body weight and metabolism may affect dosing, and what alternatives to medications are available that successfully treat psychiatric illness during pregnancy. Thus, treatment decisions must be made with little hard data.

It is also important to understand that the use of psychotropic medications during pregnancy is essentially a "marker" for a population of women with different risk factors than the general population of pregnant women. These risk factors, including health-related behaviors, associated illnesses, and other characteristics, may influence the outcomes of studies attempting to examine the risks of in utero exposure of a psychotropic medication to a child. For example, diabetes, obesity, smoking, and substance use are more common in patients with psychiatric illness than in the general population. Studies that have not controlled for the underlying psychiatric illness and its confounding behaviors and characteristics may find associations between psychotropic medications and outcomes that are not directly caused by exposure to the medication itself, but by characteristics and behaviors that are more highly prevalent in the population of patients who take psychotropic medications during pregnancy.

US FOOD AND DRUG ADMINISTRATION PREGNANCY CATEGORIES AND THE PREGNANCY AND LACTATION LABELING RULE

In 2014, the US Food and Drug Administration (FDA) published the "Pregnancy and Lactation Labeling Rule," mandating changes to the content and format of prescription drug labeling detailing use during pregnancy and breastfeeding. The labeling changes went into effect in 2015 for all new products and will be phased in over time for older medications and products. The new labeling will attempt to summarize all currently available information to help the clinician weigh the risks and benefits of prescribing a drug during pregnancy or breastfeeding.

Because the new labeling will be phased in over time, it is still important to understand the meaning of the former FDA pregnancy categories. Categories include A, B, C, D, and X, and classification is based on the amount of evidence for safety in