

Antidepressants and Pregnancy: Continued Evidence of Harm—Still No Evidence of Benefit

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Antidepressant medication use during pregnancy is increasing. It is essential that women of childbearing age, pregnant women, and their health care providers be aware of the risks, benefits, and alternatives prior to taking these agents. The best available evidence suggests that antidepressant use by pregnant women may be associated with miscarriage, birth defects, preterm birth, decreased birth weight, neonatal behavioral syndrome, persistent pulmonary hypertension in the newborn, neonatal electrocardiogram (EKG) changes, and behavioral effects. Evidence of benefit is lacking. The hope that improved maternal mood through medication would lead to better pregnancy results has not been realized; the antidepressant-exposed pregnancies are faring worse. The available evidence raises the question: Are we exposing a generation of women and their babies to drugs that are causing significantly more harm than good?

Keywords: depression; pregnancy; antidepressants; serotonin reuptake inhibitors

Whether to take an antidepressant during pregnancy is an important decision that must balance maternal mental health considerations with fetal/pregnancy exposure issues. Each pregnant woman and her health care providers must weigh the risks, benefits, and alternatives to medication use in pregnancy. Much attention has focused on the risks of antidepressant use during pregnancy. A significant misconception, however, surrounds the issue of benefit and how maternal medication use may affect obstetrical outcomes.

Numerous studies have now shown antidepressant use during pregnancy to be associated with increased rates of miscarriage (Nakhai-Pour, Broy, & Bérard, 2010), birth defects (Pedersen, Henriksen, Vestergaard, Olsen, & Bech, 2009), preterm birth (Suri et al., 2007), decreased birth weight (Oberlander, Warburton, Misri, Aghajanian, & Hertzman, 2006), neonatal behavioral syndrome (Sanz, De-las-Cuevas, Kiuru, Bate, & Edwards, 2005), persistent pulmonary hypertension in the newborn (Chambers, et al., 2006), neonatal electrocardiogram (EKG) changes (Dubnov-Raz et al., 2008), and behavioral effects (Ruchkin & Martin, 2005). No study has shown any improvement in obstetrical outcomes in women taking antidepressants.

Fluoxetine (Prozac) was launched in the late 1980s and the use of antidepressant medications has risen steadily ever since. Women of childbearing age make up a significant percentage of users, making exposure during pregnancy commonplace. Rates of use during pregnancy have increased over time and are now estimated to be as high as 13.4% (Cooper, Willy, Pont, & Ray, 2007) and rising (Bakker, Kölling, van den Berg, de Walle, & de Jong van den Berg, 2008).

The hope for all who care for pregnant women has been that antidepressant use would lead to improved maternal mood, which would translate into better maternal self-care and the avoidance of habits such as alcohol and tobacco. The improved mood and better habits would, in turn, lead to better obstetrical outcomes: for example, less preterm birth, higher birth weights, and healthier newborns.

This has been the hope for antidepressant use during pregnancy. Unfortunately, the reality tells a different story. Starting in the 1990s, questions were raised about the effects of these drugs on pregnancies. Time and again the studies have shown worsened pregnancy outcomes in those women on antidepressants. At best, some studies show no difference. It is notable that not a single study has ever shown improvement in pregnancy outcomes in those women who are taking medication. The hoped for improvements that theoretically could arise with better maternal mood have not come to fruition.

The most common explanation given for the consistent research finding of increased obstetrical complication rates among antidepressant users is that the depressed pregnant women taking medications are different from the women not on these drugs (i.e., that the between group differences are not adequately controlled for in the studies). Yet, even in the studies that have gone furthest to control for maternal mood (comparing depressed women on antidepressants vs. equally or more depressed women who are not taking medication), the obstetrical outcomes for the women on medication are consistently worse and never better.

One can make the argument that even if maternal antidepressant use worsens obstetric outcomes, antidepressants can be recommended because they improve maternal outcomes and child developmental outcomes. However, in this area too, the evidence is lacking. Although initial published studies—most of which were sponsored by pharmaceutical companies—appeared to suggest significant clinical benefit with antidepressants in nonpregnant populations, full evaluation of the data on antidepressants (including published and unpublished studies submitted to the Food and Drug Administration) has shown little clinical benefit for most patients (Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008). Several authors have drawn the same conclusion regarding this literature (Fournier et al., 2010; Ghaemi, 2008; Moncrieff & Kirsch, 2005; Turner et al., 2008).

Confusion has arisen in studies that have compared pregnant women who stop their antidepressants to those who continue on the medications (Cohen et al., 2006). Worsening symptoms in the cessation group has been interpreted as proof of benefit of the medications without appropriate consideration of the issue of withdrawal. When the serotonin-reuptake inhibitors were first introduced, they were promoted having few withdrawal effects. However, subsequent experience with these agents has demonstrated convincingly that withdrawal from these agents is real and can be associated with several distressing symptoms (Warner, Bobo, Warner, Reid, & Rachal, 2006).

Pregnant women with depression or anxiety need appropriate care and treatment, and it is not necessary to demonstrate improved pregnancy outcomes in order to argue that some women should take antidepressants during pregnancy. Obvious cases spring to mind such as those who are suicidal when not taking antidepressants or those with severe withdrawal when they stop these agents; and for every woman, the choice is personal and should be supported. It is crucial, however, that pregnant women and women of childbearing age be given accurate counseling regarding the risks, benefits, and alternatives when

making this important decision. Given the evidence of increased complication rates with antidepressant use during pregnancy, it is no longer appropriate to counsel women based on a “wishful hypothesis” that improved mood control will result in better pregnancy outcomes. There is no evidence to support that model and continually mounting evidence to the contrary.

A renewed emphasis should be placed on self-help approaches and psychological treatments. Current national guidelines recommend stopping antidepressant therapy during pregnancy in women with mild depression (National Institute for Health and Clinical Excellence [NICE], 2007). These guidelines state:

If a woman being treated for mild depression is taking an antidepressant, the medication should be withdrawn gradually and monitoring (“watchful waiting”) considered. If intervention is then needed, the following should be considered: self-help approaches (guided self-help, computerized cognitive behavioral therapy, exercise) or brief psychological treatments. (p. 27)

With greater than 50% of pregnancies unplanned, it is important that accurate counseling be available to any woman of childbearing age who is considering antidepressant use. Women of childbearing age, pregnant women, and their health care providers need to know that antidepressant use during pregnancy appears to increase the risks of miscarriage, birth defects, preterm birth, and other pregnancy complications. As a class, the agents do not appear to provide clinically significant benefit for most patients with depression when compared with placebo. The hope that improved maternal mood through medication would lead to better pregnancy results has not been realized; the antidepressant-exposed pregnancies are faring worse.

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