

Study suggests too much risk associated with SSRI usage and pregnancy

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Elevated risk of miscarriage, preterm birth, neonatal health complications and possible longer term neurobehavioral abnormalities, including autism, suggest that a class of antidepressants known as selective serotonin reuptake inhibitors (SSRI) should only be prescribed with great caution and with full counseling for women experiencing depression and attempting to get pregnant, say researchers at Beth Israel Deaconess Medical Center, Tufts Medical Center and MetroWest Medical Center.

"Depression and infertility are two complicated conditions that more often than not go hand in hand. And there are no definitive guidelines for treatment," says lead author Alice Domar, Ph.D, Obstetrics and Gynecology, Beth Israel Deaconess Medical Center and Executive Director of the Domar Center for Mind/Body Health at Boston IVF. "We hope to provide a useful analysis of available data to better inform decisions made by women and the providers who care for them."

Domar and colleagues conducted a review of published studies evaluating women with depressive symptoms who took antidepressants while pregnant. The results appear online October 31 in the journal *Human Reproduction*.

"There are three main points that stand out from our review of the scientific studies on this topic," says senior author Adam Urato, MD, Chairman of Obstetrics and Gynecology at MetroWest Medical Center and a Maternal-Fetal Medicine specialist at Tufts Medical Center. "First,

there is clear and concerning evidence of risk with the use of the SSRI antidepressants by pregnant women, evidence that these drugs lead to worsened pregnancy outcomes. Second, there is no evidence of benefit, no evidence that these drugs lead to better outcomes for moms and babies. And third, we feel strongly that patients, obstetrical providers, and the public need to be fully aware of this information."

Over the last 20 years antidepressant usage has increased 400 percent. Antidepressants are now the most commonly prescribed medication in the United States for people between 18 and 44 years of age, the childbearing years for most women. And as women enter their late 30s and early 40s they are more likely to experience infertility.

"According to the Centers for Disease Control, more than 1 percent of the babies born in the USA each year are the result of an IVF cycle," write the authors. "And most women will report symptoms of depression during infertility treatment, especially following unsuccessful treatment cycles."

As many as 11 percent of women undergoing fertility treatment report taking an SSRI to combat depressive symptoms, but Domar and colleagues found no evidence of improved [pregnancy outcomes](#) with antidepressant usage, and in fact, found the opposite. They also found plenty of controversy around SSRI efficacy. Many studies found SSRIs to be no more effective or only slightly more effective than placebos in treating depression. "More broadly, there is little evidence of benefit from the antidepressants prescribed for the majority of women of childbearing age—and there is ample evidence of risk," the authors write.

For starters, there is mounting evidence that SSRIs may decrease pregnancy rates for women undergoing fertility treatment. Additionally, studies consistently show that women using antidepressants experience increased rates of miscarriage. There is also a strong signal of congenital

abnormalities, the most noted of which is the association between the use of the antidepressant, Paxil, and cardiac defects. In 2005, this association prompted the FDA to ask Paxil's manufacturer, GlaxoSmithKline to change Paxil's risk factor from a C to a D, where a D rating indicates a demonstrated risk to the fetus.

"Preterm birth is, perhaps, the most pressing obstetrical complication," write the authors. In more than 30 studies, the evidence overwhelmingly points to increased risk for early delivery in women who are taking antidepressants. "This is a significant finding because we know that babies born before 37 weeks are at risk for many short and long-term health problems," says Urato. "Caring for premature babies adds up to billions of dollars in healthcare expenditures."

Available data also suggests that antidepressant usage, especially if it extends beyond the first trimester, leads to an increased risk of pregnancy-induced hypertension and preeclampsia. "Given the importance of the hypertensive disorders of pregnancy in terms of maternal and newborn morbidity and mortality, and the widespread use of antidepressants during pregnancy, further investigation into this area will be essential," write the authors.

Similarly, long-term exposure to SSRIs appears to correspond to an increased incidence of birth weight falling below the 10th percentile, coupled with increased rates of respiratory distress.

The health complications associated with antidepressant usage can be carried into infancy and beyond. A 2006 study showed that infants exposed to antidepressants in utero had a 30 percent risk of Newborn Behavioral Syndrome, most commonly associated with persistent crying, jitteriness and difficulty feeding. In more rare instances the syndrome can produce seizures and breathing difficulties leading to the need for intubation. Studies have also shown delayed motor development in

babies and toddlers. And a Kaiser Permanente study showed a "two-fold increased risk of autism spectrum disorders associated with maternal treatment with SSRI antidepressants during the pregnancy, with the strongest effect associated with treatment during the first trimester."

"There is enough evidence to strongly recommend that great caution be exercised before prescribing SSRI antidepressants to women who are pregnant or who are attempting to get pregnant, whether or not they are undergoing infertility treatment," says Domar. "We want to stress that depressive symptoms should be taken seriously and should not go untreated prior to or during pregnancy, but there are other options out there that may be as effective, or more effective than SSRIs without all the attendant risks."

Domar and team looked at studies assessing different treatment modalities for depression in the general population, including psychotherapy, exercise, relaxation training, yoga, acupuncture and nutritional supplements. While many of these options were shown to provide some benefit, psychotherapy, specifically cognitive behavioral therapy (CBT) showed the most promise. "There is overwhelming evidence that CBT is equivalent to antidepressant medication in the treatment of mild to moderate depression and more recent research indicates that it is effective in the treatment of severe depression as well," write the authors.

A 2008 study showed impressive results for CBT in depressed women undergoing infertility treatments. The results showed that 79 percent of women who received CBT reported a significant decrease in symptoms, compared with 50 percent of women in the medication group.

"These alternative treatment options may not be appropriate for everyone, still we think it's important for [women](#) on an antidepressant who are considering becoming pregnant to have a conversation with their

physician about the risks and benefits of continuing to take their medication," says Domar. "Because at this point in time, with no data to indicate an advantage to taking an SSRI during pregnancy, the research all points to increased risk."

Provided by Beth Israel Deaconess Medical Center

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