

Antidepressant Medications in Pregnancy

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Antidepressants are commonly used by women in child-bearing age. When antidepressants are used, they can influence the fetus in one of four ways. Antidepressants might be associated with an increased risk of miscarriage, teratogenesis, neonatal toxicity, or long-term neurobehavioral sequelae. As we shall explain later, most commonly used antidepressants were not found to be associated with an increased risk of miscarriage. Omphaloceles, gastroschisis, anencephaly, and craniosynostosis might be slightly more common in the offspring of women taking antidepressants.



Overview of Antidepressant Medications in Pregnancy

The use of [antidepressants](#) in the 3rd trimester **can cause neonatal toxicity**. Withdrawal syndromes have been previously described in neonates whose mothers were taking antidepressants near the delivery time. The long-term effects of antidepressants on the fetus and neonates are controversial.

Tricyclic Antidepressants in Pregnancy

There are no prospective or retrospective studies focusing on the topic of pregnancy loss after prenatal exposure to tricyclic antidepressants. Several prospective and retrospective **studies evaluated the possibility of teratogenicity of tricyclic antidepressants use in the first trimester**. In summary, tricyclic antidepressants do not seem to be associated with a higher risk of teratogenesis.

Neonatal toxicity after the use of tricyclic antidepressants in the third trimester has been reported before. The main **symptoms of neonatal tricyclic antidepressants withdrawal syndrome are jitteriness, irritability, and seizures**. This syndrome is reported in one-quarter of neonates who were exposed to tricyclic antidepressants in utero.

Clomipramine is the only tricyclic antidepressant known to be associated with neonatal seizures after in utero exposure. Tricyclic antidepressants are unlikely to have any long-term neurobehavioral effects on the offspring of women who used the drugs during [pregnancy](#).

Selective Serotonin Reuptake Inhibitors in Antidepressant Medications

Like tricyclic antidepressants, selective serotonin reuptake inhibitors do not seem to be associated with an increased risk of first-trimester miscarriage. Infants who were exposed to fluoxetine in utero might have a slightly increased risk of minor [malformations](#).

Note: Congenital heart defects were found to be slightly more common in infants who were exposed to fluoxetine in utero. Omphaloceles might be more common in infants who were exposed to sertraline. Citalopram, on the other hand, has been associated with a slightly increased risk of neural tube defects.

It is important to note here that while one or two studies reported a slightly increased risk of teratogenicity of selective serotonin reuptake inhibitors, most studies did not.

Paroxetine

The only selective serotonin reuptake inhibitor that might certainly influence the organogenesis of the developing fetus is paroxetine. In utero exposure to paroxetine was associated with an increased risk of atrial and ventricular septal defects; therefore, **maternal use of paroxetine during the first trimester is highly discouraged**. It normally increases the risk for cardiac malformations by 1 % and major malformations by 3 %.

Fluoxetine

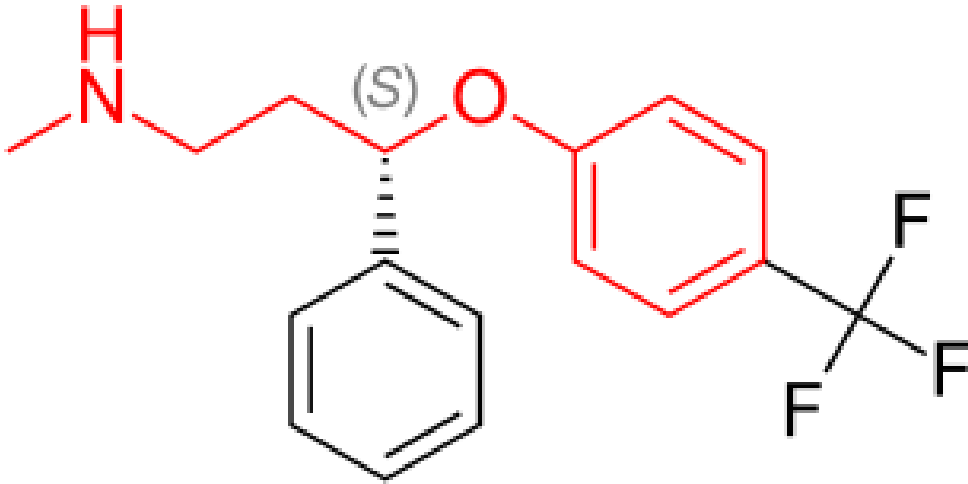


Image: "(S)-fluoxetine" by Vaccinationist. License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

Infants who were exposed to fluoxetine at the time of delivery or near delivery had respiratory distress, feeding problems, and jitteriness. These symptoms were reported as part of a withdrawal syndrome that is specific for selective serotonin reuptake inhibitors. [Persistent pulmonary hypertension](#) of the newborn (PPHN) is unlikely to be associated with in utero exposure to selective serotonin reuptake inhibitors. Only a few, poorly designed, studies reported a weak association between PPHN and maternal use of antidepressants.

Effects

Selective serotonin reuptake inhibitors are unlikely to have any long-term effects on the development of the infant. **Cognition, language, and school performance were not different** between children who were exposed to selective serotonin reuptake inhibitors in utero and those who were not. A recent study, however, pointed towards the possible association between in utero exposure to selective serotonin reuptake inhibitors and autism spectrum disorders.

Monoamine Oxidase Inhibitors (MAOIs) in Pregnancy

In contrast to selective serotonin reuptake inhibitors and tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs) are **definitely associated with an increased risk of teratogenicity**. Congenital malformations were 3.4 times more common in the offspring of women taking MAOIs during pregnancy, compared to women who do not. MAOIs were also found to be associated with an increased risk of PPHN. Because of this, MAOIs should be avoided by pregnant women.

Venlafaxine in Pregnancy

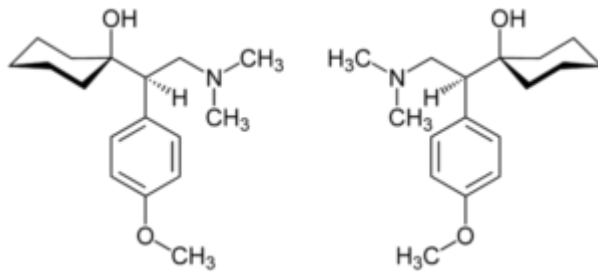


Image: "Venlafaxine Enantiomers Structural Formulae" by Jü.
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Venlafaxine was evaluated in a few studies to see if it is associated with an increased risk of teratogenicity. The use of venlafaxine during pregnancy was **not associated with an increased risk of PPHN, minor, or major congenital malformations**; therefore, venlafaxine was considered as one of the safest antidepressants during pregnancy.

Other Antidepressants and Pregnancy

Mirtazapine

Mirtazapine was evaluated in a small case series (7 pregnant women) and **was found to be safe during pregnancy**; therefore, a large prospective study was performed and it came to the same conclusion. Mirtazapine is unlikely to be associated with any significantly increased risk of congenital malformations. Nefazodone, trazodone, and vilazodone are also safe during pregnancy.

Bupropion

Bupropion might be associated with an increased risk of congenital heart defects. The incidence of congenital heart defects in infants who were exposed to bupropion in utero was 2.1 per 1,000, whereas the incidence was 0.82 per 1,000 in the general population. Accordingly, **bupropion is better avoided during pregnancy**.

Treatment Guidelines for Depressive Symptoms in Pregnancy

Exposure to antidepressants during pregnancy, even if considered as unlikely to be teratogenic, still makes the pregnancy a high-risk one; therefore, proper prenatal planning of the pregnancy is recommended.

Mild depressive symptoms

Mild depressive symptoms during pregnancy can be managed with interpersonal therapy. Women with severe depressive symptoms, those who meet the diagnostic criteria for a major depressive disorder, those with psychotic features, and women who have suicidal ideation should receive a pharmacological intervention. This pharmacological intervention is usually in the form of an antidepressant.

New-onset depression

New-onset depression during pregnancy should be treated with a **selective serotonin reuptake inhibitor**. Venlafaxine is also a reasonable first-line therapy for new-onset

depression during pregnancy. Tricyclic antidepressants are usually ineffective in the management of new-onset depression in pregnancy.

MAOIs

MAOIs should be avoided during pregnancy. Paroxetine and bupropion should be also avoided during pregnancy. The discontinuation of these antidepressants should be gradual to avoid the emergence of withdrawal symptoms or a relapse of a major depressive episode.

The early planning of the pregnancy before conception plays a critical role here, as it can make the treating physician try to gradually discontinue the offending antidepressant before pregnancy. By doing so, one can limit the in-utero exposure to such possibly teratogenic antidepressants.

Use of antidepressants during lactation

The maternal use of antidepressants during lactation is another controversial topic. Tricyclic antidepressants were found in infants' serum after maternal use during lactation; therefore, the current recommendation is to **avoid tricyclic antidepressants during lactation.**

The maternal use of **paroxetine during lactation is deemed to be the safest option.** Paroxetine is usually undetected in the serum of the infant and no side effects were reported in the infant. Changing antidepressants for the woman can cause a relapse; therefore, it might be reasonable to choose an option that is considered as safe during pregnancy and lactation.

Sertraline is reported to be quite safe during pregnancy and, despite being detected in the serum of the breastfed infant, it was not associated with any side effects; therefore, sertraline might be a reasonable option for the mother who does not want to change antidepressants.

Bupropion

Bupropion should be avoided during lactation as it has been associated with neonatal seizures. Fortunately, seizures caused by bupropion in neonates are unlikely to be epileptic and are not associated with epilepsy-specific electroencephalogram findings.

References

Ram D, Gandotra S. [Antidepressants, anxiolytics, and hypnotics in pregnancy and lactation](#). Indian Journal of Psychiatry. 2015;57(Suppl 2):S354-S371. doi:10.4103/0019-5545.161504. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539881/>

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