

The use of antidepressants during pregnancy

Unipolar depression (or major depressive disorder) can affect a woman at any point of her life, including pregnancy. The physical and emotional stresses of pregnancy can exacerbate depression, or even cause its onset. Depression occurs in 7.4% of all pregnant women during the first trimester, and by the third trimester, prevalence increases to 12%.ⁱ These women are often treated with antidepressants, or may already be taking antidepressants when they become pregnant. However, the use of antidepressants during pregnancy may pose a risk to the fetus, so therapy must be chosen carefully and the benefits and risks of such treatment be relayed to the mother. Changing the class of antidepressant or antidepressant cessation altogether can sometimes cause more harm than good to the mother and fetus. Unfortunately, guidelines on the subject are sparse.

What do the guidelines say?

NICE guidelines regarding antenatal and postnatal mental health, last updated in 2010, currently state that tricyclic antidepressants (TCAs) have lower known risks during pregnancy than other antidepressants, including selective serotonin reuptake inhibitors (SSRIs).ⁱⁱ However, a review of these guidelines in 2011 suggests that they should be updated, due to 'potential new evidence that may invalidate current recommendation(s)'.ⁱⁱⁱ The 2011 RCOG guidelines for management of women with mental health issues during pregnancy and the postnatal period state 'For women who develop mild/moderate depression or anxiety during pregnancy, self-help strategies (guided self-help, computerised cognitive behavioural therapy or exercise) should be considered'.^{iv} So what is the correct treatment of depression during pregnancy? Should women taking SSRIs switch to TCAs, and should antidepressants be stopped altogether in favour of CBT?

Is it safe to take antidepressants during pregnancy?

During pregnancy, the maternal and fetal circulations are connected, so any drug taken by the mother can potentially be metabolised by the fetus. SSRIs and TCAs, the two drug classes most commonly used to treat depression, both cross the placenta.^v The low metabolic enzyme activity of the fetus does pose a risk of drug accumulation, however it has been shown that fetal accumulation of SSRIs does not occur.^{vi} Both SSRIs and TCAs have been deemed non-teratogenic, and are safe to be taken during pregnancy, in that the risk of major fetal malformations has not been shown to be greater than the general population risk.^{vii,viii,ix,x,xi} This is with the exception of the SSRI paroxetine, which has been associated with fetal heart defects and is advised against using during pregnancy.^{xii,xiii,xiv} Although SSRIs and TCAs are safe to use in pregnancy, they do have the adverse effect of causing withdrawal in some neonates. However, symptoms persist for no longer than 1 month with either antidepressant^{xv}, suggesting that this short lived side effect may not outweigh the benefits of antidepressant treatment during pregnancy.

Should antidepressant use be stopped altogether?

There is a five-fold increase in risk of relapse of depression during pregnancy in women after cessation of antidepressants.^{xvi} So lack of antidepressant use is potentially detrimental to the

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mother and may alter her care of her baby. Untreated depression during pregnancy can potentially cause the fetus to suffer from chronic antenatal stress, where both maternal and fetal plasma cortisol are raised.^{xvii} Chronic antenatal stress has been linked with shyness, anxiety disorders and, most often, attention deficit hyperactivity disorder in childhood.^{xviii}

Should SSRI use be stopped in favour of TCA use?

SSRIs have already replaced TCAs as the first choice of drug to treat depression in non-pregnant patients, due to their more bearable side effects and their increased safety in overdose.^{xix,xx} Yet NICE guidelines currently recommend TCA use based on the fact that they 'have been in use for a relatively long period of time, and are considered to have the lowest known risk in pregnancy and breastfeeding'^{xxi}. Given the potential detrimental effect that switching class of antidepressant can cause on a mother's management of her depression, are SSRIs being unnecessarily sidelined for use in pregnancy? The research showing that SSRIs and TCAs are safe for use in pregnancy also shows no difference in the safety between the two drug classes (see ref. 7-11). Furthermore, Reis *et al.* have shown TCAs to have higher risks during pregnancy than SSRIs (except paroxetine), including an increased rate of congenital malformations, an increase in premature births and an increase in low birth weight, although further studies are needed before definitive conclusions can be drawn from this.^{xxii} Additionally, TCAs^{xxiii,xxiv} and SSRIs^{xxv,xxvi,xxvii,xxviii} produce comparable rates of withdrawal in the neonate.

What are the longterm effects on the mental health of the fetus?

Early child development is not affected by maternal use of TCAs or fluoxetine, as measured by scores for IQ, language and behaviour^{xxix,xxx}. However, there is a serious lack of studies on the longterm neurological side effects of SSRI exposure *in utero*. This is surprising given that serotonin is known to be involved in aspects of brain development, such as synaptogenesis and cell differentiation. Croen *et al* in 2011 showed in what they called a 'preliminary' study that there is a moderate, increased risk of autism spectrum disorders (ASDs) with prenatal SSRI, but not TCA use.^{xxxi} Further research is needed to confirm these longterm effects on mental health.

The effects of changing antidepressants during pregnancy, or stopping use altogether, on both the mother and the fetus should be explained to the patient and discussed thoroughly before any decision is reached. Antidepressant cessation is not an appropriate choice for every woman, since it may cause a depression relapse. Alteration of antidepressant class may also negatively affect a woman's treatment of her depression unnecessarily, especially considering there is no real evidence that TCAs are safer than SSRIs for use during pregnancy. It can be argued that if a mother's depression is treated well, it will allow them to be the best mother they can be to their baby, which would be the best outcome of all.

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