Risks of untreated depression in pregnancy

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Abstract

Question In my family practice, I tell my female patients of reproductive age who have depression that untreated depression in pregnancy might be more harmful than the unproven risks of antidepressants. However, I recently read in a national news magazine that there is actually no evidence for this advice. Have I missed something?

Answer You did not miss anything, so you should continue to advise your pregnant patients as before. News magazines can have substantial bias, as the reporters often only interview "experts" who support their beliefs, as was probably the case in this article. Most glaringly, in this instance, no perinatal psychiatrists were interviewed and none of the experts were clinically involved with pregnant women. We believe that media statements like the one you mentioned might lead women to abruptly discontinue their antidepressants, putting themselves at risk of relapse, hospitalization, and even suicide. Your balancing role in providing your patient with evidence-based information is critical.

Les risques de la dépression non traitée durant la grossesse

Résumé

Question Dans ma pratique familiale, je dis à mes patientes en âge de procréer qui souffrent de dépression que leur maladie laissée sans traitement durant la grossesse pourrait être plus dommageable que les risques non prouvés des antidépresseurs. Par ailleurs, j'ai lu dans une revue nationale d'actualités qu'il n'y a pas réellement de données probantes étayant ce conseil. Aurais-je manqué quelque chose?

Réponse Vous n'avez rien manqué et vous devriez continuer à prodiguer les mêmes conseils qu'auparavant à vos patientes enceintes. Les revues d'actualités sont susceptibles d'avoir un parti pris puisque souvent, les journalistes n'interviewent que les «experts» en accord avec leurs convictions, comme c'était probablement le cas dans cet article. C'est particulièrement évident dans le cas présent, puisqu'aucun psychiatre périnatal n'a été interviewé et qu'aucun des experts cités n'était cliniquement concerné par des femmes enceintes. Nous croyons que les déclarations médiatiques comme celle que vous avez mentionnée pourraient inciter des femmes à discontinuer abruptement leurs antidépresseurs, ce qui les mettrait à risque de rechute, d'hospitalisation et même de suicide. Votre rôle consistant à faire le juste équilibre et à donner à vos patientes des renseignements fondés sur des données probantes est d'autant plus essentiel.

Up to 1 in 5 pregnant women is affected by depression, but unfortunately many of these cases are undiagnosed or untreated.[1] To help prevent the consequences of untreated depression, it is crucial to use screening tools and be up to date on the effectiveness and safety of pharmacotherapy.

Risks of untreated depression

For some pregnant women, appropriate pharmacotherapy is necessary, as maternal depression has been associated with various detrimental health concerns for both the baby and the mother. Babies born to women with untreated depression are at risk of prematurity, low birth weight, and intrauterine growth restriction.[2,3] The negative consequences of untreated maternal depression might also affect childhood development. Higher impulsivity, maladaptive social interactions, and cognitive, behavioural, and emotional difficulties have been shown to occur.[4,5] The adverse outcomes of untreated maternal depression might also be detrimental to the mother. Importantly, pregnant women with depression are more at risk of developing postpartum depression and suicidality.[6] Increased hospital admissions and pregnancy complications such as preeclampsia have also been linked to untreated maternal depression.[6,7] It has also been shown that pregnant women with depression are more likely to engage in high-risk health behaviour. Some examples include smoking, illicit substance and alcohol abuse, and

poor nutrition.[8] To prevent this behaviour, antidepressant treatment might be needed.

A large National Institutes of Health multicentre trial found that women who discontinued their antidepressant therapy relapsed significantly more frequently compared with women who maintained their antidepressant use throughout pregnancy (hazard ratio 5.0; $P<.001$). In that study, 68% of women who discontinued their medication had major depressive relapses compared with only 26% of women who maintained their medication, and those who discontinued their medication were 3 times more likely to be hospitalized and experience complications.[9]

Antidepressant risks

With these findings and the consequences of untreated depression, it is important to establish a risk-benefit ratio when counseling patients. The risks of untreated depression must be balanced with what is reported in the peer-reviewed literature regarding fetal exposure to antidepressants. To date, most of the more than 30 published studies, including thousands of pregnancy outcomes, reported negligible or no fetal risks. The main concern appears to be the increased risk of cardiac malformations—usually ventricular septal defects, most of which close spontaneously early in life. The increased risk was marginal and it was unknown if the spontaneously resolving minor ventricular septal defects were included in some of the studies.[10] A very large Danish study reported that this apparent increase in cardiac defects occurred also among women who did not treat their depression with antidepressants, strongly suggesting that this result is probably owing to ascertainment and reporting bias, and not the antidepressants.[11]

Although more research needs to be conducted, the results of studies examining long-term development of children exposed in utero to selective serotonin reuptake inhibitors are reassuring, with no apparent adverse effects in the children.[12]

Health care providers should be aware that women might require increased doses of their antidepressant medications in late pregnancy owing to pharmacokinetic changes. In pregnancy, the volume of distribution and renal drug elimination increase. Additionally, the metabolic activities of CYP (cytochrome P450) 3A4 and CYP2D6, enzymes responsible for the metabolism of many selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors, have been shown to be increased.[13] It is generally recommended that patients be treated with the minimum effective dose and monitored closely. It is important to communicate to the patient that owing to these pharmacokinetic changes, an increase in dose might be required if breakthrough symptoms occur.

Conclusion

For some women, untreated depression can have tragic consequences, the most serious being death by suicide. Unfortunately, at Motherisk we have been made aware of cases in which pregnant women have died by suicide following abrupt discontinuation of their antidepressants, a tragedy that could possibly have been avoided with continuing treatment.

Antidepressants should always be prescribed judiciously by physicians in all patients, most especially pregnant women. However, it is clear from examination of all the current evidence-based information, and application of an individualized risk-benefit ratio, that women with clinically serious depression should be offered drug therapy.[10] Whether or not they take it is ultimately their decision; however, they will be armed with scientific information, rather than with non-expert opinions expressed in news magazines.

Competing interests
None declared

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Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future **Motherisk Updates**. Published Motherisk Updates are available on the *Canadian Family Physician* website (**www.cfp.ca**) and also on the Motherisk website (**www.motherisk.org**).