



Motherisk Update

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New antidepressants in pregnancy

ABSTRACT

QUESTION I have read that fluoxetine is the drug of choice for treating depression during pregnancy. One of my patients, who did not respond to the “old” selective serotonin reuptake inhibitors, is doing well on venlafaxine and is now 6 weeks pregnant. What advice should I give her?

ANSWER Fluoxetine is recommended because to date it has the most evidence of its safety. It is important that women be treated appropriately for depression during pregnancy, and some research on the newer antidepressants, such as venlafaxine, will be useful to you and your patient in making an informed decision regarding treatment.

RÉSUMÉ

QUESTION J’ai lu que la fluoxétine est le médicament de première intention pour traiter la dépression durant la grossesse. L’une de mes patientes, qui n’a pas bien réagi aux «traditionnels» inhibiteurs spécifiques du recaptage de la sérotonine, répond bien à la venlafaxine et est maintenant enceinte de 6 semaines. Quels conseils devrais-je lui donner?

RÉPONSE La fluoxétine est recommandée parce que, jusqu’à présent, son innocuité est corroborée par le plus grand nombre de données scientifiques. Il importe que les femmes soient adéquatement traitées contre la dépression durant la grossesse et certaines recherches sur les plus récents antidépresseurs, comme la venlafaxine, vous seront utiles à vous et à votre patiente dans la prise d’une décision éclairée concernant la thérapie.

Many women of childbearing age suffer from depression and, because at least 50% of pregnancies are unplanned,¹ some women are exposed to antidepressants early in pregnancy. In a previous study we showed that misinformation and fear of teratogenicity led many women to abruptly discontinue needed antidepressants after pregnancy was diagnosed.² Today, physicians feel comfortable prescribing selective serotonin reuptake inhibitor (SSRI) antidepressants, such as fluoxetine, because these drugs have been available for many years and a large body of evidence documents their safety

during pregnancy.³⁻⁶ Physicians continue to be concerned, however, about the newer antidepressants.

Several studies have documented how important it is to treat depression during pregnancy. A British study showed that depression during pregnancy has been relatively neglected compared with postpartum depression, even though it is more prevalent and approximately 25% of postpartum depressions actually begin during pregnancy.⁷

The American Psychiatric Association’s Committee on Research on Psychiatric Treatments identified treatment of major depression during pregnancy as

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a priority in clinical management. Based on this, a position paper was published on risk-benefit decision making for such treatment.⁸ The authors concluded there was no evidence that antidepressants caused harm to unborn babies and that pregnant women should be treated as long as benefits and possible risks are well explained to them. A recent survey of 3472 pregnant women in the United States revealed that one in five had symptoms of depression, but few (24%) actually received treatment during pregnancy.⁹

In the 1990s, newer non-SSRI antidepressants were introduced and were used by women who became pregnant while taking them. Motherisk has been studying these newer drugs and has published the only study currently available on the safety of venlafaxine, a phenethylamine bicyclic derivative chemically unrelated to other antidepressants.¹⁰ We followed 150 women who had all been exposed to venlafaxine in the first trimester (35 [23%] were exposed throughout pregnancy) and compared them with two control groups. In the venlafaxine group, there were 125 live births, 18 spontaneous abortions, seven therapeutic abortions, and two major malformations. There were no statistically significant differences among groups for any of the end points examined.

We also published the only study examining the fetal safety of trazodone and nefazodone, both phenylpiperazine antidepressants structurally unrelated to other antidepressants.¹¹ Among 147 women, there were 121 live births (two babies had major malformations), 20 spontaneous abortions, and six therapeutic abortions. In all cases, exposure occurred during the first trimester (52 [35%] were exposed throughout pregnancy). There were no statistically significant differences among the three groups in any end points examined. Trazodone has actually been on the market for many years, but, since it is structurally similar to nefazodone and there have been no studies on its safety during pregnancy, we decided to include both drugs in our study.

Bupropion, an antidepressant of the amineketone class, is indicated for two conditions: depression and smoking cessation. To date, no

studies have been published of its effect on human pregnancy. The manufacturer has a registry in which the outcomes of 266 pregnancies of women exposed during the first trimester are documented. There appeared to be no increased risk of major malformations. There was, however, no comparison group. At Motherisk, we are currently enrolling pregnant women and women planning pregnancy who have been exposed to bupropion along with comparison groups matched for smoking and depression.

Mirtazapine, a tetracyclic antidepressant that enhances noradrenergic and specific serotonergic transmission, has been available in Canada since 2001. There is no information on its safety during pregnancy, but animal studies revealed no adverse effects on reproduction, and there have been no reports of adverse effects in babies of mothers who took it during pregnancy. Motherisk is studying this drug also. If you have patients taking either bupropion or mirtazapine, please ask them to get in touch with the Motherisk Program at (416) 813-6780 or 1-800-670-6126.

If women do not respond to or suffer adverse effects from SSRIs and require antidepressants, available information suggests the newer antidepressants are safe. This evidence-based information should help patients and their physicians work out a risk-benefit ratio and make an informed decision about treatment. Pregnant women with depression should be treated appropriately to ensure that they are in optimal mental health to interact and bond with their babies. 

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Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto, Ont. **Ms Einarson** is a member and **Dr Koren** is Director of the Motherisk Program. **Dr Koren**, a Senior Scientist at the Canadian Institutes for Health Research, is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation and, in part, by a grant from the Canadian Institutes for Health Research.

Do you have questions about the safety 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 College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in The Motherisk Newsletter and on the Motherisk website (www.motherisk.org) also.