

Prescribing antidepressants to pregnant women

What is a family physician to do?

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During the past year, the time we have spent at the Motherisk Program counseling pregnant women and their health care providers on the safety and risks of antidepressant use during pregnancy has increased dramatically. Physicians and pregnant women from across Canada have been calling, e-mailing, and faxing us in increasing numbers with questions regarding the safety of antidepressants during pregnancy. This is most likely due to a number of recent studies that have been published in this field. These studies have had conflicting results that add to the already mixed messages regarding the safety of this class of drugs during pregnancy.

What prompted us to write this editorial was our experience with a pregnant woman from Nova Scotia who was advised by a family physician to stop taking her antidepressants abruptly. When this woman was 12 weeks pregnant, she moved to a small town 3 hours from Halifax. She was taking citalopram prescribed by her family physician in Halifax for depression and had been prescribed it before becoming pregnant. When she required a refill, she visited the only family physician in the very small town to which she had moved. Upon discovering that she was pregnant, he advised her that he would not renew the prescription because antidepressants were unsafe to take during pregnancy. She offered to call her physician in Halifax for confirmation, but the new physician still refused, and subsequently she had to make a trip to Halifax to see her previous family physician in order to get her medication.

We wondered what would have prompted this physician to be so adamant about refusing to refill a prescription for an antidepressant for a pregnant woman? The answer might be because the evidence regarding the safety of antidepressants during pregnancy is not clear, and he thought he was "being on the safe side." This is a common refrain we hear from physicians and other health care providers when it comes to prescribing drugs during pregnancy, especially psychotropic drugs. However, until recently, according to evidence-based information in the literature, antidepressants have been considered relatively safe to use during pregnancy and were not associated with increased risk of birth defects or other adverse effects.¹ In the past year, several studies have been published that contradict this evidence.

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Studies documenting increased risks

Last year, the drug company GlaxoSmithKline published on their website (not in a peer-reviewed journal) that there was an increased risk of cardiovascular defects in infants whose mothers had taken paroxetine during early pregnancy. This was a very small increased risk, however, 1.5% compared with 1% in the general population, and the authors did not indicate whether the defect resolved spontaneously, which is a fairly common occurrence.² Two other studies both found the same increased risk with use of paroxetine (between 1% and 2%).^{3,4} Another study documented an increased risk of persistent pulmonary hypertension of the newborn (PPHN), but that is a rare condition and would not occur in 99% of cases.⁵

In another study of antidepressants in general, the authors stated that a statistically significant difference of 28 g in birth weight translated into an increased risk of low birth weight.⁶ Another recent study on antidepressants as a group found an increased risk of congenital malformations but did not distinguish between major and minor congenital anomalies, and minor anomalies by definition cause no functional impairment.⁷

Some case series have documented neonatal withdrawal in infants whose mothers took antidepressants during late pregnancy. The withdrawal was mostly self-limiting and not life-threatening, and approximately 30% of all infants exposed in utero to antidepressants might have some withdrawal symptoms.^{8,9}

Studies documenting little or no increased risk

During the same period, a meta-analysis and 2 studies of antidepressants as a group that looked at a combined total of 4500 pregnancy outcomes did not find an increased risk of major malformations.¹⁰⁻¹² In a recent Motherisk study we conducted in response to reports of cardiovascular defects associated with use of paroxetine during pregnancy,²⁻⁴ we collected 1170 prospectively ascertained outcomes of infants exposed to paroxetine in the first trimester of pregnancy from 8 teratogen information services from around the world. We compared them with the outcomes of a group of non-exposed infants. We found the rate of cardiovascular defects to be similar in both groups (0.7%),¹³ which is the rate expected in the general population.¹⁴

In addition, 2 papers were recently published in the *New England Journal of Medicine* on this topic. Despite conducting many statistical tests between groups, which would increase the probability of finding significant results with no clinical importance, the authors found few, if any, teratogenic effects of these drugs. To their credit, the authors stressed the importance of treating the mothers' underlying depression.^{15,16} Finally, an abstract presented at this year's meeting of the American Psychiatric Association reported the results of another study on use of selective serotonin reuptake inhibitors (SSRIs) during pregnancy. These authors found no association between taking SSRIs (as a group) and increased risk of major malformations, including both PPHN and cardiovascular birth defects.¹⁷

Consideration of maternal illness

In prescribing antidepressants to pregnant women, we have to keep in mind the possible adverse effects of maternal illness on fetuses and infants. It is important that pregnant women be in the best possible mental health to ensure that they become involved and caring mothers. In a recent study, 86 of 201 (43%) women experienced a relapse of major depression during pregnancy. Among the 82 women who maintained their medication throughout pregnancy, 21 (26%) relapsed, but among the 65 women who discontinued their medication, 44 (68%) relapsed. The authors concluded that women with a history of depression should continue their antidepressant medication during pregnancy.¹⁸

Limitations of studies

Prospective cohort studies, case-control studies, pregnancy registries, prescription database studies, and health care insurance database studies, as well as meta-analyses, are the types of studies usually used to determine the outcomes of infants of mothers who took particular drugs during pregnancy. There are limitations to all of these studies; however, because conducting randomized controlled trials among pregnant women would be unethical, we have to use information from the studies we are able to conduct. For example, Motherisk published a study where we documented that women using antidepressants during pregnancy had a 30% higher utilization rate of ultrasound scans. In addition, we found that infants of women who took SSRIs during pregnancy underwent twice as many echocardiograms in the first year of life.¹⁹

Conclusion

Despite all this new information, there are no current clinical practice guidelines for treatment of depression during pregnancy. There is a Health Canada website that discusses the treatment of depression during pregnancy, but regarding use of antidepressants, it

New resource for health care professionals

While information about the effect of psychotropic medications and substance use on individuals has grown steadily over the years, data on how they affect pregnant and breastfeeding women, their fetuses, infants, and children has unfortunately lagged behind. The Canadian Mental Health Association and the Motherisk Program at Sick Children's Hospital in Toronto, Ont, have collaborated on a new resource, *Exposure to psychotropic medications and other substances during pregnancy and breastfeeding: A handbook for health care providers*. This is perhaps the first handbook ever to provide busy health care professionals with easily accessible data on this subject, including current research and medical recommendations. Written for a range of health care providers, including physicians, it contains information on stigma, counseling, and screening, as well as evidence-based information on the safety or risk of using psychotropic medications and other substances, such as alcohol and psychotropic drugs, during pregnancy and breastfeeding. This project was financially supported by a grant from Health Canada and is provided free of charge to health care professionals throughout Canada. It is available from the Canadian Mental Health Association in Toronto (www.cmha.ca).

only states, "Discuss with your physician" (www.gfmer.ch/Guidelines/Pregnancy_newborn/Pregnancy_newborn_mt.htm).

It has been estimated that up to 20% of all pregnant women suffer from some degree of depression,²⁰ so it is important that they are treated appropriately, and if necessary, with pharmacotherapy. The decision to take an antidepressant during pregnancy should be made by physician and patient together using evidence-based information. Although information is available in the literature, it can be difficult for physicians to understand the limitations of the various types of studies. A best-practice guideline would be very helpful for physicians assisting their patients with making decisions about taking medications during pregnancy.

We have received many reports of physicians advising their patients to discontinue their antidepressants abruptly upon confirmation of pregnancy. This is definitely not a good practice as stopping them abruptly can have serious ramifications for mothers.²¹ If, following discussion with her physician, a woman decides she does not wish to take an antidepressant during pregnancy, the medication should be slowly tapered off over a number of weeks. 

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Competing Interests

None declared

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