

MOTHERISK UPDATE

Maternal obesity and risk of neural tube defects

Gideon Koren, MD, FRCPC

abstract

QUESTION One of my patients is taking olanzapine for schizophrenia. She has gained a lot of weight, which, I understand, often happens with some of the new atypical antipsychotics. Due to her weight gain, she failed to notice she had become pregnant. Is she at risk?

ANSWER Experience with olanzapine is relatively slight, but available prospective data do not show increased teratogenic risk. Adiposity, on the other hand, is associated with increased risk of neural tube defects. Only some of this risk can be reduced by folate supplementation.

résumé

QUESTION Une de mes patientes prend de l'olanzapine pour la schizophrénie. Elle a pris beaucoup de poids ce qui, selon ce que j'ai appris, se produit fréquemment avec les nouveaux antipsychotiques atypiques. À cause de son gain de poids, elle n'a pas remarqué qu'elle était devenue enceinte. Court-elle des risques?

RÉPONSE L'expérience avec les effets de l'olanzapine n'est pas très étendue, mais les données prospectives disponibles ne démontrent pas de risques tératogènes accrus. Par ailleurs, l'adiposité est associée à un risque plus élevé de malformation du tube neural. Un supplément d'acide folique peut, en partie seulement, réduire ce risque.

Obesity during pregnancy is associated with a long list of acknowledged health risks, including higher prevalence of cesarean section,¹ hypertension,² deep vein thrombosis,³ and diabetes mellitus.⁴ In this Motherisk Update, however, we will focus on the relatively unknown risk of neural tube defects (NTDs).

Several epidemiologic studies have suggested that being overweight before pregnancy is a risk factor for NTDs. A large case-control study of 604 fetuses or infants with NTDs, and 1658 fetuses or infants with other major malformations, showed that risk of NTDs increased from 1.9 (95% confidence interval [CI] 1.2 to 2.9) for women weighing 80 to 89 kg to 4.0 (95% CI 1.6 to 9.9) for women weighing 110 kg or more.⁵ The reference group for comparison consisted of women weighing between 50 and 59 kg.

After controlling for folate intake, there was still a threefold higher risk of NTDs in the heaviest groups. Intake of 400 µg or more of folate reduced NTD risk by 40% among women weighing less than 70 kg, but did not decrease risk at all among heavier women. These results suggest that inadequate folate intake is not the mechanism leading to increased risk of NTDs among the babies of obese women.

It is now generally accepted that a body mass index >29 kg/m² doubles the risk of NTDs.⁶ A recent

study has shown that the elevated risk encompasses open or closed, isolated, nonisolated, high, low, or open/isolated/high phenotypes of spina bifida. Risk appears to be higher among female offspring.⁷

With the introduction of atypical antipsychotics, such as clozapine, olanzapine, and others, it will be important to ensure appropriate intake of folic acid to account for the increased body mass commonly associated with these medications.⁸ Because many women taking these drugs become obese, it makes clinical

sense to monitor them with ultrasound and α -feto-protein to rule out NTDs. These patients should also be referred to high-risk perinatal programs for diagnosis and management of other complications related to weight gain (eg, hypertension, diabetes, and deep vein thrombosis). ❖

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.

Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto, Ont. **Dr Koren** is Director of the Motherisk Team and a Senior Scientist in the Canadian Institutes of Health Research.

clinical challenge

défi clinique

.....

References

1. Kaiser PS, Kirby RS. Obesity as a risk factor in a low-risk population. *Obstet Gynecol* 2001;97:39-43.
2. Broughton PF, Roberts JM. Hypertension in pregnancy. *J Hum Hypertens* 2000;14:705-24.
3. Samama MM. An epidemiologic study of risk factors for deep vein thrombosis in medical outpatients: the Sirius study. *Arch Intern Med* 2000;160:3415-20.
4. Moore LL, Singer MR, Bradlee ML, Rothman KJ, Milunsky A. A prospective study of the risk of congenital defects associated with maternal obesity and diabetes mellitus. *Epidemiology* 2000;11:689-94.
5. Werler MM, Louik C, Shapiro S, Mitchell AA. Prepregnant weight in relation to risk of neural tube defects. *JAMA* 1996;275:1089-92.
6. Shaw GM, Velie EM, Schaffer D. Risk of neural tube defect-affected pregnancies among obese women. *JAMA* 1996;275:1093-6.
7. Shaw GM, Todoroff K, Finnell RH, Lammer EJ. Spina bifida phenotypes in infants or fetuses of obese mothers. *Teratology* 2000;61:376-81.
8. Karagianis J. Olanzapine and weight gain [letter]. *Can J Psychiatry* 2000;45:493.

...