Is ondansetron safe for use during pregnancy?

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Abstract

Question While I usually prescribe doxylamine-pyridoxine for morning sickness, some of my patients with severe nausea and vomiting of pregnancy (NVP) receive ondansetron in hospital. I have read some new precautions recommended by the US Food and Drug Administration (FDA). Is ondansetron safe to use during pregnancy?

Answer During the past decade ondansetron has been increasingly used in the United States for NVP, owing to the lack of an FDA-approved drug for this condition. While fetal safety data for doxylamine-pyridoxine are based on more than a quarter of a million pregnancies, the fetal safety data for ondansetron are based on fewer than 200 births. Moreover, a recent case-control study suggested there was an increased risk of cleft palate associated with ondansetron. Recently, the FDA issued a warning about potentially serious QT prolongation and torsade de pointes associated with ondansetron use; the warning included a list of precautions and tests that must be followed. The drug is not labeled for use in NVP in either the United States or Canada. Based on the data available today, ondansetron use cannot be assumed to be safe during pregnancy.

L'ondansétron est-il sécuritaire durant la grossesse?

Résumé

Question Je prescris habituellement de la doxylamine-pyridoxine pour la nausée matinale, mais certaines de mes patientes qui ont des problèmes sévères de nausées et de vomissements de la grossesse (NVG) reçoivent de l'ondansétron à l'hôpital. J'ai lu à propos de nouvelles précautions recommandées par la Food and Drug Administration des États-Unis (FDA). L'utilisation de l'ondansétron est-elle sécuritaire durant la grossesse?

Réponse Au cours de la dernière décennie, on a utilisé de plus en plus l'ondansétron aux États-Unis pour les NVG, en l'absence d'un médicament approuvé par la FDA pour ce problème. Quoique l'innocuité pour le fœtus de la doxylamine-pyridoxine soit démontrée en se fondant sur plus d'un quart de million de grossesses, les données sur la sécurité de l'ondansétron pour le fœtus ne se basent que sur moins de 200 naissances. De plus, une récente étude cas-témoin fait valoir qu'il y avait un risque accru de fentes palatines associées à l'ondansétron. Récemment, la FDA a émis un avertissement au sujet de la prolongation de l'intervalle QT et de torsades de pointe potentiellement sérieuses associées avec l'usage de l'ondansétron; l'avertissement comporte une liste de précautions à prendre et de tests à effectuer. Le médicament n'est homologué pour l'utilisation dans les cas de NVG ni États-Unis ni au Canada. En se fondant sur les données disponibles actuellement, on ne peut pas présumer que l'utilisation de l'ondansétron soit sécuritaire durant la grossesse.

Ondansetron, a potent antiemetic agent, is a 5-hydroxytryptamine receptor 3 antagonist that blocks the effects of serotonin. It was designed originally for chemotherapy-induced nausea and vomiting. The drug is also labeled for use in nausea and vomiting associated with radiation therapy, anesthesia, and surgery. However, because there is no drug approved by the US Food and Drug Administration (FDA) for morning sickness in the United States, an increasing number of American women experiencing nausea and vomiting of pregnancy (NVP) have been treated with ondansetron.

Fetal safety

Fetal safety of ondansetron was addressed by the Motherisk program in 2004 through a prospective cohort study of 176 women, mostly American, in whom we could not detect an increased teratogenic risk.[1] However, this sample size ruled out only a 5-fold increased risk of major malformations, and not any specific malformation. Moreover, the lack of other, similar cohort studies precluded conducting a meta-analysis to increase the sample size.

Importantly, a recent large control study by the Slone Epidemiology Center in Boston, Mass, and the Centers for Disease Control and Prevention in Atlanta, Ga, detected a 2-fold increased risk of cleft palate associated with ondansetron taken for NVP in the first trimester of pregnancy (odds ratio 2.37 [95% CI 1.28 to 4.76]).[2]

Maternal safety

In September 2011 the FDA issued a warning about possible serious QT prolongation and torsade de pointes among people receiving ondansetron.[3] The FDA requires strict follow-up of patients receiving ondansetron to rule out long QT syndromes, electrolyte imbalance, congestive heart failure, or receiving concomitant medications that prolong the QT interval.[3] In the context of NVP, quite a few women with severe NVP might have electrolyte imbalances (hypokalemia or hypomagnesemia). Currently, through Motherisk counseling of women who receive ondansetron for morning sickness, it is evident that none of the FDA precautions are being followed.

Because the paramount challenge of treating pregnant women with medications is fetal and maternal safety, ondansetron should be used cautiously only after drugs with better safety records that have been labeled for use in pregnancy (eg, doxylamine-pyridoxine) have been tried.

Competing interests
Dr Koren has served as a consultant for Duchesnay Inc in Blainville, Que.

References
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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**.

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