Motherisk Update

Changes in drug handling during pregnancy

What it might mean for your patients

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ABSTRACT

QUESTION A pregnant patient taking lithium for bipolar depression is clinically uncontrolled despite a high dose. She insists that she is taking the medication. Her lithium serum levels have fallen from 1 mEq/L to 0.6 mEq/L. What is the reason for this change?

ANSWER Lithium is eliminated by the kidney. In late pregnancy the glomerular filtration rate increases substantially and hence elimination of the drug can almost double. Liver biotransformation pathways might also increase the rate of elimination of various drugs, causing lower levels and, potentially, suboptimal therapy.

RÉSUMÉ

QUESTION La dépression bipolaire d'une patiente enceinte, malgré une forte dose de lithium, n'est pas cliniquement contrôlée. La patiente insiste qu'elle prend ses médicaments. Ses taux sériques de lithium ont baissé de 1 milliéquivalent par litre à 0,6. Comment peut-on expliquer ce changement?

RÉPONSE Le lithium s'élimine par les reins. À la fin de la grossesse, le taux de filtration glomérulaire augmente considérablement et, par conséquent, l'élimination du médicament peut presque doubler. Les cheminements de la biotransformation par le foie peuvent aussi augmenter le taux d'élimination de divers médicaments et, éventuellement, se traduire par une thérapie sous-optimale.

Several pregnancy-induced changes in drug disposition can cause expecting mothers to handle medications very differently than before or after gestation. This can have important implications for medication dosage and monitoring among pregnant patients. Several changes should be considered: compliance, increase in body weight, increase in glomerular filteration rate, and changes in hepatic drug metabolism.

Compliance

Pregnant women are often reluctant to take medications, even for life-threatening conditions, owing to misperception of fetal risks. If patients do not respond to therapy that worked in the past, always consider the possibility of decreased compliance.

In an interesting and novel move, a Canadian manufacturer is now marking an indicia silhouette of a pregnant woman on its morning sickness medication tablets to encourage pregnant women to take them. Such a sign is documented to improve women's perceptions of safety.

Increase in body weight

The increase in body weight in late pregnancy means a decrease in dose per kilogram. Because steady state concentrations (and therefore drug effects) are the ratio between dose rate and clearance rate, such changes in weight are likely to cause some women to be suboptimally treated.

Increase in glomerular filtration rate

In late pregnancy there is a 50% increase in cardiac output and glomerular filtration rate. This will lead to decreased serum concentrations, and potentially to decreased effectiveness, for renally eliminated drugs such as lithium, digoxin, and aminoglycosides.

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Changes in hepatic drug metabolism

Metabolism of some drugs is enhanced during pregnancy. Medications metabolized by cytochrome P-450 2D6 (fluoxetine,[1] citalopram[2]), P-450 2A6 (nicotine[3]), and P-450 3A4 (eg, protease inhibitors[4]) exhibit substantially lower serum concentrations in late pregnancy. In contrast, there is substantial decrease in activity of cytochrome P-450 1A2, which metabolizes caffeine.[1-5]

For some pregnant women, lower serum concentrations might necessitate higher dosages to achieve therapeutic effects. Changes in dose mean that monitoring patients' responses to their medications must be vigilant during the second part of pregnancy.

References

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MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Dr Koren** is Director of the Motherisk Program and is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation and, in part, by a grant from the Canadian Institutes of Health Research. He holds the Ivey Chair in Molecular Toxicology at the University of Western Ontario in London.

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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