Motherisk Update

Safety of gadolinium during pregnancy

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ABSTRACT

QUESTION A pregnant patient who underwent magnetic resonance imaging (MRI) because of an acute abdomen, was told that MRI contrast agents (ie, gadolinium-based contrast agents) are contraindicated during pregnancy. What is the risk to her baby?

ANSWER Current radiology practices and recommendations discourage the use of gadolinium-based contrast agents during pregnancy because their safety for the fetus has not yet been proven. In line, however, with the European Society of Radiology guidelines and based on the available evidence, gadolinium-based contrast agents appear to be safe in pregnancy. Gadolinium use should be considered when the diagnostic study is important for the health of the mother.

RÉSUMÉ

QUESTION Une patiente enceinte a subi un examen à l'aide de l'imagerie par résonance magnétique (IRM) en raison d'un abdomen aigu. On lui a dit que les agents de contraste en IRM (p. ex. les agents de contraste à base de gadolinium) sont contre-indiqués durant la grossesse. Quels sont les risques pour son nouveau-né?

RÉPONSE Les pratiques et les recommandations actuelles en radiologie ne sont pas favorables à l'utilisation des agents de contraste à base de gadolinium durant la grossesse parce que leur innocuité pour le fœtus n'a pas encore été éprouvée. Par ailleurs, si l'on se fonde sur le guide de pratique de la Société européenne de radiologie et les données scientifiques accessibles, les agents de contraste à base de gadolinium semblent sûrs durant la grossesse. On devrait envisager recourir au gadolinium lorsque l'étude diagnostique est importante pour la santé de la mère.

Magnetic resonance imagining (MRI) is considered safe during pregnancy, as magnetic energy has been shown not to be harmful for the developing fetus.[1,2]

On the other hand, most radiology service providers consider gadolinium-based contrast agents for MRI (eg, gadopentetate, gadodiamide, gadolinium DPTA, gadoterate meglumine) to be relatively or absolutely contraindicated during pregnancy; these paramagnetic agents are not recommended by the Food and Drug Administration because they cross the placenta and their long-term effects are unknown. All pregnant patients are expected to consult their obstetricians before undergoing MRI examination.

Gadolinium-based contrast agents are excreted almost exclusively by the kidneys through glomerular filtration. Their volume of distribution is equal to the volume of extracellular water, and binding to plasma proteins is negligible. These agents possess a very high safety index in human beings.[3]

Although there have not been any long-term animal studies to evaluate the carcinogenic potential of gadolinium-based contrast agents, no carcinogenic or mutagenic effects have been observed and no teratogenic or other long-term effects occurred in mice exposed in utero to gadolinium-based contrast agents.[4-7] Pregnant mice exposed to MRI with and without gadolinium had no differences in litter size, number of live offspring, fetal weight, morphology, or development, compared with unexposed controls.[4]

Gadolinium-based contrast agents have been detected in the placenta in animals and human beings.[8-10] In women during the second and third trimesters of pregnancy, uptake of gadolinium-based contrast agents by the placenta was sufficient for MRI imaging.[11,12] These agents have also been observed in animals, and occasionally in human beings, to cross the placenta into the fetal circulation and to be excreted by the fetal kidneys, appearing in the fetal bladder only minutes after administration to the mother.[3,13,14] Gadolinium-based contrast

agents are believed to diffuse from the fetus back to the mother, given the high clearance rate observed in fetal rats.[15]

Inadvertent exposure

Inadvertent human exposure during the first trimester of pregnancy has not been associated with adverse effects in the fetus.[16,17] Reports on use of gadolinium-based contrast agents during the second or third trimester are not rare,[10-13,18] underscoring the usefulness of these agents in diagnosing various conditions. No harm to the fetus has been documented in these circumstances.

Guidelines

The European Society of Radiology has issued a guideline[19] discussing gadolinium use during pregnancy. Their conclusion is that gadolinium is probably safe during pregnancy, as excessive quantities are not expected to cross the placenta or to be toxic to the fetus if they do.[19] These guidelines also state that, given that gadolinium is mainly distributed in extracellular water and rapidly eliminated by the kidney, in the unlikely event that some gadolinium reached the baby, it would be rapidly eliminated into urine.[19]

Conclusion

Current radiology practices and recommendations discourage the use of gadolinium-based contrast agents during pregnancy because their safety for the fetus has not been proven. Yet available evidence suggests it is unlikely that these compounds have an adverse effect on the developing fetus; therefore, their use should not be limited, particularly given the important clinical reasons for MRI examinations during pregnancy (eg, to rule out serious abdominal diseases).

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MOTHERISK

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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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Pre-emptive treatment for severe morning sickness

Invitation to join a new study

Alon Shrim, MD **Gideon Koren,** MD, FRCPC **Motherisk Program**

Nausea and vomiting of pregnancy (NVP) is the most common medical condition in pregnancy. Very little research, however, has focused on the etiology, characteristics, implications, and management of NVP.

In a recent prospective, non-randomized study by the Motherisk Program, we found that women who were pre-emptively treated for NVP had substantial improvement in their symptoms, suggesting that pre-emptive management is effective in preventing severe NVP.

Based on this study, Motherisk is currently conducting a randomized, prospective trial. Women who call the Motherisk NVP Line with a history of severe NVP in previous pregnancies and who are planning to become pregnant or who are already pregnant but have not yet experienced symptoms of NVP can be recruited. They will be randomized to receive doxylamine succinate and pyridoxine HCl, either as soon as they become aware of the pregnancy (and before NVP starts) or only once NVP symptoms start.

All patients will be interviewed during the pregnancy for severity of NVP as well as other factors. The primary outcome measured will be the rate of severe NVP in each of the 2 groups. For women who participate in either group of the study who do not have drug coverage, the medication will be supplied at no charge by the Hospital for Sick Children.

Based on our pilot study and supplementary reports, we believe that NVP, as well as its financial and social consequences, can be substantially reduced by this treatment.

If your patients are suitable *please contact* **Ms Caroline Maltepe** *by e-mail at* **caroline.maltepe@sickkids.ca** *or by telephone at 800436-8477; or* **Dr Alon Shrim** *by e-mail at* **alon.shrim@utoronto.ca.**