Motherisk Update

Tumour necrosis factor alpha and use of infliximab

Safety during pregnancy

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ABSTRACT

QUESTION A 27-year-old patient of mine with rheumatoid arthritis has been treated with infliximab for the last 5 years. She is planning her first pregnancy. How should I advise her regarding use of infliximab during pregnancy, bearing in mind that infliximab substantially improved her medical condition?

ANSWER Infliximab (Remicade) has not been tested in pregnant animals because it does not interact with non–human tumour necrosis factor (TNF) alpha. Several case reports describing women who used infliximab during pregnancy do not suggest a strong association with adverse pregnancy outcomes. More studies are required to determine infliximab's safety during pregnancy.

RÉSUMÉ

QUESTION Une de mes patientes de 27 ans souffrant d'arthrite rhumatoïde reçoit un traitement à l'infliximab depuis 5 ans. Elle planifie sa première grossesse. Quels conseils devrais-je lui donner concernant l'utilisation de l'infliximab durant sa grossesse, en tenant compte du fait que l'infliximab a considérablement amélioré son état physique?

RÉPONSE L'infliximab (Remicade) n'a pas été mis à l'essai chez les animaux en gestation parce qu'il n'a pas d'interaction avec le facteur de nécrose tumorale alpha (TNF) non humain. Plusieurs rapports de cas décrivant des femmes qui utilisaient l'infliximab durant la grossesse ne font pas valoir l'existence d'une forte association avec des conséquences défavorables pour la grossesse. Il faudrait plus d'études pour déterminer l'innocuité de l'infliximab durant la grossesse.

Infliximab is a monoclonal antibody to human tumour necrosis factor (TNF) alpha. It is used to treat Crohn disease and arthritis.[1] The product label indicates that infliximab has not been tested in pregnant experimental animals because it does not interact with non–human TNF alpha (although it does react with chimpanzee TNF alpha).

Several case reports describe women who used infliximab during pregnancy. A 26-year-old woman with Crohn disease complicated by a rectovaginal fistula became pregnant while she was receiving infliximab infusions. She delivered a baby weighing 681 g at 24 weeks' gestation. The neonate had intracerebral and intrapulmonary bleeding, was disconnected from the life support system on day 3, and died shortly thereafter. The patient conceived when her inflammatory bowel disease was active, but other medications she was taking and the severity of her condition could also have affected the outcome of her pregnancy.[2]

Katz et al[3] have reported on data extracted from the infliximab postmarketing surveillance database regarding exposure before or during pregnancy. Of 96 pregnancies with known outcome, 64 (67%) resulted in live births, 14 (15%) in miscarriages, and 18 (19%) in therapeutic termination. There were

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five reports of infants born with complications. One infant born at 24 weeks' gestation did not survive; a second infant had a complicted neonatal course with no apparent congenital anomalies; a third child was born with tetralogy of Fallot, and a fourth child had intestinal malrotation. Another infant (of a twin pregnancy) had delayed development and hypothyroidism.[3]

In a study designed to evaluate the practice and recommendations of rheumatologists in the United States (175 rheumatologists, all members of the American College of Rheumatology), physicians answered a detailed questionnaire addressing their experience of and beliefs about the safety of infliximab use during pregnancy. Only 46.5% of them were likely to agree that pregnancy is contraindicated for women taking infliximab.[4] The figure is probably low because there is little information on the teratogenic effects of the drug.

There is no doubt that more women will be exposed to infliximab during pregnancy in the near future. The little information currently available does not suggest a strong association with adverse pregnancy outcomes. More studies are needed, however, to provide extensive evidence of the safety of infliximab during pregnancy.

The scarcity of data has to be considered when giving the drug to pregnant women. It seems prudent to use it only when the well-being of the mother and particularly the viability of the pregnancy are highly dependent on use of infliximab.

References

1. Khanna D, McMahon M, Furst DE. Safety of tumor necrosis factor-alpha antagonists. *Drug Saf* 2004;27(5):307-24.
2. Srinivasan R. Infliximab treatment and pregnancy outcome in active Crohn's disease. *Am J Gastroenterol* 2001;96(7):2274-5.
3. Katz JA, Antoni C, Keenan GF, Smith DE, Jacobs SJ, Lichtenstein GR. Outcome of pregnancy in women receiving infliximab for the treatment of Crohn's disease and rheumatoid arthritis. *Am J Gastroenterol* 2004;99(12):2385-92.
4. Chakravarty EF, Sanchez-Yamamoto D, Bush TM. The use of disease modifying antirheumatic drugs in women with rheumatoid arthritis of childbearing age: a survey of practice patterns and pregnancy outcomes. *J Rheumatol* 2003;30(2):241-6.

MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Dr Shrim is a member and Dr Koren is Director of the Motherisk Program. Dr Koren holds the Ivey Chair in Molecular Toxicology at the University of Western Ontario in London 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.

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.

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