MOTHERISK *UPDATE*

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Taking drugs during pregnancy

How safe are the unsafe?

abstract

QUESTION I prescribed misoprostol to one of my patients with a peptic ulcer. When she found out she was pregnant while on the drug, both she and, admittedly, I were very scared to learn that the drug is teratogenic in that it causes Möbius syndrome. How great is the risk?

ANSWER Very small. Although women who use misoprostol during the first trimester have a 30-fold higher risk of having babies with Möbius syndrome, the malformation is so rare that, even if you see 1000 women who took misoprostol during embryogenesis, you might not see a single child with the syndrome. It is crucial to explain the *size* of the risk; otherwise women tend to believe the risk is huge even when, in fact, it is hardly measurable.

résumé

QUESTION J'ai prescrit du misoprostol à une patiente souffrant d'ulcères gastriques. Lorsqu'elle a appris qu'elle était enceinte alors qu'elle suivait cette pharmacothérapie, elle, et moi de même, il va sans dire, avons été très inquiets d'apprendre que le médicament est tératogène, en ce sens qu'il cause le syndrome de Mœbius. Quelle est l'ampleur du risque?

RÉPONSE Très minime. Même si les femmes qui prennent du misoprostol durant le premier trimestre de leur grossesse ont 30 fois plus de risque de mettre au monde un enfant souffrant du syndrome de Mœbius, cette malformation est si rare que, même si vous voyiez 1 000 femmes ayant pris du misoprostol durant l'embryogenèse, vous pourriez ne voir aucun enfant qui souffrirait du syndrome. Il est essentiel d'expliquer l'ampleur du risque; autrement, les femmes peuvent être portées à croire qu'il est immense alors qu'en réalité, il est presque impossible à mesurer.

Ever since we discovered in the late 1950s that thalidomide caused fetal malformations, women and health professionals have commonly believed that every drug is potentially harmful to a fetus. When asked, even women exposed to nonteratogenic drugs believe they have a 25% risk of having children with major malformations, apparently the size of the risk with thalidomide itself.[1] This unrealistic perception leads pregnant women to avoid medications even when they clearly need them.[2]

Teratogenicity in humans is studied in different ways. It is important for family physicians to understand the advantages and limitations of certain types of studies, so they can inform patients not just whether there is increased risk, but also of the magnitude of that risk.

Cohort studies focus on finding the proportion of children who are malformed after exposure to a certain drug and comparing it with the proportion in an unexposed group. For example, Motherisk recently showed that rates of major malformations among babies born to women exposed occupationally to organic solvents were significantly higher than in a control group consisting of women not working with these chemicals.[3]

Because major malformations occur in 1% to 3% of the general population and any particular malformation is rare, it is not easy to prove that a specific malformation is caused by a specific drug.

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.

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clinical challenge
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défi clinique

A much more sensitive method is a case-control study because it focuses on a specific child with a specific malformation.

In a study conducted in Brazil, we showed that children born with Möbius syndrome (facial paralysis and anomalies such as limb deformities) were 30 times more likely to have been exposed to misoprostol in utero than children with other malformations, such as neural tube defects.[4] In Brazil, where therapeutic abortion is illegal, young women use misoprostol as an abortifacient. An odds ratio of 30 sounds scary, but Möbius syndrome is so rare in the general population (one in 50 000 to 100 000 births) that even an odds ratio of 30 is hardly measurable.

Indeed, a prospective cohort study in Brazil showed that none of 86 women who took misoprostol during the first trimester had children with Möbius syndrome.[5] We think misoprostol most likely causes Möbius deformities through vascular disruption, but the risk is marginal.

References

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