

Bias against the null hypothesis

Scaring pregnant women about drugs in pregnancy

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Abstract

Question Since the thalidomide disaster, medicine is practised as if every drug is teratogenic, when in fact very few medications are. Pregnant women are often ready to refuse treatment even for life-threatening conditions owing to misinformation and misperceptions about fetal risks. How can I reassure my patients and prevent misinformation from affecting their treatment?

Answer Physicians must provide evidence-based counseling to their patients. For example, antihistamines for morning sickness have been proven safe in numerous studies, but are commonly the subject of media reports overstating the risks to the fetus. Family physicians and obstetricians must take an active role in preventing pregnant patients from being misinformed.

Biais contre l'hypothèse nulle

Effrayer les femmes enceintes au sujet des médicaments durant la grossesse

Résumé

Question Depuis le désastre de la thalidomide, on pratique la médecine comme si tous les médicaments étaient tératogènes, alors qu'en réalité, très peu le sont. Les femmes enceintes sont souvent prêtes à refuser un traitement même en cas de problèmes qui menacent leur vie à cause de renseignements et de perceptions erronés au sujet des risques pour le fœtus. Comment puis-je rassurer mes patientes et empêcher que la désinformation nuise à leur traitement?

Réponse Les médecins doivent fournir à leurs patientes des conseils fondés sur des données probantes. Par exemple, les antihistaminiques pour les nausées matinales se sont révélés sécuritaires dans nombreuses études, mais ils font souvent l'objet de reportages médiatiques exagérant leurs risques pour le fœtus. Les médecins de famille et les obstétriciens doivent jouer un rôle actif pour empêcher que les patientes enceintes soient mal informées.

Histamine-type 1 blockers (antihistamines) have been widely used in different products aimed at treating morning sickness, which affects up to 80% of all pregnancies.¹ The fetal safety of antihistamines has been repeatedly documented in numerous studies, and 5 different meta-analyses have corroborated the safety of their use.²⁻⁶ In fact, one of these analyses⁴ even pointed out that antihistamines had an apparent protective effect against malformations. The authors of 2 studies opined that it is not the antihistamines that protect the baby, but rather the nausea and vomiting of pregnancy itself, which is known to confer favourable pregnancy outcomes including prevention of miscarriages and malformations, and to have a beneficial effect on long-term development.^{7,8} A recent study re-analyzed this original meta-analysis, and excluded 2 of 24 studies, which accounted for more than 40 000 women, because the authors could not locate the

articles (the original paper had several references out of order and one missing). The authors concluded that antihistamines do not confer a protective effect, but are still safe for the fetus.⁹ An analysis that includes the missing references from the original meta-analysis corroborates the initial results, showing an apparent protective effect of antihistamines.¹⁰

The authors of the new, erroneous re-analysis brought it to the attention of a national newspaper, which published a headline insinuating that antihistamines were not safe in pregnancy,¹¹ prompting readers to react in panic. At the time the newspaper's report was published, the journalist was aware of the errors in the re-analysis, but he did not include these details in his report. Moreover, he did not make it clear that "lack of protective effect" of antihistamines is a long way from "risk," and that 4 other meta-analyses confirmed the safety of antihistamines.

Bias in scientific information

Because the Motherisk program is consulted by up to 200 women and their health professionals every day about the use of drugs and exposure to chemicals in pregnancy, we are painfully aware of the misinformation and misperceptions that pregnant women and their families encounter.

Bias against the null hypothesis is the term used to describe the tendency to report adverse events of drugs more often than reporting on their safety. We have shown that a study of a medication that shows no increase in risk is much less likely to get published in meeting abstracts and journals, and to be reported by the media.¹²⁻¹⁶ As a result, the medical literature is often distorted toward alarming rather than relieving fears, even with use of safe drugs such as antihistamines for morning sickness. **Box 1** presents the numerous ways in which this distortion is created, promoted, and sustained.¹²⁻¹⁶

Not surprisingly, pregnant women exposed to nonteratogenic drugs tend to assume these medications carry high fetal risks, and this misperception leads many of them to consider terminating otherwise-wanted pregnancies.^{17,18}

We have shown that more vulnerable women (eg, women with depression, single mothers) are more likely to be negatively affected by misinformation, with higher tendencies to terminate otherwise-wanted pregnancies.^{19,20} The silver lining here is that evidence-based counseling of pregnant women can avoid terminations.¹⁸

Conclusion

Physicians in general, and obstetricians in particular, must take an active role in preventing misinformation from adversely affecting the management of pregnant patients.

Box 1. How the bias against the null hypothesis is created

The following situations explain how the bias against the null hypothesis is created:

- Abstracts are more likely to be presented at meetings if they have adverse results than if they show no increase in risk
- Papers are more likely to be published if they report on adverse results than if they report on results that show no increase in risk
- Media reports are much more likely for papers that find adverse results than for those that show no increase in risk
- Physicians are much more likely to cite adverse results than results that show no increase in risk in subsequent research
- Journal reviewers are more likely to accept articles with adverse results for publication than articles with results that show no increase in risk

Data from Koren et al.¹²⁻¹⁶

The Motherisk program is always pleased to talk to and counsel your patients directly in cases in which physicians believe this can help women and their families.

Competing interests

Motherisk research is supported by Duchesnay Inc, manufacturers of Diclectin (pyridoxine-doxylamine) for morning sickness.

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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. Published Motherisk Updates are available on the *Canadian Family Physician* website (www.cfp.ca) and also on the Motherisk website (www.motherisk.org).