Motherisk Update

Guidelines for maternal codeine use during breastfeeding

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ABSTRACT

QUESTION In light of the recent evidence of adverse events in infants whose mothers use codeine medication, we have been struggling with the issue of how to manage codeine analgesia in our postpartum patients. What are some guidelines for the safe use of codeine during breastfeeding?

ANSWER Motherisk has summarized recent scientific evidence into suggested guidelines for the safe use of codeine during breastfeeding.

RÉSUMÉ

QUESTION Compte tenu des récentes données scientifiques sur les événements indésirables survenus chez des nourrissons dont les mères prenaient des médicaments avec codéine, nous nous demandons comment procéder en ce qui a trait à l’administration postpartum d’analgésiques avec codéine à nos patientes. Existe-t-il des directives sur l’utilisation sans danger de la codéine pendant l’allaitement?

RÉPONSE Motherisk a résumé les données scientifiques récentes sous forme de lignes directrices proposées pour l’utilisation sécuritaire de la codéine durant l’allaitement.

It is widely recognized that maternal pain should be managed following delivery, but the issue of how to adequately provide this pain relief has not been resolved. Any medication prescribed during the postpartum period must be safe and effective for mothers without causing harm to breastfed infants. Although there is an absence of scientific data supporting its use,1 many institutions in North America prescribe the combination of acetaminophen (300 mg), codeine (30 mg), and caffeine (15 mg) (ie, Tylenol No. 3) for analgesia following cesarean section or episiotomy.2 The rationale for choosing codeine analgesia appears to be institutional tradition and years of experience in the hospital setting. However, mothers rarely have follow-up appointments once discharged from the hospital, and recent evidence of adverse drug reactions in breastfed infants whose mothers are prescribed outpatient codeine medication3-5 necessitates guidelines in this population (Boxes 1 and 2).

Postpartum use

A review of the pharmacologic mechanism of codeine analgesia sheds light on issues surrounding its postpartum use.6 Codeine is a prodrug that must be metabolized via the cytochrome P450 2D6 (CYP 2D6) enzyme into morphine to elicit an analgesic effect.7,8; however, the CYP 2D6 gene is highly polymorphic.9 While codeine is effective for most individuals worldwide who possess 2 functional copies of the gene, about 8% of Europeans do not possess any active gene copies, and thus are unable to receive analgesia.10 On the other hand, functional duplications of the CYP 2D6 gene (which range from 2% to 40% of individuals, depending on ethnic background10) enhance morphine biotransformation from codeine11 and have been associated with adverse events,12,13 including death in a breastfed infant.4,5 There are commercial tests available for CYP 2D6 genetic screening; however, clinical trials supporting its introduction in the hospital setting have not yet been performed.

While maternal genotype should certainly be considered before codeine is prescribed, patient education might be an equally important preventive measure.4,5

Box 1. Codeine use during breastfeeding

A large number of women are treated for pain following cesarean section or episiotomy.

- It is important to effectively treat postpartum pain.
- Codeine is widely used for postpartum pain, mostly in combination with acetaminophen. Tylenol No. 3 is the most common codeine-acetaminophen combination in clinical use.
- Recent research from Motherisk suggests that codeine might not be safe for all breastfed infants, as in a minority of cases it might cause CNS depression and apnea.
- A minority of mothers might convert more codeine to morphine in their bodies, putting their babies at risk of side effects or even death.
- Infants appear to be more sensitive to the effects of narcotic opioids, such as morphine, than older children or adults.

CNS—central nervous system.
The strategy of replacing codeine with another opioid analgesic is troublesome in the absence of safety data and clinical experience. However, if codeine is to remain the first-line treatment of postpartum pain, practitioners, as well as patients, should be educated on its risks.

Competing interests
None declared

References

In most cases, the occurrence of CNS depression is consistent between the mother and the baby. If the mother suffers from symptoms of CNS depression (eg, somnolence, grogginess), a physician should examine the baby for signs of CNS depression as well.

• If the baby is not fed well, does not wake up to be fed, does not gain weight, or shows limpness, he or she should be examined by a physician.
• Central nervous system depression in the baby appears to worsen after 4 days, probably owing to the accumulation of morphine with more breastfeeding. If possible, codeine should not be used for longer than 4 days. If pain still necessitates codeine, an attempt should be made to decrease the dose or to switch to non-codeine painkillers (eg, NSAIDs).
• Women who convert more codeine to morphine have a duplication of the gene encoding for cytochrome P450 2D6. This genetic predisposition can be detected by genetic test. This test, although not available in most hospitals, is available on the market.
• Although codeine is widely used in North America,9 randomized studies comparing the use of codeine with various NSAIDs in laparotomy cases (ie, abdominal surgery) have failed to show codeine to be superior in pain relief.

CNS—central nervous system, NSAIDs—nonsteroidal anti-inflammatory drugs.

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Dr Madadi, Ms Moretti, Ms Bozzo, and Des Djukanovic and Itlo are members of the Motherisk Program. Dr Nulman is Associate Director and Dr Koren is Director of the Motherisk Program. Dr Koren is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation. He holds the Ivey Chair in Molecular Toxicology in the Department of Medicine 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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