

Use of over-the-counter cough and cold medications in children

Allan E. Shefrin MD FRCPC Ran D. Goldman MD MSc FRCPC

ABSTRACT

QUESTION Every winter I see numerous children in my office with cold symptoms. Is it safe and effective to use over-the-counter cough and cold medications to alleviate their symptoms?

ANSWER Over-the-counter cough and cold medications are not effective in treating children with the common cold and might cause serious side effects, including death. New recommendations restricting use in Canada to those older than 6 years of age are effective immediately, with relabeling of products starting in the fall of 2009.

RÉSUMÉ

QUESTION Chaque hiver, beaucoup d'enfants se présentent à mon cabinet avec des symptômes du rhume. Est-il sûr et efficace d'utiliser des médicaments en vente libre contre la toux et le rhume pour atténuer leurs symptômes?

RÉPONSE Les médicaments en vente libre contre la toux et le rhume ne sont pas efficaces pour traiter les enfants qui ont le rhume et pourraient causer des effets secondaires sérieux, y compris la mort. De nouvelles recommandations préconisant de ne pas utiliser ces médicaments au Canada chez les enfants de moins de 6 ans sont en vigueur immédiatement et l'étiquetage de ces produits doit être modifié à compter de l'automne 2009.

Every week 10% of American children will use over-the-counter cough and cold medications (OTC CCM). The OTC CCM preparations are usually a combination of at least 2 types of medications, including antihistamines, antitussives, expectorants, decongestants, and antipyretics (Table 1). Children 2 to 5 years of age are the most common users of such preparations, followed by children younger than 2 years of age.¹

The Food and Drug Administration (FDA) first endorsed the use of OTC CCMs in children in 1976, despite the absence of data supporting their safety and efficacy in the pediatric population. Dosing guidelines were established using adult dosages without testing their appropriateness for children. The suggested dose was half of the adult dose for children between the ages of 5 and 12 and a quarter of the adult dose for children between the ages of 2 and 5. There were no dosing guidelines suggested for children younger than 2 years of age. The FDA did not review this approval until 2007.²

Recently, concern about the safety of children using OTC CCMs has grown. Accordingly, both Health Canada and the FDA released statements amending their positions.^{3,4}

Effectiveness

The Cochrane Collaboration maintains 3 reviews directly related to the use of OTC medications to treat the

common cold. The most relevant Cochrane meta-analysis reviewed OTC CCMs in ambulatory patients with viral-induced cough; this meta-analysis reviewed 25 studies, with 8 pediatric trials among them, representing 3492 people, including 616 children. The primary end points of this meta-analysis were frequency and severity of cough, cough counts, sputum production, and physician assessments. The evidence was neither for nor against the use of OTC medications in either pediatric or adult populations.⁵

In a meta-analysis of 35 studies on antihistamine formulations for the treatment of upper respiratory tract infections in adults and children, there was no clinically significant effect found. Almost 9000 patients were included in this study, with end points including alleviation of nasal congestion, rhinorrhea, sneezing, and

Table 1. Examples of ingredients in over-the-counter cough and cold medications, by category

CATEGORY	EXAMPLES OF INGREDIENTS
Antihistamines	Chlorpheniramine, diphenhydramine, hydroxyzine
Antipyretics	Acetaminophen, ibuprofen
Antitussives	Dextromethorphan
Decongestants	Pseudoephedrine, phenylpropanolamine, phenylephrine
Expectorants	Guaifenesin

subjective improvement. Side effects, such as sedation, were noted when first-generation antihistamines were used. Combined therapy with decongestants yielded no benefit in small children (<5 years of age) while a possible benefit of unknown clinical significance was seen in older children and adults.⁶ In another Cochrane review, nasal decongestants were shown to have a statistically significant effect on nasal congestion (6% difference, 95% confidence interval 3% to 9%). However, no pediatric studies met the criteria for inclusion, and these results cannot be applied to patients younger than 12 years of age.⁷

Safety

Multiple studies suggest there is no benefit to the use of OTC CCMs, but is there potential for harm? Yes. In recent years, several published reports have linked OTC CCM ingredients, when used both correctly and incorrectly, with morbidity and mortality.

The US National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance program reported that OTC CCM preparations were responsible for 7091 visits to emergency departments (EDs) during 2004 and 2005 in children younger than 12 years old. This represented almost 6% of total ED visits related to medication. Of these cases, 66% were due to unsupervised ingestion. A quarter of cases were due to properly administered medications with undesired outcomes. Eight times more children presented with effects of medication errors related to OTC CCMs compared with other medications. While children aged 2 to 5 years represented the largest group in this study, children younger than age 2 had the highest rate of adverse reactions.⁸ Providing further evidence of the ED burden related to OTC CCMs, the Centers for Disease Control reported that 1519 patients younger than the age of 2 were treated in American EDs in 2005 for problems related to OTC CCMs.⁹

The true prevalence of OTC CCMs in pediatric illness might be underreported. Physicians might not consider the role of such medications in various presentations, such as apparent life-threatening events (ALTEs). Pitetti et al reported 13 out of 274 (5%) patients presenting with ALTEs had evidence of OTC CCM use on toxicology testing.¹⁰ This raised concern about the potential role of OTC CCMs in ALTEs and led the authors to conclude that toxicology screening should be performed in all cases of ALTEs.¹⁰

Ingredients of OTC CCM have also been linked to several pediatric deaths. During postmortem toxicology evaluation of children with unclear causes of death, OTC CCM ingredients were found. In these cases, OTC CCMs were used as directed or in order to induce side effects such as sedation or to cause intentional overdose.^{11,12} Two earlier case series reported 4 deaths in children younger than 9 months of age that were best explained by OTC

CCM ingredients.^{9,13} A recent review of unexplained infant deaths in Arizona yielded 10 cases linked to OTC CCM use. Toxicology was available for only 21 of the 90 children in the review, and the study results might underestimate the link. Five of these children came from non-English-speaking families, and OTC CCM use was prescribed by a physician in one other case.¹⁴

More recent data regarding OTC CCM and pediatric deaths were published in 2009. An expert panel of pediatricians and toxicologists published a report after reviewing deaths due to OTC CCM use in patients younger than 12 years of age. Five sources of data were looked at including the medical literature, the FDA database, and manufacturers' data. The panel found that of 189 cases, 118 were judged to be possibly, likely, or definitely related to OTC CCM ingredients. Of the 118 cases, 103 involved nonprescription drugs, with 88 involving overdose. The authors found several factors associated with the fatalities: age younger than 2 years, use of the medication for sedation, use in a day care setting, combining 2 or more medications containing the same ingredient, failure to use a measuring device, product misidentification, and use of products intended for adults. Finally, review of the information showed that 6 of the children died after an attempt to sedate them, 3 were cases of abuse, and in 10 cases homicide was suspected.¹⁵

The number of studies suggesting OTC CCMs have played a role in pediatric morbidity and mortality should provide evidence there is a real risk in using these preparations in children. Recent recommendations by Health Canada and the FDA appear to be addressing these concerns.

Recent recommendations

In the fall of 2008, Health Canada and the FDA released separate statements regarding the use of OTC CCMs in children. Citing a lack of evidence of efficacy and growing concerns about adverse reactions, Health Canada advised against the use of all OTC CCM formulations in children younger than 6 years of age and suggested caution be exercised when these formulations were used in children older than 6 years of age.³ For similar reasons, the FDA is advising against the use of OTC CCMs in children younger than 4 years of age.⁴

Competing interests

None declared

Correspondence

Dr Ran D. Goldman, BC Children's Hospital, Department of Pediatrics, Room K4-226, Ambulatory Care Building, 4480 Oak St, Vancouver, BC V6H 3V4; telephone 604 875-2345, extension 5217; fax 604 875-2414; e-mail rgoldman@cw.bc.ca

References

1. Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Pseudoephedrine use among US children, 1999-2006: results from the Slone survey. *Pediatrics* 2008;122(6):1299-304.
2. Sharfstein JM, North M, Serwint JR. Over the counter but no longer under the radar—pediatric cough and cold medications. *N Engl J Med* 2007;357(23):2321-4.

3. Health Canada [website]. *Health Canada's decision on cough and cold medicines*. Ottawa, ON: Health Canada; 2008. Available from: www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2008/2008_184info1-eng.php. Accessed 2009 Jul 14.
4. Food and Drug Administration. *Using over-the-counter cough and cold products in children*. Silver Spring, MD: Food and Drug Administration; 2008. Available from: www.fda.gov/ForConsumers/ConsumerUpdates/ucm048515.htm. Accessed 2009 Aug 28.
5. Smith SM, Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. *Cochrane Database Syst Rev* 2008;(1):CD001831.
6. Sutter AI, Lemiengre M, Campbell H, Mackinnon HF. Antihistamines for the common cold. *Cochrane Database Syst Rev* 2003;(3):CD001267.
7. Taverner D, Latte G. Nasal decongestants for the common cold [retracted in: *Cochrane Database Syst Rev* 2009;(2):CD001953]. *Cochrane Database Syst Rev* 2007;(1):CD001953.
8. Schaefer MK, Shehab N, Cohen AL, Budnitz DS. Adverse events from cough and cold medications in children. *Pediatrics* 2008;121(4):783-7. Epub 2008 Jan 28.
9. Centers for Disease Control and Prevention (CDC). Infant deaths associated with cough and cold medications—two states, 2005. *MMWR Morb Mortal Wkly Rep* 2007;56(1):1-4.
10. Pitetti RD, Whitman E, Zaylor A. Accidental and nonaccidental poisonings as a cause of apparent life-threatening events in infants. *Pediatrics* 2008;122(2):e359-62.
11. Marinetti L, Lehman L, Casto B, Harshbarger K, Kubiczek P, Davis J. Over-the-counter cold medications—postmortem findings in infants and the relationship to cause of death. *J Anal Toxicol* 2005;29(7):738-43.
12. Boland DM, Rein J, Lew EO, Hearn WL. Fatal cold medication intoxication in an infant. *J Anal Toxicol* 2003;27(7):523-6.
13. Gunn VL, Taha SH, Liebelt EL, Serwint JR. Toxicity of over-the-counter cough and cold medications. *Pediatrics* 2001;108(3):e52.
14. Rimsza ME, Newberry S. Unexpected infant deaths associated with use of cough and cold medications. *Pediatrics* 2008;122(2):e318-22.
15. Dart RC, Paul IM, Bond GR, Winston DC, Manoguerra AS, Palmer RB, et al. Pediatric fatalities associated with over the counter (nonprescription) cough and cold medications. *Ann Emerg Med* 2009;53(4):411-7. Epub 2008 Dec 19.



Child Health Update is produced by the Pediatric Research in Emergency Therapeutics (PRETx) program at the BC Children's Hospital in Vancouver, BC. Dr Shefrin is a member and Dr Goldman is Director of the PRETx program. The mission of the PRETx program is to promote child health through evidence-based research in therapeutics in pediatric emergency medicine.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in children? We invite you to submit them to the PRETx program by fax at 604 875-2414; they will be addressed in future Child Health Updates. Published Child Health Updates are available on the *Canadian Family Physician* website (www.cfp.ca).