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Treating cough and cold: Guidance for caregivers of children and youth

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Despite the widespread use of over-the-counter (OTC) cough and cold medications (CCMs), the effectiveness of most CCMs has not been proven in children. A meta-analysis summarizing trials using OTC CCMs for viral-induced cough found no evidence for or against the use of OTC medicines in both paediatric and adult populations when cough frequency and severity, as well as physician assessments, were compared. Furthermore, North American data suggest that OTC CCMs may be associated with medication errors and adverse events, resulting in visits to emergency departments and even leading to death. The present article provides information on current evidence for cough and cold therapies, including fluid intake, humidified air, antihistamines, echinacea, zinc, honey and vitamin C, for caregivers of children and youth.

Key Words: Children; Cough and cold; Medications; Over-the-counter (OTC) medications

EPIDEMIOLOGY

It is estimated that more than one-half of children younger than 12 years of age use one or more medicinal products in a given week; over-the-counter (OTC) products, mostly cough and cold medications (CCMs) account for the majority of medication exposures (1). The preparations are usually a combination of several medications including antitussives, expectorants, antihistamines, decongestants and antipyretics such as acetaminophen.

When CCMs were first approved in the United States in 1976, no data supporting their safety and efficacy were available for the paediatric population, and dosing recommendations were derived using adult dosages. For children younger than two years of age, no dosing guidelines were offered. The Food and Drug Administration (FDA) did not review this approval until 2007 (2).

The effectiveness of most CCMs has not been proven in children. A Cochrane meta-analysis of ambulatory adults and children with viral-induced cough (3) found eight paediatric trials, representing 616 children. No evidence was found for or against the use of OTC medicines in both the paediatric and adult population when frequency and severity of cough, cough counts, sputum production and physician assessments were compared (3).

POTENTIAL HARM

The United States National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance program reported that CCM preparations were responsible for 6% (n=7091) of total

Le traitement de la toux et du rhume : des conseils pour ceux qui s'occupent d'enfants et d'adolescents

Malgré l'utilisation généralisée de médicaments contre la toux et le rhume (MCTR) en vente libre, l'efficacité de la plupart des MCTR n'est pas démontrée chez les enfants. Une méta-analyse résumant les essais faisant appel aux MCTR en vente libre contre le rhume d'origine virale n'a permis de produire aucune donnée probante pour ou contre les médicaments en vente libre au sein des populations pédiatrique et adulte en matière de comparaison de la fréquence et de la gravité de la toux et de l'évaluation par les médecins. De plus, selon les données nord-américaines, les MCTR en vente libre pourraient s'associer à des erreurs de médication et à des événements indésirables qui entraînent des visites à l'urgence et même des décès. Le présent article fournit aux personnes qui s'occupent d'enfants et d'adolescents de l'information sur les données probantes à jour au sujet des traitements contre la toux et le rhume, y compris la consommation de liquide, l'air humidifié, les antihistaminiques, l'échinacée, le zinc, le miel et la vitamine C.

emergency department (ED) visits related to medication use during 2004 and 2005 in children younger than 12 years of age (4). The Centers for Disease Control and Prevention (USA) reported that 1519 patients younger than two years of age were treated in American EDs in 2005 for problems related to CCMs (5). In one report (6), 5% of 274 patients presenting with apparent life-threatening events showed evidence of CCM use on toxicology testing. Recently, CCMs were associated with paediatric deaths (7). An expert panel of paediatricians and toxicologists reviewed deaths in patients younger than 12 years of age. Of 189 cases, 118 were found to be possibly, likely or definitely related to CCM ingredients. Of these, 103 involved a nonprescription drug and, of these, 88 involved an overdose. Factors associated with fatalities are presented in Table 1.

Using a stratified probability sample of 63 American EDs, it was recently reported that visits for CCM-related adverse events among children younger than 12 years of age were substantially reduced after withdrawal of OTC infant CCMs. For children younger than two years of age, the estimate was 1248 visits (13.3%) versus 2790 visits (28.7%) in the postwithdrawal period compared with the prewithdrawal period (difference -15.4% [95% CI -25.9% to -5.0%]) (8). Similarly, a significant decrease in the annual rates of therapeutic errors in children younger than two years of age reported to poison centres in Maryland (USA) followed the voluntary withdrawal of OTC CCMs (45.2 per 100,000 children [95% CI 30.7 to 66.6] versus 83.8 per 100,000

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children [95% CI 67.6 to 104.0] in the prewithdrawal period; $P < 0.02$) (9).

Similarly, OTC CCMs were among the most common medications to be associated with medication errors in Ireland (10).

In the fall of 2008, Health Canada and the FDA released separate statements regarding the use of CCMs in children. Health Canada advised against the use of all CCM formulations in children younger than six years of age, with caution being exercised when these formulations were used in children older than six years of age (11). The FDA recommended that CCMs should not be used in children younger than two years of age (12).

Based on these recent recommendations, what other measures can paediatricians suggest to families to support children with cough and cold symptoms likely due to a viral illness?

OTHER INVESTIGATED TREATMENTS

Fluid intake

Consumption of fluids during an illness with cough and cold is considered by many to be the mainstay of treatment in children. Staying hydrated and softening secretions are the mechanisms of potential benefit.

Humidified air

Humidified air (cold or warm) is frequently used by parents and recommended by health care providers. The mechanism of action is unclear and may involve enhanced drainage of congested upper airways. One Cochrane review (13) assessed the benefit of steam inhalation and was unable to recommend its use in the treatment of common cold symptoms, despite the fact that three of six studies found benefits of steam for symptom relief in children with the common cold. No significant adverse events were reported.

Nonsteroidal anti-inflammatory drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs), mostly ibuprofen, are used by many parents and children to improve comfort during febrile illness, including during illness with cold and cough. When compared with placebo and other treatments in a recent Cochrane review with nine randomized controlled trials (RCTs), describing 37 comparisons (placebo or other NSAIDs) and more than 1000 patients (14), NSAIDs did not significantly reduce the total symptom score or duration of the cold, but were found to be beneficial for discomfort or pain caused by the viral illness.

Antihistamines

A Cochrane review (15), including 32 articles with almost 9000 people with the common cold, found large differences in study designs, participants, interventions and outcomes. The reviewers found no evidence of any clinically significant effect in children regarding general recovery when antihistamines were used as monotherapy. First-generation antihistamines showed a small effect on rhinorrhea and sneezing, but these effects were overshadowed by side effects including sedation of these patients. Combination of antihistamines with decongestives in small children failed to show any positive effect. In older children (and adults), the majority of studies showed some small effects on general recovery and on nasal symptom severity, but it was unclear whether these effects were clinically significant (15).

Echinacea

A 2006 Cochrane collaboration review identified 16 controlled trials on the effect of echinacea for cough and the common cold (16). Due to multiple methodological limitations in many of the

TABLE 1
Factors associated with fatalities from over-the-counter cough and cold medications in children

Age younger than two years
Use of the medication for sedation
Use in a daycare setting
Combining two or more medications with the same ingredient
Failure to use a measuring device
Product misidentification
Use of products intended for adults

Adapted from reference 7

studies, the reviewers suggested there were no sufficient data to suggest the effectiveness of echinacea in children. The use of echinacea for eight to 12 weeks as a prophylactic measure did not result in effective prevention of the common cold.

Zinc

It has been suggested that zinc can inhibit viral growth (17). As such, the treatment of cough and cold with zinc was tested in several studies. While some of them showed benefits, especially if used within 24 h of the onset of common cold symptoms (18), others failed to show the same effect (19). At the present time, the use of zinc in children with cough and cold is not recommended.

Honey

Pasteurized honey can safely be used in children older than one year of age. It is inexpensive, has an excellent safety profile, a good demulcent effect and antioxidant properties, and it increases cytokine release, which may result in antimicrobial effects (20). It was recently shown to have potential benefit for cough and cold. In paired comparisons, honey was significantly superior to no treatment or honey-flavoured dextromethorphan for cough frequency and severity, bothersome nature of the cough, and the child/parent sleep quality, as rated by the parents (21).

A Cochrane collaboration review (22) included one RCT, and concluded that there was not enough evidence to advise for or against the use of honey. More recently, an RCT with 139 children (24 to 60 months of age) suffering from cough due to upper respiratory tract infection reported that 2.5 mL of honey before sleep improved cough frequency and severity, as well as sleep quality in a mean of 59% of children (23). This was a better improvement compared with dextromethorphan, diphenhydramine or placebo.

Vitamin C

Vitamin C (ascorbic acid) is widely sold and used as part of a multivitamin regimen or by itself, for both prevention and therapy of the common cold. In a Cochrane review of more than 30 comparisons, including vitamin C, involving more than 11,000 participants, no significant improvement of symptoms was noticed with the use of vitamin C. When comparisons were made among thousands of patients for prophylaxis of respiratory episodes, a consistent benefit was observed with vitamin C, representing a reduction in cold duration of more than 13% among children. Of interest, among 642 marathon runners, skiers and soldiers on sub-arctic exercises, a pooled RR of 50% for developing a cold while taking prophylactic vitamin C was found in six studies (24). While these results in children are promising, no clear recommendation can be found with respect to the dose of vitamin C or whether any interaction with other drugs or adverse events can be anticipated when using vitamin C on a regular basis.

CONCLUSIONS

Despite their widespread use among children, the use of OTC CCMs is not effective in most cases and is potentially harmful. Several alternatives such as fluids, humidified air, NSAIDs, anti-histamines, echinacea, zinc and vitamin C, have been investigated and, so far, show little benefit in the paediatric population. Honey may have beneficial effects, but dosing is yet to be determined. Identifying specific groups of children who may benefit from one or more of these alternatives is an effort justified by the large number of children suffering from the common cold, and the frequency of this illness. Large clinical trials of these products are needed.

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REFERENCES

- Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Medication use among children <12 years of age in the United States: Results from the Slone Survey. *Pediatrics* 2009;124(2):446-54.
- 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.
- 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.
- Schaefer MK, Shehab N, Cohen AL, Budnitz DS. Adverse events from cough and cold medications in children. *Pediatrics* 2008;121(4):783-7.
- 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.
- 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.
- Dart RC, Paul IM, Bond GR, et al. Pediatric fatalities associated with over the counter (nonprescription) cough and cold medications. *Ann Emerg Med* 2009;53(4):411-7.
- Shehab N, Schaefer MK, Kegler SR, Budnitz DS. Adverse events from cough and cold medications after a market withdrawal of products labeled for infants. *Pediatrics* 2010;126(6):1100-7.
- Klein-Schwartz W, Sorkin JD, Doyon S. Impact of the voluntary withdrawal of over-the-counter cough and cold medications on pediatric ingestions reported to poison centers. *Pharmacoepidemiol Drug Saf* 2010;19(8):819-24.
- Cassidy N, Duggan E, Williams DJ, Tracey JA. The epidemiology and type of medication errors reported to the National Poisons Information Centre of Ireland. *Clin Toxicol (Phila)* 2011;49(6):485-91.
- Health Canada. Health Canada's decision on cough and cold medicines. <http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2008/2008_184info1-eng.php> (Accessed on September 22, 2011).
- FDA releases recommendations regarding use of over-the-counter cough and cold products. <<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116839htm>> (Accessed on September 22, 2011)
- Singh M, Singh M. Heated, humidified air for the common cold. *Cochrane Database Syst Rev* 2011;(5):CD001728.
- Kim SY, Chang YJ, Cho HM, Hwang YW, Moon YS. Non-steroidal anti-inflammatory drugs for the common cold. *Cochrane Database Syst Rev* 2009;(3):CD006362.
- De Sutter AI, Lemiengre M, Campbell H. Withdrawn: Antihistamines for the common cold. *Cochrane Database Syst Rev* 2009;(4):CD001267.
- Linde K, Barrett B, Wölkart K, Bauer R, Melchart D. Echinacea for preventing and treating the common cold. *Cochrane Database Syst Rev* 2006;(1):CD000530.
- Suara RO, Crowe JE Jr. Effect of zinc salts on respiratory syncytial virus replication. *Antimicrob Agents Chemother* 2004;48(3):783-90.
- Hulisz D. Efficacy of zinc against common cold viruses: An overview. *J Am Pharm Assoc* 2004;44(5):594-603.
- Caruso TJ, Prober CG, Gwaltney JM Jr. Treatment of naturally acquired common colds with zinc: A structured review. *Clin Infect Dis* 2007;45(5):569-74.
- Gheldof N, Wang XH, Engeseth NJ. Identification and quantification of antioxidant components of honeys from various floral sources. *J Agric Food Chem* 2002;50(21):5870-7.
- Paul IM, Beiler J, McMonagle A, Shaffer ML, Duda L, Berlin CM Jr. Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. *Arch Pediatr Adolesc Med* 2007;161(12):1140-6.
- Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. Honey for acute cough in children. *Cochrane Database Syst Rev* 2010;(1):CD007094.
- Shadkam MN, Mozaffari-Khosravi H, Mozayan MR. A comparison of the effect of honey, dextromethorphan, and diphenhydramine on nightly cough and sleep quality in children and their parents. *J Altern Complement Med* 2010;16(7):787-93.
- Douglas RM, Hemilä H, Chalker E, Treacy B. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev* 2007;(3):CD000980.

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