Cough and Cold Medications in Children:

Are They Effective?

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Presented at the 2008 Annual Meeting of the Ontario Pharmacists' Association, September, 2008.

The common cold is an acute inflammatory reaction to viral infection of the upper airway, characterized clinically by a sore throat followed by a runny nose, nasal congestion, sneezing and cough. The cold begins when virus particles in droplets enter and infect cells lining the nasopharynx and throat. There are > 100 different viruses which can cause the common cold, of which some of the more common are *Rhinovirus*, *Coronavirus*, *Myxovirus*, *Adenovirus*, *Echovirus* and *Coxsackievirus*. Once the viral infection has developed, the subsequent immune response results in nasal congestion, fever and the clinical manifestations of the common cold. Symptoms develop typically two to five days after infection and can last for seven to 14 days. The natural history is of resolution, although as noted, secondary infections can occur and the common cold can also trigger an exacerbation of existing pulmonary problems such as asthma.

Although the mortality associated with the common cold is low, there is significant morbidity, in part related to frequency. The common cold is very, very common. Estimates are that there is a new case of the common cold every second in North America, with more than a billion cases per year. In children of school age, Canadian data suggests that, in any given year, more than half will develop a cold.[1] Colds account for more days of work or school missed than any other single diagnosis. In addition, colds can be followed by secondary infections such as pneumonia or otitis media. The yearly economic burden for Canada has been estimated to be between two and three billion dollars.[2]

Therapeutic options for the common cold in children

The high frequency and considerable morbidity associated with the common cold suggest that therapeutic options would be of benefit. Regrettably, the wide viral repertoire associated with the common cold has effectively precluded any conventional antiviral therapy and current management is primarily supportive and symptomatic.

Supportive therapy includes antipyretics for fever, fluids and rest. While this does not decrease the duration of symptoms, this does make the patient more comfortable.

Symptomatic therapy includes therapies that aim to specifically target the symptoms of a cold, these including runny nose, nasal congestion, sneezing and cough. There is a long history of symptomatic therapy for the common cold and a number of products developed for use in adults have over the years been modified for use as therapy in children.[3] The efficacy of these products, even in adults, has been controversial.[4-6]

Despite this, they have been very popular and there are > 700 types of cough and cold medication for children on the North American market. They have also been widely used. In 1994, the Center for Disease Control estimated that 50% of all children in the US received a cough or cold medication in any given month.

While the issue of safety and efficacy of these products in children has been debated for some time, recent events have forced a critical analysis of the data supporting the use of cough and cold medications in children as to whether these products in fact are generally safe and effective. Specifically, a Citizen's Petition in the US (Docket #2007P-0074) was filed in 2007 that held that children's cough and cold medications sold on an OTC basis were not generally recognized as safe and effective.[7]

What are the therapeutic agents in question?

The four major groups of drugs used to treat cough and cold symptoms in children are:

- Nasal decongestants
- Antihistamines
- Expectorants
- Antitussives

Nasal decongestants such as xylometazoline (topically) or pseudoephedrine (systemically) are used to reduce nasal stuffiness and congestion. Antihistamines such as diphenhydramine or brompheniramine are used systemically to reduce histamine-related symptoms such as runny nose and watery eyes, while the anticholinergic effects of these agents can also dry the nasal mucosa. Expectorants such as guaifenesin are used to reduce the viscosity and surface tension of secretions such as mucous, making it easier to eliminate mucous. Antitussives such as dextromethorphan are used to reduce the frequency and intensity of non-productive cough. Frequently these agents are used in combination.

The basis of the Citizen's Petition was that these products, when used in children, did not in fact provide symptomatic relief and were associated with risk. What is the evidence for and against these claims?

In 1994, the Center for Disease Control estimated that 50% of all children in the US received a cough or cold medication in any given month.

Efficacy

The question of the efficacy of children's cough and cold preparations has been controversial for some time. While there have been studies addressing this issue in adults, in children the majority of the scant number of studies performed have been underpowered and have often used non-validated instruments to measure the primary outcome. Thus, much of the available evidence must be obtained from meta-analysis or by systematic reviews of all trials available.

In the case of nasal decongestants, Taverner and Latte were unable to find any research in children that meet the standards required for systemic review.[8] Their review of available adult studies concluded that there was no data supporting the use of nasal decongestants for therapy of colds in children < 12-years-of-age.[8]

A larger number of studies were reviewed by De Sutter, *et al* to determine the role of antihistamines in the therapy of colds.[9] This review of 32 studies with > 8,900 patients, showed that

antihistamines alone were not an effective therapy for the symptoms of the common cold and while a small beneficial effect was demonstrated when they were used in combination with decongestants, there was no evidence for benefit in small children.[9]

There are very few studies on the use of guaifenesin in adults and none at all in children. The studies to date show slight subjective improvement when studied in small numbers of adults with chronic cough and mucous production, but there is no evidence that guaifenesin is any more effective than water, which is known to be a natural expectorant.

Antitussives, when studied in adults, have produced a slight decrease in cough frequency but not intensity. This may not be the case in children. In a meticulously well-done study of 105 children with colds, a teaspoon of buckwheat honey was found to reduce nocturnal symptoms significantly better than either dextromethorphan or placebo.[10]

There are a small number of studies assessing the use of combination products in children. The majority of these studies have not found significant differences in outcome between treatment combinations or with placebo.[11-15]

In addition to conventional therapy, there are a small number of studies of natural products and herbal medications for the therapy of the common cold.[1] While some agents have promise, it would be safe to say that the overall results are disappointing, with most natural or herbal products performing no better than placebo.

Thus, the best available evidence suggests that, for young children, there is no evidence of efficacy for cough and cold preparations, alone or in combination.

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Safety

The consideration of the safety of cough and cold medications for children should start with the observation that these medications are mainly very safe. However, very safe is not completely safe and this is especially true in the context of an OTC medication. While medications with major toxicities are routinely used by children, this is in the context of a learned intermediary (*i.e.*, a healthcare professional—often two [physician and pharmacist]) who will advise the family on safe administration, therapeutic plan and monitoring. In contrast, with an OTC preparation it is possible for a parent to obtain the medication in most cases with the only contact being the retail clerk who charges them for the drug in question. Thus, the safety standards that OTC medication must reach are very high.

Safety concerns with children's cough and cold medications have been raised for some time with respect to case reports. The Citizen's Petition noted above drew on another source, this being Poison Control Center reports. The Petition cited the Maryland Poison Control Database, which in 2004 reported 1,078 calls regarding ingestion of cough and cold medications in children (out of 18,575 calls for children < 18-years-of-age), of which five were serious. All resolved without significant sequelae. A six-year study of calls banked by the American Association of Poison Control Centers disclosed that, between 2000 and 2007, there were 774,960 calls for ingestion of cough and cold medications in children, 99% at home and 97% were not severe. However, there were 35 deaths, primarily in infants and toddlers and mainly related to therapeutic overdosing.

Thus, the best available evidence suggests that, in situations of therapeutic overdose, there is a small but significant risk associated with the use of cough and cold medications in children.[16]

The current situation

As a result of the Citizen's Petition and subsequent hearings, the US FDA has stated that cough and cold medications should not be given to children under the age of two.[7] The issue of use of these medications for children between the ages of two and 12 years is under active debate, both by the FDA and Health Canada.

Clinical implications

This raises the obvious issue of what a practitioner should do when confronted with a young child with a cold. The parents should be advised with respect to supportive therapy (*i.e.*, rest, plenty of fluids and the use of an antipyretic [acetaminophen or ibuprofen] in appropriate doses). A frank discussion on the lack of evidence for safety and the potential for harm from cough and cold medications would be prudent.

There are a few caveats. Some children with strong allergic histories who develop a cold during a time when their seasonal allergies are active may benefit from judicious use of an antihistamine. Children with histories of reactive airway disease and nocturnal cough, especially when the cough is persistent for more than a week, may benefit from the use of an inhaled β_2 agonist such as salbutamol. For children older than one-year-of-age, the study by Paul, *et al* suggests that a teaspoon of buckwheat honey at night may be effective in reducing the intensity of cough and improving the quality of sleep.[10]

This also raises the issue of anticipatory guidance. Given the frequency with which colds are seen among children, it is prudent for primary care practitioners who have families with young children to include advice on home care of colds when seeing children for routine healthcare visits.

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For references, please contact **cme@sta.ca**