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DIAGNOSIS AND MANAGEMENT OF ACUTE COUGH

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Abstract:

Introduction: *The common cold is considered an acute upper respiratory syndrome, often because of viral infection, with symptoms consisting of rhinorrhea and nasal obstruction. Common cold is often supplemented by sore throat, sneezing, body aches, low-grade fever, and cough. Cough linked with the common cold is a common and especially bothersome symptom for patients in the ambulatory setting. A new Internet survey showed that cough outlasted other cold symptoms in seventy percent of the survey respondents. Adults in the US average 2 to 3 colds in a year, and this number is even greater in children. 52% of adult participants from a new survey showed that cough/cold affected their daily lives. 3 A total of seventy five percent of survey respondents tried to manage the cough associated with the common cold (CACC), most often with over the counter (OTC) syrup or a throat lozenge. In 2015, the average American household made twenty six trips to retail outlets and spent about $338 every year on OTC products. The new Cough Expert Panel believed it would be helpful to conduct a systematic review to update the recommendations of the 2006 guideline.*

Aim of work: *In this review, we will discuss acute cough.*

Methodology: *We did a systematic search for Acute cough using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.*

Conclusions: *Regrettably, there has not been much change in the management options for cough because the common cold since publication of the 2006 CHEST cough guidelines. Many of the published studies are small and have marked limitations and potential biases. Data pooling was not possible, making it hard to provide definitive recommendations. Cold symptoms are one of the most common reasons for seeking medical attention, and cough is one of the most irritating and persistent cold symptoms.*

Key words: *acute cough; common cold; pharmacologic and nonpharmacologic treatment.*

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INTRODUCTION:

The common cold is considered an acute upper respiratory syndrome, often because of viral infection, with symptoms consisting of rhinorrhea and nasal obstruction. Common cold is often supplemented by sore throat, sneezing, body aches, low-grade fever, and cough. Cough linked with the common cold is a common and especially bothersome symptom for patients in the ambulatory setting. A new Internet survey showed that cough outlasted other cold symptoms in seventy percent of the survey respondents. [1] Adults in the US average 2 to 3 colds in a year, and this number is even greater in children. [2]

52% of adult participants from a new survey showed that cough/cold affected their daily lives. A total of seventy five percent of survey respondents tried to manage the cough associated with the common cold (CACC), most often with over the counter (OTC) syrup or a throat lozenge. In 2015, the average American household made twenty six trips to retail outlets and spent about $338 every year on OTC products.

The new Cough Expert Panel believed it would be helpful to conduct a systematic review to update the recommendations of the 2006 guideline. [3] In this review, we will discuss the most recent evidence regarding acute cough

METHODOLOGY:

We did a systematic search for Acute cough using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.
The terms used in the search were: acute cough, presentation, diagnosis, management, pharmacological, non pharmacological.

Key Clinical Question 1

Is there proof of clinically significant management effects for acetylcysteine or carbocysteine in decreasing the duration of cough?

The Chalumeau and Duijvestijn[4] systematic review studied 6 trials that compared acetylcysteine or carbocysteine vs placebo for upper or lower respiratory tract infections in children. There were only 3 trials tested cough as a primary outcome, measuring after six days. The technique of assessing cough were not discussed. Generally, these studies were small in size and had a greater risk of bias. It was challenging to account for other therapies and, in many cases, antibiotics were given. Moreover, many of the patients were hospitalized, which is not routine for the treatment of the common cold.

The Chalumeau and Duijvestijn systematic review recognized 34 studies, with a total of 2,064 participants, that assessed product safety. Though limited data are noted for children < 2 years, there were 59 cases of paradoxically increased bronchorrhea in this age group, and many (86%) needed hospitalization or extended hospitalization. For other age groups, the products were generally safe, with minor GI symptoms reported in 2% of all participants.

Key Clinical Question 2

Is there proof of clinically significant management effects for decongestants and antihistamines in decreasing the duration of CACC?

The De Sutter et al[5] systematic review recognized four RCTs that assessed the effects of antihistamine and decongestant combinations on the severity of cough. The data included 672 cold episodes. Data pooling was not possible due to many treatments and combinations.

Generally, the evidence were inconsistent, making it challenging to form any conclusion regarding the effectiveness of this combination of products. The De Sutter et al systematic review recognized 2 RCTs of antihistamine and analgesic combinations.

The De Sutter et al systematic review recognized 2 RCTs with a total of 249 subjects managed with a decongestant and analgesic combination. No effect on cough was observed. The De Sutter et al systematic review assessed 3 RCTs of antihistamine, decongestant, and analgesic combinations. 2 studies included 555 adult subjects, and one pediatric study included 201 children. Data pooling was impossible, and study results were inconsistent. The two adult studies did show some treatment results on cough with the combination of dextromethorphan, doxylamine, paracetamol, and ephedrine. The author concluded that this combination may be efficient for CACC in adults. But, there is no marketed product available in the United States that includes this combination of ingredients. The pediatric study using the combination of acetaminophen, diphenhydramine, and pseudoephedrine showed no effect on cough; however, dextromethorphan was not included in the combination product administered in the pediatric study.

One possible eligible trial was identified from an updated literature search of the De Sutter review.

This trial by Dicpinigaitis et al[6] assessed the effect of diphenhydramine on cough reflex sensitivity in 22 healthy subjects with acute viral infection by administering a capsaicin challenge on 3 separate days. Diphenhydramine was successful in inhibiting the cough reflex in subjects with acute cough during viral respiratory tract infection. After review, it was concluded that this study was not relevant to the clinical question. The available recently marketed products in the United States do not include the combination of ingredients that may be effective for CACC in adults; so, no specific recommendations could be made for the use of antihistamine, decongestant, and analgesic combinations to treat CACC in adults. Additionally, there were no pediatric studies of antihistamine, decongestant, and analgesic combination products that showed efficacy for CACC. For adult and pediatric patients with cough due to the common cold.

Key Clinical Question 3
Is there proof of clinically significant effects for NSAIDs on CACC?

The Kim et al[7] systematic review recognized 2 RCTs of 77 patients receiving NSAIDs and 82 placebo comparisons. The 2006 cough guidelines suggested a combination of first-generation antihistamine and nasal decongestant or naproxen for CACC. The Kim et al systematic review showed no clear evidence that treatment with NSAIDs is effective for treatment of CACC. These studies were small with wide CIs. In adult patients with cough due to the common cold, we suggest against the use of nonsteroidal anti-inflammatory agents until they have been shown to make cough less severe or resolve sooner (Ungraded Consensus-Based Statement).

Key Clinical Question 4
Is there proof of clinically significant treatment effects for honey in decreasing the duration of CACC in pediatric patients?[8]

The Oduwole et al [9] systematic review recognized a total of 3 RCTs. Two RCTs included a comparison of honey to dextromethorphan for decreasing the numbers of cough. Both trials were judged to be at high risk of bias. There were 149 total participants in these study arms (75 received honey and 74 received dextromethorphan). Generally, there was no difference between treatment groups.

One trial also involved a comparison of honey to diphenhydramine. This comparison showed honey can be better than diphenhydramine in decreasing the numbers of cough and severity of cough. Two other comparisons in the two RCTs showed that honey was probably better compared with no treatment in 154 participants for frequency of cough and cough severity.

Key Clinical Question 5
Is there proof of clinically significant treatment effects for zinc regarding the time to resolution of cough or change in the cough symptom score?

The Singh and Das [10] systematic review published in 2013 recognized four RCTs in which zinc was assessed for time to resolution of cough. 1 study was excluded because the zinc was given as syrup, while the other three studies used zinc lozenges. In the three lozenge studies, 122 patients received zinc lozenges and 137 patients received placebo therapy. Data pooling was not possible given the diverse populations and varying dosage frequency.

Key Clinical Question 6
Is there proof of clinically significant treatment effects for OTC medications in decreasing the duration of CACC?

The Smith et al[11] systematic review, evaluated to be of excellent quality, involved 6 trials with a total of 1,526 adult patients that compared antitussive agents with placebo. The antitussive agents studied included codeine, dextromethorphan, and moguisteine. Four trials of antitussive studies were identified in 327 pediatric subjects. Generally, the studies had love quality with variable results.

The Smith et al systematic review recognized 3 trials that compared the expectorant guaifenesin with placebo in 304 subjects. Data quality was poor, and studies had conflicting results. No studies were identified that reported outcomes with the use of expectorants in pediatric subjects.

The Smith et al systematic review recognized one trial of 99 subjects that compared the mucolytic agent bromhexine with placebo. One pediatric trial compared the mucolytic letosteine with placebo in 40 subjects. Generally, the data quality for mucolytic agents was very low, and data pooling was not possible. 1 trial did find reduced cough frequency with mucolytic therapy. 4 studies evaluated other product combinations against placebo in 836 adults; 3 of the studies found antihistamines to be no more effective than placebo in relieving cough symptoms. 2 studies evaluated other product combinations in 99 pediatric patients. Generally, these studies were small

and heterogeneous, using widely varied drug preparations and dosing frequencies.

These limitations cannot result in possible data pooling. None of the pediatric studies showed a benefit over placebo for antitussive therapy, antihistamines, decongestants, or antitussive/bronchodilator treatment. A trial by Paul et al[12] was recognized in the updated literature search of Smith et al. Paul et al assessed a single dose of Vicks VapoRub (camphor, menthol, and eucalyptus oils in a petroleum base) compared with
petrolatum and no treatment for nocturnal cough caused by respiratory tract infections in 138 children. The study was blinded, but parents who used VapoRub correctly
guessed their treatment group 86% of the time, as did 89% of the petrolatum-treating control group. Parents rated VapoRub most favorably for symptomatic relief of
nocturnal cough. This study was assessed as low quality.

Though the mechanism is not completely clear, menthol has been proven to improve the nasal sensation of airflow and may lead to improved sleep. Another trial was identified in the update of Smith et al. Paul et al[13] compared the effects of agave nectar with placebo and no treatment on acute nocturnal cough in 119 infants and toddlers. This study was evaluated as low quality. Although a placebo effect was showed, there was no additional benefit from agave nectar.

In adult and pediatric patients with the common cold, we find no evidence to support or refute the use of OTC antitussive agents, expectorants, mucolytic agents, antihistamines, or combination products for decreasing cough.

Discussion

This review discussed six key clinical questions regarding the treatment of CACC. It could make no specific recommendation regarding the use of acetylcysteine or carbocysteine for key clinical question 1. Regarding key clinical question 2, no specific recommendation can be made based on the responsibility of decongestants and antihistamines. For key clinical question 3, no evidence was found to support the use of nonsteroidal anti-inflammatory agents. For key clinical question 4, we suggested that honey may offer more relief than diphenhydramine, no treatment, or placebo; but, honey is not more effective than dextromethorphan for adults and children.

The first hydrocodone and guaifenesin combination product (Vituz; Hawthorn Pharmaceuticals) was sold in 2013. No new clinical studies were required by the FDA for approval of this combination product; efficacy was based on the shown bioequivalence of the active ingredients to their respective reference products. The same pathway of approval has been used for several other cough and cold preparations over the past 3 years; hydrocodone bitartrate and guaifenesin oral solution (Obredon; Sovereign Pharmaceuticals), [14]

In January 2008, the FDA published a consumer update strongly recommending that “over-the-counter (OTC) cough and cold products should not be used for infants and children under two years of age because serious and potentially life-threatening adverse effects might happen.” [15]

In pediatric patients (aged < 18 years) with cough due to the common cold, studies suggest avoiding use of codeine-containing medications because of the potential for serious side effects including respiratory distress (Ungraded Consensus-Based Statement).

_ Development of clinical studies to confirm the use of multi-ingredient prescription and nonprescription cough therapies42

_ Development of effective antitussive medications that are safe for children and adults
_ RCTs with proper comparators

CONCLUSIONS:

Regrettably, there has not been much change in the management options for cough because the common cold since publication of the 2006 CHEST cough guidelines. Many of the published studies are small and have marked limitations and potential biases. Data pooling was not possible, making it hard to provide definitive recommendations. Cold symptoms are one of the most common reasons for seeking medical attention, and cough is one of the most irritating and persistent cold symptoms.

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