Cochrane for Clinicians

Putting Evidence into Practice

Oral Antihistamine/Decongestant/Analgesic Combinations for the Common Cold

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Dr. Salisbury-Afshar presents a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://summaries.cochrane.org/CD004976.

EB CME

This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 807.

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Clinical Scenario

A 32-year-old otherwise healthy man presents with three days of low-grade fever (99°F to 100°F [37.2°C to 37.8°C]), nasal congestion, headache, itchy throat, sinus pressure, and an intermittent cough. You explain that he likely has a viral upper respiratory tract infection. He asks if any over-the-counter medications will ease his symptoms.

Clinical Question

Are over-the-counter antihistamine/decongestant/analgesic combinations effective in alleviating the symptoms and reducing the duration of the common cold in adults and children?

Evidence-Based Answer

Combination cold medications, including antihistamine/decongestant/analgesic, antihistamine/decongestant, antihistamine/analgesic, and analgesic/decongestant formulations, provide modest symptom relief in adults and older children, but are not effective in young children. Only the analgesic/decongestant formulation is associated with a statistically significant increased risk of adverse effects.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

The common cold is a mild upper respiratory tract illness that may cause sneezing, nasal congestion and discharge, sore throat, and cough. Rhinovirus is the most common cause, accounting for 30 to 50 percent of all upper respiratory tract infections. Coronavirus, respiratory syncytial virus, parainfluenza virus, and adenovirus are other major viruses that cause the common cold.[2]

The average adult has two to four colds per year, whereas young children have six to eight. Colds are usually self-limited and last seven to 10 days, although some patients have symptoms for up to three weeks.[2] Despite being self-limited, colds have a considerable impact on lost time from work and school. Estimates suggest that adults miss 20 million work days and children miss 22 million school days in the United States each year as a result of colds.[3] Also, upper respiratory tract infections account for about 25 million primary care visits annually.[4]

Currently, no antiviral medications are available to treat the common cold, so the goal of care is symptom relief. All of the four combination medications in this analysis produced greater overall symptom relief compared with the control.[1] The antihistamine/decongestant trials reported the greatest benefit, with four patients needing to be treated for one additional patient to have symptom improvement. However, because the confidence intervals overlapped, there is insufficient evidence to conclude that one combination provides more benefit than another.

Higher rates of adverse effects were reported for each of the combination medications, but only the analgesic/decongestant combination had significantly more adverse effects than the control group. The number needed to treat to see one additional harmful outcome was 14. The most common adverse effects associated with this combination were dizziness/lightheadedness and gastrointestinal upset.

Of the 27 studies in this analysis, two studies included children younger than two years, and two other studies included children two to four years of age. The meta-analysis

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Cochrane Abstract

Background: Although combination formulas containing antihistamines, decongestants, and/or analgesics are sold over the counter in large quantities for the common cold, the evidence of effectiveness is limited.

Objectives: To assess the effectiveness of antihistamine/decongestant/analgesic combinations in reducing the duration and alleviating the symptoms of the common cold in adults and children.

Search Methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2011, Issue 4), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, OLDMEDLINE (1953 to 1965), MEDLINE (1966 to November 2011), and EMBASE (1990 to December 2011).

Selection Criteria: Randomized controlled trials investigating the effectiveness of antihistamine/decongestant/analgesic combinations compared with placebo, other active treatments (excluding antibiotics), or no treatment in children and adults with the common cold.

Data Collection and Analysis: Two review authors independently extracted and summarized data on general recovery, nasal obstruction, rhinorrhea, sneezing, cough, and side effects. We categorized the trials according to the active ingredients.

Main Results: We included 27 trials (5,117 participants) of common cold treatments. Fourteen trials studied the antihistamine/decongestant combinations; two, antihistamine/analgesic combinations; six, analgesic/decongestant combinations; and five, antihistamine/decongestant/analgesic combinations. In 21 trials, the control intervention was placebo, and in six trials it was an active substance. Reporting of methods in most trials was poor and there were large differences in design, participants, interventions, and outcomes. Pooling was possible only for a limited number of studies and outcomes.

Antihistamine/decongestant: 12 trials. Eight trials reported on global effectiveness and six could be pooled (n = 309 on active treatment and 312 on placebo). The odds ratio (OR) of treatment failure was 0.27 (95% confidence interval [CI], 0.15 to 0.50). The number needed to treat for an additional beneficial outcome (NNTB) was four (95% CI, 3 to 5.6). On the final evaluation day, 41 percent of participants in the placebo group had a favorable response compared with 66 percent of those on active treatment. Of the two trials that were not included in the pooling, one showed some global effect and the other showed no effect.

Antihistamine/analgesic: three trials. Two reported on global effectiveness, and data from one study were presented (n = 290 on active treatment and 292 on ascorbic acid). The OR of treatment failure was 0.33 (95% CI, 0.23 to 0.46) and the NNTB was 6.67 (95% CI, 4.76 to 12.5). After six days of treatment, 43 percent of participants in the control group were cured, compared with 70 percent in the active treatment group. The second study also showed an effect in favor of active treatment.

Analgesic/decongestant: six trials. One trial reported on global effectiveness: 73 percent of participants on active treatment benefited, compared with 52 percent of the control group, who took paracetamol (available as acetaminophen in the United States). The OR was 0.28 (95% CI, 0.15 to 0.52).

Antihistamine/decongestant/analgesic: five trials. Four trials reported on global effectiveness, and two could be pooled. Reported global effect (less than one severity point on a four- or five-point scale) was 52 percent with active treatment and 34 percent with placebo. The OR of treatment failure was 0.47 (95% CI, 0.33 to 0.67) and the NNTB was 5.6 (95% CI, 3.8 to 10.2). Two other trials found no beneficial effect. Two other studies did not show any effect.

Two studies of antihistamine/decongestant combinations (113 children) could not be pooled. The active treatment had no significant effect.

Adverse effects: The combination of antihistamine/decongestant caused more adverse effects than the control intervention, but the difference was not significant: 157 of 810 participants (19 percent) versus 60 of 477 (13 percent) had one or more adverse effects (OR = 1.58; 95% CI, 0.78 to 3.21). Participants taking analgesic/decongestant combinations had significantly more adverse effects than the control group (OR = 1.71; 95% CI, 1.23 to 2.37). The number needed to treat for an additional harmful outcome was 14. Neither of the other two combinations caused significantly more adverse effects. Eleven of 90 participants (12 percent) taking the antihistamine/analgesic combination had one or more adverse effects versus nine of 91 (10 percent) taking the control medication (OR = 1.27; 95% CI, 0.50 to 3.23). In one study of the antihistamine/decongestant/analgesic combination, five of 224 participants (2 percent) on active treatment experienced adverse effects versus nine of 208 (4 percent) on placebo. Two other trials reported no differences between treatment groups, but numbers were not reported.

Authors' Conclusions: Current evidence suggests that antihistamine/decongestant/analgesic combinations have some general benefit in adults and older children. These benefits must be weighed against the risk of adverse effects. There is no evidence of effectiveness in young children.

These summaries have been derived from Cochrane reviews published in the Cochrane Database of Systematic Reviews in the Cochrane Library. Their content has, as far as possible, been checked with the authors of the original reviews, but the summaries should not be regarded as an official product of the Cochrane Collaboration; minor editing changes have been made to the text (http://www.cochrane.org).

found that the combination medications provided no benefits for young children. In 2008, the U.S. Food and Drug Administration recommended that over-the-counter cough and cold medications not be given to children younger than two years because of the risk of "serious and potentially life-threatening side effects."[5] The 2010 National Poison Data System reported that antihistamines and "cold and cough preparations" were among the top 10 substances most commonly involved in the deaths of children younger than five years.[6]

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