



Q/ Do OTC remedies relieve cough in acute URIs?

Lauren DeAlleume, MD
University of Colorado Health
Sciences Center, Denver

Beth Tweed, MLIS, AHIP
University of Colorado Health
Sciences Center, Denver

EVIDENCE-BASED ANSWER

A / **SOME DO. DEXTROMETHORPHAN** (DM) for adults and honey for children provide some relief. DM may modestly decrease cough in adults compared with placebo (strength of recommendation [SOR]: **B**, systematic review of inconsistent or limited evidence). The data supporting zinc for the common cold are mixed (SOR: **B**, meta-analysis with inconsistent results). Antihistamines, antihistamine-decongestant combinations, and guaifenesin don't provide greater relief than placebo in adults (SOR: **B**, systematic review of inconsistent or limited evidence).

In children, antihistamines, decongestants, DM, or combinations of them don't relieve cough better than placebo (SOR: **A**, systematic review). Honey may modestly decrease frequency and severity of cough compared with DM or no treatment (SOR: **B**, small, randomized controlled trial [RCT]).

Clinical commentary

It appears that all of the common, troublesome symptoms of an upper respiratory infection can be managed just as well with over-the-counter (OTC) medications as with prescriptions: DM for cough; acetaminophen or naproxen sodium for fever and aches; decongestants or vapor rubs for nasal congestion. Spread the word!

It would be wonderful if the office visit for upper respiratory infection became a rarity—the health care system would save a lot of money. Presumably, patients would still come in wondering if they had something worse than a cold, but education during the first visit would help prevent repeat trips.

Jon O. Neher, MD
Valley Medical Center
Family Practice Residency,
University of Washington, Renton

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Evidence summary

A Cochrane review found DM to be modestly effective in 2 of 3 studies.¹ In the first study—a meta-analysis of 6 industry-sponsored RCTs of 710 adults—a single 30-mg dose of DM decreased coughing bouts by 12% ($P=.004$) and increased the time between bouts by 17% ($P=.002$) in the 3 hours after treatment.

A second study of 3 successive industry-sponsored, blinded RCTs enrolling a total of 451 adults found that 30 mg of DM decreased cough counts between 19% and 36% ($P<.05$) over a 3-hour follow-up period. Neither of the 2 studies specified whether the outcome assessors were blinded to treatment groups.

A third double-blinded RCT evaluating a single 30-mg dose of DM in 43 adults during a 3-hour follow-up period showed no statistically significant improvement in cough outcomes compared with placebo.

A split decision on guaifenesin

The same Cochrane review also evaluated other medications for cough related to upper respiratory infection in adults.¹ The results of 2 guaifenesin trials were split. In a double-blinded RCT of 239 adults, more patients taking guaifenesin reported decreased cough frequency and intensity (75% vs 31%; $P<.01$). However, another double-blinded RCT of

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65 patients found guaifenesin to be no more effective than placebo in reducing subjective cough frequency.

Antihistamines don't help, adding a decongestant isn't much better

Three trials of antihistamines in a total of 1900 adults found that the drugs didn't relieve cough symptoms more effectively than placebo. Antihistamine-decongestant combination trials produced split results. In 1 double-blinded RCT of 283 adults, loratadine-pseudoephedrine (5 and 120 mg, respectively) twice daily for 4 days didn't decrease subjective cough scores more than placebo and was associated with more dry mouth, dizziness, headache, and insomnia (30% vs 21%; *P* value not reported).

Another partially double-blinded RCT of 73 adults reported that dexbrompheniramine-pseudoephedrine (6 and 120 mg, respectively) twice daily for 1 week decreased subjective cough severity (1.4 vs 2.0; *P* < .05) on a scale of 0 to 4 during days 3 to 5 of treatment. The combination was associated with increased dizziness and dry mouth, however (exact data not reported; *P* ≤ .01).

Codeine works no better than placebo

Two partially double-blinded RCTs of 163 adults found codeine (sold OTC in Canada) to be no more effective than placebo in relieving cough caused by the common cold.¹

Zinc lozenges show mixed results

Zinc lozenges containing 13.3 mg of zinc acetate taken every 2 to 3 hours decreased the duration of cough from 5.35 to 2.14 days (*P* < .001) in a double-blinded placebo-controlled RCT of 50 adults.² The most recent systematic review showed mixed results: Half the studies found no benefit for zinc in treating upper respiratory infection.³

In children, forget DM, antihistamines, decongestants

The previously mentioned Cochrane review¹ also summarized studies in children. DM was no more effective than placebo for decreasing cough in 2 RCTs enrolling a total of 107 children. Another single-blinded RCT of 100 children showed that neither DM

nor diphenhydramine relieved cough better than placebo.

Two RCTs involving a total of 237 children compared antihistamines with placebo. One double-blinded trial reported that clemastine and chlorpheniramine were no more effective than placebo. The other partially double-blinded trial found that diphenhydramine didn't decrease cough frequency more than placebo.

Two double-blinded RCTs (total of 155 children) showed that antihistamine-decongestant combinations (brompheniramine-phenylpropanolamine and brompheniramine-phenylephrine-propranolamine) didn't reduce cough more than placebo. No studies have evaluated guaifenesin in children.¹

Honey appears to help

In a partially double-blinded RCT (the "no treatment" group was not blinded) of 105 children, a single dose of buckwheat honey decreased cough frequency, as assessed by parents, by 1.89 points on the 7-point Likert scale compared with DM (1.39) and no treatment (0.92; *P* < .001). Overall improvement in symptom score averaged 10.71 out of a total 30 points for honey compared with 6.41 for no treatment (*P* = .04). Cough frequency and overall symptom scores for DM didn't differ significantly from no treatment. Hyperactivity, nervousness, and insomnia were reported more often with honey (5 patients) than DM (2 patients) or no treatment (0 patients); (*P* = .04).⁴

Placebos work, but why?

In a review of 8 RCTs, the average reduction in cough in the placebo group (both capsules and syrups) was approximately 85% of that seen in the active medication group (range 56%-105%).⁵ Several factors may account for the efficacy of placebo, including lubrication of the pharynx by increased salivation caused by sweet or bitter vehicles. Sweet vehicles also may stimulate endogenous opioids that may suppress cough. In an unblinded RCT of 54 patients, a capsule placebo significantly decreased the number of coughs during a 15-minute follow-up compared with no treatment (18 vs 3; *P* = .0003).⁶

Recommendations

The American College of Chest Physicians recommends a first-generation antihistamine-decongestant combination or naproxen for acute cough in the common cold (SOR: **A**). Newer-generation, nonsedating antihistamines are not recommended (SOR: **D**).⁷

The US Food and Drug Administration (FDA) advises against using OTC cough and cold medicines in children younger than 2 years because of the risk of “serious and potentially life-threatening side effects.” The FDA also recommends taking significant pre-

cautions if these products are used in children older than 2 years, pending a complete FDA review of the medications for children 2 to 11 years. Manufacturers of children’s cough and cold remedies have changed the labels on the medications voluntarily to recommend that they not be given to children younger than 4 years.⁸

The American Academy of Pediatrics recommends that physicians clearly educate parents about the potential risks and lack of benefits of DM- and codeine-containing cough remedies.⁹

JFP

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