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EVIDENCE-BASED REVIEW

Non-antibiotic treatments for upper-respiratory tract infections (common cold)☆

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Heated humidified air;
Vitamin C;
Zinc

Summary
Objectives: To review the seven Cochrane reviews of non-antibiotic treatment for the common cold.
Methods: Each Cochrane review was read and summarized, and results presented as relative risks and, where possible, numbers needed to treat.
Results: The main theme that runs through these Cochrane reviews is the variable quality of the primary studies. In general, the reviewers are fairly cautious about the benefits of any of the treatments other than first-dose decongestants and antihistamine–decongestant combinations. For antihistamines alone, the reviewers were clear about the lack of efficacy except in the high-quality studies in which a global improvement in symptoms was noted. Some studies were statistically significant, but the Cochrane reviewers were guarded about how clinically significant they were. For Echinacea, problems were found with the quality of the studies and the wide range of different forms of this substance. Heated humidified air seemed to be effective in the UK and Israel, but not the USA, making definitive statements about efficacy difficult. Over-the-counter medication for cough seemed to have no documented benefit in children under the age of 5 years. Letosteine (a mucolytic) may be effective in children but is not available in the UK. Bisolvon (a mucolytic) was found to be effective for cough in only one study. For older children and adults, dextromethorphan may be effective (two out of three studies showed benefit), and guiafenesin (an expectorant) showed mixed benefit in two trials. Dexbrompheniramine (a sedating antihistamine)/pseudoephedrine (6 mg/120 mg twice daily for 1 week) was significantly more effective than placebo for severity of cough, whereas, in another study, loratadine (a non-sedating antihistamine)/pseudoephedrine (5 mg/120 mg twice daily for 4 days) did not show any difference between the study groups. Vitamin C may have a small role in preventing the common cold, with possibly a greater role in high-intensity physical activity and sub-arctic conditions. Zinc

☆Please see reference list for Cochrane reviews cited in this evidence-based review.

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lozenges seemed to be effective, but the issue of unblinding due to taste was a methodological issue of concern to the reviewers. The benefits and harms are calculated as numbers needed to treat for one person to benefit (NNTB) and numbers needed to treat for one person to harm (NNTH), and were calculated by the author. *Conclusion:* Most non-antibiotic treatments for the common cold are probably not effective. The most promising are dextromethorphan, bisolvon and guiaphenesin for cough, antihistamine–decongestant combinations for a wide range of symptoms, nasal decongestants (at least for the first dose) and possibly zinc lozenges.

Introduction

This paper evaluates the seven Cochrane systematic reviews that deal with non-antibiotic treatments for upper-respiratory tract infection. This was originally intended to include the review of anti-viral treatment for the common cold, but this review has been removed from the library as it was not updated. The treatments in this review are those that may be self-administered in many jurisdictions (e.g. heated humidified air), as well as being recommended in others by clinicians and even subsidized by some health funders. Thus, the term ''over-the-counter'' (OTC) is not strictly correct. Most of the clinical syndromes in this review fit the definition of the common cold, but, as mentioned in the earlier review in this series on ''antibiotics for upper-respiratory tract infections: a review of Cochrane reviews,[1]'' there is the issue of microbiological aetiology to consider. It is not always clear if an infection is of a viral, bacterial or mixed nature. In this paper, infections are assumed to be mainly viral, but the microbiology is not usually known or sought by clinicians.

In this overview, effects may be reported as the NNTB (number needed to treat for one person to benefit) and the NNTH (number needed to treat for one person to harm). The NNTB is the inverse of the absolute risk reduction (ARR) resulting from a particular treatment in a particular group of patients.[2] It is felt that it is better to report the ARR than the relative risk reduction, as this term refers to the benefit of a treatment without any reference to the baseline risk. Both the ARR and the NNTB (the reciprocal of ARR) take these factors into consideration. The same applies to the NNTH for harm. The NNTB and the NNTH were only reported in this review if they were from statistically significant studies or statistically significant pooled relative risks. The latter is calculated by obtaining a pooled relative risk from the meta-analysis and applying it to the patient expected event rate (PEER). The PEER is the rate of events that occur in the group taking the placebo medication in a randomized trial comparing drug with placebo. Therefore, if the relative risk is less than 1 then the $\text{NNTB} = 1/\{(1-\text{RR}) \times \text{PEER}\}$, and if the relative risk is greater than 1 then the $\text{NNTB} = 1/\{(\text{RR}-1) \times \text{PEER}\}$.[2]

A number of issues affect the quality of the reviews covered in this paper. These include a wide range of design quality in the studies reviewed. The dose and quality of some of the medicinal components and combination medications are also issues of concern. The latter two of these apply particularly to OTC medications. Issues are also raised by different methods of measuring end points, such as continuous scales compared with dichotomous outcomes (i.e. feeling well or absence of cough). As some of the medications are designed for specific purposes (e.g. cough suppressant), then absence of cough will be appropriate. For decongestants, it will be nasal discharge and stuffiness. This raises the question of what would be the appropriate outcome for an antihistamine for the common cold.

Ideally, the primary outcomes are specified beforehand. However, it is not always possible to tell if the analysis was done on the outcomes of primary interest or on the secondary outcomes. In this particular field, underpowering because of small study size is also an issue. NNTB can only be calculated if dichotomous outcomes are used, but they can be calculated for different symptoms, providing some practical information to guide treatment decisions.

Antihistamines for the common cold

The systematic review on antihistamines for the common cold[3] was undertaken because the use of antihistamines for the common cold is widespread yet there was concern that they may not be effective. The review contained 32 papers with 35 comparisons; 22 trials were of monotherapy and 13 were of a combination of antihistamines with other medication. The number of participants totalled 8930. The authors reported large differences in