Cochrane Library

Cochrane Database of Systematic Reviews

Honey and lozenges for children with non-specific cough (Review)

Mulholland S, Chang AB

Mulholland S, Chang AB.
Honey and lozenges for children with non-specific cough.
Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD007523.
DOI: 10.1002/14651858.CD007523.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Honey and lozenges for children with non-specific cough

Selamawit Mulholland[1], Anne B Chang[2]

[1]Queensland Respiratory Centre, Royal Children's Hospital, Brisbane, Australia. [2]Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Queensland Children's Respiratory Centre and Queensland Children's Medical Research Institute, Brisbane, Australia

Contact address: Selamawit Mulholland, Queensland Respiratory Centre, Royal Children's Hospital, Herston Road, Herston, Brisbane, Queensland, Australia. selamawit.mulholland@uqconnect.edu.au.

Editorial group: Cochrane Airways Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 2, 2011.
Review content assessed as up-to-date: 27 October 2010.

Citation: Mulholland S, Chang AB. Honey and lozenges for children with non-specific cough. *Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD007523. DOI: 10.1002/14651858.CD007523.pub2.

ABSTRACT

Background

Chronic non-specific cough is a chronic, dry cough of in the absence of identifiable respiratory disease or known aetiology. Although it is usually not reflective of an underlying severe illness, it does cause significant morbidity, and as such relief from it is often sought. The use of honey and lozenges to soothe upper respiratory tract irritation is common, inexpensive, and potentially more effective in treating the symptoms than pharmacological interventions.

Objectives

To evaluate the efficacy of honey and/or lozenges in the management of children with chronic non-specific cough.

Search methods

The Cochrane Airways Group searched the Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, OLDMEDLINE, and EMBASE databases in October 2010.

Selection criteria

All randomised controlled trials comparing honey or lozenges with a placebo in treating children with chronic non-specific cough.

Data collection and analysis

The results of the searches were assessed according to the pre-determined criteria. None of the trials identified by the searches were eligible for inclusion, leaving no data available for analysis in this review.

Main results

The search did not provide any applicable randomised controlled trials that investigated the efficacy of honey and lozenges in treating children with non-specific chronic cough. Data from acute studies suggest a potential role for honey in relieving cough, but whether this is applicable to chronic cough is unknown.

Authors' conclusions

Clinically, this review was unable to provide any justifiable recommendation for or against honey and/or lozenges due to the lack of evidence. The absence of applicable studies highlights the need for further research into the area of treating children with chronic non-specific coughs with honey and/or lozenges. These treatments are not recommended when managing very young children (as lozenges are a potential choking hazard, and honey may cause infant botulism in children under one year of age).

PLAIN LANGUAGE SUMMARY

Honey and lozenges for children with non-specific cough

Symptomatic relief is often sought for children with chronic non-specific cough (which is defined as a dry, non-productive cough with no known cause lasting longer than four consecutive weeks). This review aimed to assess the efficacy of treating children with such coughs using honey or lozenges, as these options are inexpensive. No randomised controlled trials were found to be applicable to this review, primarily due to the participants in the studies not fulfilling the inclusion criteria. However, studies on the efficacy of these treatments in treating acute cough in children showed that honey has the potential to be beneficial in children over a year old. Further research evaluating the efficacy of honey and lozenges in treating chronic non-specific coughs in children is needed.

BACKGROUND

Description of the condition

Non-specific cough has been defined as non-productive cough in the absence of identifiable respiratory disease or known aetiology (Chang 2001). While some children with chronic non-specific cough have asthma, the majority do not (Chang 1999). In adults, chronic cough is defined as cough of over eight weeks duration but the definition commonly accepted in children is that of over 4 weeks, based on the known differences between paediatric and adult cough (Chang 2005).

Description of the intervention

Honey and lozenges are both commonly used remedies for cough. Honey is a popular choice due to its inexpensive and potentially effective antitussive properties, and (other than being contraindicated in infants younger than one year) is generally regarded as a safe treatment (Paul 2007). As such, recommended doses are not required for safety purposes, but many of the studies evaluate honey against cough syrups and hence use comparable doses.

Lozenges vary in pharmacological composition from those that contain analgesic ingredients (such as benzocaine and menthol) to those that are primarily effective due to their physiologic properties (such as the promotion of salivation).

How the intervention might work

General management of children with non-specific cough currently involves the 'watch, wait, and review' approach (Chang 2006), as the aetiology of the cough is, by definition, unknown. Interventions can therefore only be symptomatic, not curative, so honey and lozenge treatments need to be evaluated in this regard. Antitussive treatments have been noted to work on at least three levels: pharmacological, physiological, and placebo (i.e. that obtained by using a placebo treatment) (Eccles 2002). Honey comprises recognised antimicrobial and antioxidant properties, in addition to working physiologically by soothing the epipharynx and stimulating saliva production. Lozenges would differ pharmacologically depending on specific active ingredients, but would uniformly be physiologically effective through saliva production. Those lozenges that contain agents such as menthol would also exhibit cooling abilities, another important physiological aspect of certain antitussives (Eccles 2002).

Either treatment may demonstrate physiological or placebo-related improvements. One proposed mechanism for this effect is the production of endogenous opioids in response to taking perceived antitussive medication; this is effective as opioids suppress the cough reflex (Eccles 2002).

Why it is important to do this review

Cough is the most common symptom presenting to general practitioners (Britt 2002; Cherry 2003). Worldwide, the desire to re-

duce the impact of the symptom of cough is reflected in the billions of dollars spent on over-the-counter cough and cold medications. Cochrane reviews on over-the-counter medications for acute cough and that related to pneumonia are available (Schroeder 2004; Chang 2007). However, the aetiology and management of acute cough is not necessarily the same as that for chronic non-specific cough. Chronic cough in children causes significant burden and stress to parents (Marchant 2008), and resolution of the cough results in a subsequent improvement in quality of life (Newcombe 2008).

Honey and lozenges superficially appear to be relatively safe therapies when compared to the adverse effects of some pharmacological interventions. However, some risk exists, as honey may cause harm from allergy or anaphylaxis, and lozenges are both potential choking hazards (and consequently contraindicated in the very young) and possibly contain potent pharmacological agents that may be harmful to young children. Thus a systematic review of the efficacy of simple remedies (such as honey and lozenges) for chronic non-specific cough would be useful in assessing the risk vs benefit details of the therapy, therefore helping to guide clinical practice.

OBJECTIVES

To evaluate the efficacy of honey and/or lozenges in the management of children with chronic non-specific cough.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials comparing honey or lozenges to a control group (placebo or usual treatment) in children with non-specific cough.

Types of participants

Children with chronic (>4 weeks) non-specific cough (dry and non-productive cough without any other respiratory symptom, sign or systemic illness).

Exclusion criteria: acute (<2 weeks) or sub-acute (2 to 4 weeks) cough, cough related to mycoplasma, pertussis and chlamydia, presence of underlying cardio-respiratory condition, current or recurrent wheeze (>2 episodes), presence of other respiratory symptoms (productive cough, haemoptysis, dyspnoea), presence of other respiratory signs (clubbing, chest wall deformity, respiratory noises such as wheeze on auscultation and other adventitious sounds), presence of any sign of systemic illness (failure to thrive, aspiration, neurological or developmental abnormality), presence of lung function abnormality.

Types of interventions

All randomised controlled trials comparing honey or any type of lozenges to a control group (placebo or usual treatment).

Types of outcome measures

Primary outcomes

a) proportions of participants who were not cured or not substantially improved at follow up (clinical failure).

Secondary outcomes

b) proportions of participants who were not cured at follow up,
c) proportions of participants who not substantially improved at follow up,
d) mean difference in cough indices (cough diary, cough frequency, cough scores),
e) proportions experiencing adverse effects of the intervention,
f) proportions experiencing complications e.g. requirement for medication change, etc.

The proportions of participants who failed to improve on treatment and the mean clinical improvement were to be determined using the following hierarchy of assessment measures (i.e. where two or more assessment measures are reported in the same study, the outcome measure that is listed first in the hierarchy will be used):

i) Objective measurements of cough indices (cough frequency, cough receptor sensitivity)
ii) Symptomatic (Quality of life, Likert scale, visual analogue scale, level of interference of cough, cough diary) - assessed by the patient (adult or child)
iii) Symptomatic (Quality of life, Likert scale, visual analogue scale, level of interference of cough, cough diary) - assessed by the parents/carers
iv) Symptomatic (Likert scale, visual analogue scale, level of interference of cough, cough diary) - assessed by clinicians

Search methods for identification of studies

Electronic searches

The following topic search strategy was used to identify the relevant randomised controlled trials listed on the electronic databases:
("cough" OR "bronchitis", all as (textword) or (MeSH)) AND ("honey" OR "lozenges") AND ("child" OR "children" OR "pediatrics" all as (textword) or (MeSH))
The full strategies are listed in Appendix 1.

Trials were sought from the following sources:
1. The Cochrane Central Register of Controlled Trials (CENTRAL), Issue 4 2008, which includes the Cochrane Airways Group Specialised Trials Register.
2. MEDLINE (1966 to October wk 2, 2008).
3. OLDMEDLINE (1950 to 1965).
4. EMBASE (1980 to wk 42, 2008).

Searching other resources

5. The list of references in relevant publications.
6. Written communication with the authors of trials included in the review.
The most recent search was done in October 2010.

Data collection and analysis

Selection of studies

Retrieval of studies: From the title, abstract, or descriptors, we both independently reviewed literature searches to identify potentially relevant trials for full review. Searches of bibliographies and texts were conducted to identify additional studies. From the full text using specific criteria, we were to independently select trials for inclusion. It was planned that agreement would measured using kappa statistics, and disagreement would be resolved by consensus.

Data extraction and management

Trials that satisfied the inclusion criteria were to be reviewed and the following information recorded: study setting, year of study, source of funding, patient recruitment details (including number of eligible subjects), inclusion and exclusion criteria, other symptoms, randomisation and allocation concealment method, numbers of participants randomised, blinding (masking) of participants, care providers and outcome assessors, dose and type of intervention, duration of therapy, co-interventions, numbers of patients not followed up, reasons for withdrawals from study protocol (clinical, side-effects, refusal and other), details on side-effects of therapy, and whether intention-to-treat analyses were possible. It was planned that data would be extracted on the outcomes described previously. Further information was to be requested from the authors where required.

Assessment of risk of bias in included studies

It was planned that in order to assess the risk of bias, we were both to independently assess the quality of the studies included in the review according to the criteria described by Jüni 2001.

Allocation concealment

Allocation concealment in each study was to be assessed as follows:
1. Adequate, if the allocation of participants involved a central independent unit, on-site locked computer, identically appearing numbered drug bottles or containers prepared by an independent pharmacist or investigator, or sealed opaque envelopes;
2. Unclear, if the method used to conceal the allocation was not described;
3. Inadequate, if the allocation sequence was known to the investigators who assigned participants or if the study was quasi-randomised.

Generation of the allocation sequence

Each study was to be graded for allocation concealment as follows:
1. Adequate, if methods of randomisation include using a random number table, computer-generated lists or similar methods;
2. Unclear, if the trial is described as randomised, but no description of the methods used to allocate participants to treatment group was described;
3. Inadequate, if methods of randomisation include alternation; the use of case record numbers, dates of birth or day of the week, and any procedure that is entirely transparent before allocation.

Blinding (or masking)

Each study was to be graded for blinding as follows:
1. Blinding of clinician (person delivering treatment) to treatment allocation;
2. Blinding of participant to treatment allocation;
3. Blinding of outcome assessor to treatment allocation.

Follow-up

Each study was to be graded as to whether numbers of and reasons for dropouts and withdrawals in all intervention groups were described, or if it was specified that there were no dropouts or withdrawals.

Dealing with missing data

We planned to request further information from the primary investigators where required.

Assessment of heterogeneity

We planned to describe any heterogeneity between the study results and test this to see if it reached statistical significance using the chi-squared test. We consider heterogeneity to be significant when the P value is less than 0.10 (Higgins 2008).

Assessment of reporting biases

If combining the data and meta-analysis were possible, we were to assess publication bias using a funnel plot. We aimed to try to identify and report on any selective reporting in the included trials.

Data synthesis

For the dichotomous outcome variables of each individual study, relative and absolute risk reductions were to be calculated using a modified intention-to-treat analysis. This analysis assumes that children not available for outcome assessment have not improved (and probably represents a conservative estimate of effect). An initial qualitative comparison of all the individually analysed studies of all the individually analysed studies examines whether pooling of results (meta-analysis) is reasonable. This takes into account differences in study populations, inclusion/exclusion criteria, interventions, outcome assessment, and estimated effect size.

The results from studies that met the inclusion criteria and reported any of the outcomes of interest were to be included in the subsequent meta-analyses. The summary weighted risk ratio and 95% confidence interval (fixed effects model) would have been calculated using Revman 5. For cross-over studies, mean treatment differences were planned to be either calculated from raw data, extracted or imputed, then entered as fixed effects generic inverse variance (GIV) outcome in order to provide summary weighted differences and 95% confidence intervals. In cross-over trials, only data from the first arm was to be included in meta-analysis if data is combined with parallel studies (Elbourne 2002). Numbers needed to treat (NNT) was to be calculated from the pooled OR and its 95% CI applied to a specified baseline risk using an online calculator (Cates 2003). The cough indices would have been assumed to be normally distributed continuous variables so the mean difference in outcomes can be estimated (weighted mean difference). If studies reported outcomes using different measurement scales, the standardised mean difference would be estimated. Any heterogeneity between the study results was to be described and tested to see if it reached statistical significance using a chi-squared test. The 95% CI estimated using a random effects model were to be included, as part of sensitivity analysis, whenever there are concerns about statistical heterogeneity.

Subgroup analysis and investigation of heterogeneity

An a priori sub-group analysis was planned for:

1. children aged less than 7 years and 7 years and above
2. combined versus mono interventions

Sensitivity analysis

Sensitivity analyses were also planned to assess the impact of the potentially important factors on the overall outcomes:

1. variation in the inclusion criteria;
2. differences in the medications used in the intervention and comparison groups;
3. differences in outcome measures;
4. analysis using random effects model;
5. analysis by “treatment received”; and
6. analysis by “intention-to-treat”.

RESULTS

Description of studies

The searches identified a total of 466 abstracts, of which 20 potential randomised controlled trials were retrieved. However, none were eligible for the purposes of this review. See Characteristics of excluded studies

Included studies

Not relevant as no studies fulfilled inclusion criteria.

Excluded studies

Of the 20 randomised controlled trials evaluated, most were excluded for not specifically involving child participants (14 studies). Four of the remaining six studies that focused on children were ineligible due to their focus on other remedies (such as dextromethorphan and codeine), and while the Macknin 1998 and Paul 2007 studies focused on using honey or lozenges to treat children, these papers dealt solely with acute infectious coughs.

Risk of bias in included studies

Not applicable.

Effects of interventions

As mentioned above, none of the studies fulfilled the pre-determined inclusion criteria. Two trials investigated the efficacy of honey (Paul 2007) or lozenges (Macknin 1998) in treating acute coughs in children. Honey was found to be beneficial in reducing severity and duration of acute viral cough in children, while the study involving zinc showed no significant difference to placebo in the intervention.

DISCUSSION

We found no relevant studies that could be included in this review. None of the trials dealt with chronic coughs in children.

From the results of one excluded study, honey was shown to have beneficial effects on acute coughs in children (Paul 2007). Another study focused on the effects of zinc lozenges on acute coughs in patients under 18 years of age, but found them to have no specific advantage to placebo, but increased the risk of bad taste and nausea (Macknin 1998). Additionally, treating children with these therapies is somewhat more complicated, as honey is relatively contraindicated in infants under 1 year of age, and lozenges in young children are a potential choking hazard. Nevertheless, the review has identified data from acute cough that should be studied for chronic cough.

Lozenges can contain pharmacologic properties that may be antimicrobial, and honey has also been noted to have antimicrobial and antioxidant properties. Honey has been found to be effective in acute cough but whether this can be extended to non-acute cough is unknown. Parents of children with chronic non-specific cough are put under considerable stress in trying to alleviate their child's symptoms (Marchant 2008). Consequently, a study on the efficacy of inexpensive and effective interventions (such as honey and lozenges) would be helpful in tackling this problem.

AUTHORS' CONCLUSIONS

Implications for practice

Clinically, this review was unable to provide any justifiable recommendation for or against honey and/or lozenges due to the lack of evidence. These treatments are not recommended when managing very young children (as lozenges are a potential choking hazard, and honey can cause infant botulism in children under one year of age)

Implications for research

The fact that none of the search results were applicable to this review highlights the need for specific research into this area. Although a chronic non-specific cough is usually not reflective of an underlying severe illness, it causes morbidity and as such relief from it is often sought. Some children are prescribed various medications and are thus exposed to the potential side-effects of pharmacological therapies. Consequently, studying the efficacy of relatively inexpensive and safe treatments, such as honey and lozenges, could greatly improve both the therapeutic regimes and outcomes of this clinical problem. Studies should be parallel double blind randomised controlled trials as non-placebo trials are subjected to bias for the outcome of cough.

ACKNOWLEDGEMENTS

We thank Toby Lasserson, Dr Chris Cates and Liz Arnold from the Airways Group for their advice, supportive role and comments to the protocol and review. We also thank the Australian Cochrane Airways Group in awarding SM a scholarship.

REFERENCES

References to studies excluded from this review

Abdul 1999 *{published data only}*
Abdul Manap R, Wright CE, Gregory A, Rostami-Hodjegan A, Meller ST, Kelm GR, et al. The antitussive effect of dextromethorphan in relation to CYP2D6 activity. *British Journal of Clinical Pharmacology* 1999;**48**(3):382–7.

Eby 2006 *{published data only}*
Eby GA, Halcomb WW. Ineffectiveness of zinc gluconate nasal spray and zinc orotate lozenges in common-cold treatment: a double-blind, placebo-controlled clinical trial. *Alternative Therapies in Health and Medicine* 2006;**12**(1):34–8.

Fischer 2002 *{published data only}*
Fischer J, Pschorn U, Vix JM, Peil H, Aicher B, Muller A, de Mey C. Efficacy and tolerability of ambroxol hydrochloride lozenges in sore throat. Randomised, double-blind, placebo-controlled trials regarding the local anaesthetic properties. *Arzneimittel-Forschung* 2002;**52**(4):256–63.

Fujimori 1998 *{published data only}*
Fujimori K, Suzuki E, Arakawa M. Effects of oxatomide, H1-antagonist, on postinfectious chronic cough; a comparison of oxatomide combined with dextromethorphan versus dextromethorphan alone. *Japanese Journal of Allergology* 1998;**47**(1):48–53.

Gilbert 2008 *{published data only}*
Gilbert G. Single dose of honey effective for cough in kids. *Journal of the National Medical Association* 2008;**100**(4): 459.

Grattan 1995 *{published data only}*
Grattan TJ, Marshall AE, Higgins KS, Morice AH. The effect of inhaled and oral dextromethorphan on citric acid induced cough in man. *British Journal of Clinical Pharmacology* 1995;**39**(3):261–3.

Haidl 2001 *{published data only}*
Haidl P, Kemper P Sr, Butnarasu J, Klauke M, Wehde H, Kohler D. Influence of the inhalation of a 1% L-menthol-solution in the premedication of fiberoptic bronchoscopy on cough and the sensation of dyspnea. *Pneumologic* 2001; **55**(3):115–9.

Lee 2000 *{published data only}*
Lee PC, Jawad MS, Eccles R. Antitussive efficacy of dextromethorphan in cough associated with acute upper respiratory tract infection. *The Journal of Pharmacy and Pharmacology* 2000;**52**(9):1137–42.

Macknin 1998 *{published data only}*
Macknin ML, Piedmonte M, Calendine C, Janosky J, Wald E. Zinc gluconate lozenges for treating the common cold in children: a randomized controlled trial. *The Journal of the American Medical Association* 1998;**279**(24):1962–7.

Matthys 1983 *{published data only}*
Matthys H, Bleicher B, Bleicher U. Dextromethorphan and codeine: objective assessment of antitussive activity in patients with chronic cough. *The Journal of International Medical Research* 1983;**11**(2):92–100.

Mizoguchi 2007 *{published data only}*
Mizoguchi H, Wilson A, Jerdack GR, Hull JD, Goodale M, Grender JM, Tyler BA. Efficacy of a single evening dose of syrup containing paracetamol, dextromethorphan hydrobromide, doxylamine succinate and ephedrine sulfate in subjects with multiple common cold symptoms. *International Journal of Clinical Pharmacology and Therapeutics* 2007;**45**(4):230–6.

Mossad 1996 *{published data only}*
Mossad SB, Macknin ML, Medendorp SV, Mason P. Zinc gluconate lozenges for treating the common cold. A randomized, double-blind, placebo-controlled study. *Annals of Internal Medicine* 1996;**125**(2):81–8.

Paul 2004 *{published data only}*
Paul IM, Yoder KE, Crowell KR, Shaffer ML, McMillan HS, Carlson LC, Dilworth DA, Berlin CM, Jr. Effect of dextromethorphan, diphenhydramine, and placebo on nocturnal cough and sleep quality for coughing children and their parents. *Pediatrics* 2004;**114**(1):85–90.

Paul 2007 *{published data only}*
Paul IM, Beiler J, McMonagle A, Shaffer ML, Duda L, Berlin CM Jr. Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. *Arch Pediatr Adolesc Med* 2007;**161**:1140–1146.

Prasad 2000 *{published data only}*
Prasad AS, Fitzgerald JT, Bao B, Beck FW, Chandrasekar PH. Duration of symptoms and plasma cytokine levels in patients with the common cold treated with zinc acetate. A randomized, double-blind, placebo-controlled trial. *Annals of Internal Medicine* 2000;**133**(4):245–52.

Prasad 2008 *{published data only}*
Prasad AS, Beck FW, Bao B, Snell D, Fitzgerald JT. Duration and severity of symptoms and levels of plasma interleukin-1 receptor antagonist, soluble tumour necrosis factor receptor, and adhesion molecules in patients with common cold treated with zinc acetate. *The Journal of Infectious Diseases* 2008;**197**(6):795–802.

Scavino 1985 *{published data only}*
Scavino Y. Combination therapy in patients with the common cold. *Current Therapeutic Research* 1985;**38**(5): 746–54.

Schutz 2002 *{published data only}*
Schutz A, Gund HJ, Pschorn U, Aicher B, Peil H, Muller A, de Mey C, Gillissen A. Local anaesthetic properties of ambroxol hydrochloride lozenges in view of sore throat. *Arzneimittel-Forschung* 2002;**52**(3):194–9.

Taylor 1993 *{published data only}*
Taylor JA, Novack AH, Almquist JR, Rogers JE. Efficacy of cough suppressants in children. *Journal of Pediatrics* 1993; **122**(5 Pt 1):799–802.

Weippl 1984 *{published data only}*
Weippl G. Therapeutic approaches to the common cold in children. *Clinical Therapeutics* 1984;**6**(4):475–82.

Yoder 2006 *{published data only}*
Yoder KE, Shaffer ML, La Tournous SJ, Paul IM. Child assessment of dextromethorphan, diphenhydramine, and placebo for nocturnal cough due to upper respiratory infection. *Clinical Pediatrics* 2006;**45**(7):633–40.

Additional references

Britt 2002
Britt H, Miller GC, Knox S, Charles J, Valenti L, Henderson J, et al. Bettering the Evaluation and Care of Health - A Study of General Practice Activity. Australian Institue of Health and Welfare Cat. No. GEP-10 2002.

Cates 2003 [Computer program]
Cates C. Visual Rx. Online NNT Calculator. http://www.nntonline.net/: Cates C, 2003.

Chang 1999
Chang AB. State of the art: cough, cough receptors, and asthma in children. *Pediatric Pulmonology* 1999;**28**:59–70.

Chang 2001
Chang AB, Asher MI. A review of cough in children. *Journal of Asthma* 2001;**38**(4):299–309.

Chang 2005
Chang AB. Cough: are children really different to adults?. *Cough* 2005;**1**:7.

Chang 2006
AB Chang, WB Glomb. Guidelines for Evaluating Chronic Cough in Pediatrics. *Chest* 2006;**129**(1):260S–83S.

Chang 2007
Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) cough medications to reduce cough as an adjunct to antibiotics for acute pneumonia in adults and children. *Cochrane Database of Systematic Reviews* 2007, Issue 4. [DOI: 10.1002/14651858.CD006088.pub2]

Cherry 2003
Cherry DK, Burt CW, Woodwell DA. National Ambulatory Medical Care Survey: 2001 summary. *Adv Data* 2003;**337**: 1–44.

Eccles 2002
R Eccles. The Powerful Placebo in Cough Studies?. *Pulmonary Pharmacology and Therapeutics* 2002;**15**:303–8.

Elbourne 2002
Elbourne DR, Altman DG, Higgins JPT, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. *International Journal of Epidemiology* 2002;**31**(1):140–9.

Higgins 2008
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0 [updated Feruary 2008]. The Cochrane Collaboration (Available from www.cochrane-handbook.org) 2008.

Jüni 2001
Jüni P, Altman DG, Egger M. Systematic reviews in health care: Assessing the quality of controlled clinical trials. *BMJ* 2001;**232 (7303)**:42–6.

Marchant 2008
JM Marchant, PA Newcombe, EF Juniper, JK Sheffield, SL Stathis, AB Chang. Chronic cough in children and its burden on parents. *Chest* 2008;**134**:303–9.

Newcombe 2008
PA Newcombe, JK Sheffield, EF Juniper, JM Marchant, Halstead R, Masters IB, AB Chang. Development of a parent-proxy cough-specific QOL questionnaire: clinical impact vs psychometric evaluations. *Chest* 2008;**133**: 386–395.

Paul 2007
IM Paul, J Beiler, A McMonagle, ML Shaffer, L Duda, CM Berlin Jr. Effect of Honey, Dextromethorphan, and No Treatment on Nocturnal Cough and Sleep Quality for Coughing Children and Their Parents. *Archives of Paediatrics and Adolescent Medicine* December 2007;**161** (12):1140–6.

Schroeder 2004
Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings (Cochrane review). *Cochrane Database of Systematic Reviews* 2004, Issue 4. [DOI: 10.1002/14651858.CD001831.pub2]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdul 1999	Adult study. Compared the antitussive effect of variations on dextromethorphan. No specific focus on cough types (i.e. chronic or non-specific)
Eby 2006	Adult study. Assessed efficacy of zinc lozenges and zinc nasal sprays in controlling symptoms of the common cold. Zinc improved cold symptoms in 20% more of the participants, but there was no specific focus on coughs or chronic symptoms
Fischer 2002	No focus on children. Assessed efficacy of ambroxol hydrochloride lozenges in acute uncomplicated sore throat relief
Fujimori 1998	Adult study. Participants had chronic coughs of a specific nature (i.e. postinfectious), and were treated with variants of dextromethorphan to test the efficacies of the treatments
Gilbert 2008	Report on Paul et al's 2007 study
Grattan 1995	Adult study. Compared inhaled and oral dextromethorphan in treating citric acid induced coughs
Haidl 2001	Adult study on menthol efficacy in treating cough and dyspnoea. Those undergoing fibreoptic bronchoscopy were treated before, after, or with placebo, and the results showed no significant difference between the groups
Lee 2000	Adult study. Assessed efficacy of dextromethorphan in treating acute upper respiratory tract infection
Macknin 1998	Assessed efficacy of zinc gluconate lozenges in treating common cold symptoms in children, but no specific focus on coughs. The study found no benefit in treating with zinc lozenges in children and adolescents
Matthys 1983	Adult study dealing with chronic stable coughs. Participants were treated with dextromethorphan or codeine and results compared, finding dextromethorphan to be a more suitable antitussive
Mizoguchi 2007	No focus on children. Assessed efficacy of syrup containing paracetamol, dextromethorphan hydrobromide, doxyamine succinate, and ephedrine sulfate in treating symptoms of the common cold
Mossad 1996	Adult study assessing the use of zinc gluconate lozenges for treating symptoms of the common cold. Results showed fewer days with coughing in lozenge-treated group (2 days compared with 4.5 days in placebo group)
Paul 2004	Examined the use of dextromethorphan, diphenhydramine, and placebo in children with coughs related to upper respiratory tract infection
Paul 2007	Studied the ability of honey to treat cough in children, including participants from 2-18 years and comparing honey to dextromethorphan and no treatment. Coughs were due to acute viral respiratory infections. Those receiving honey showed greater improvements in cough severity and sleep disruption

(*Continued*)

Prasad 2000	Adult study testing efficacy of zinc acetate lozenges in reducing duration and severity of symptoms of common cold. Lozenges were found to reduce duration and severity of cough in this study
Prasad 2008	Adult study testing efficacy of zinc acetate lozenges in reducing duration and severity of symptoms of common cold. Found lozenges reduced duration of coughs
Scavino 1985	No focus on children. Assessed efficacy of treating common cold symptoms with dextromethorphan hydrobromide syrup compared with placebo
Schutz 2002	Adult study examining the local anaesthetic properties of ambroxol hydrochloride lozenges in the context of sore throat
Taylor 1993	Evaluated treating acute night coughs in children with dextromethorphan, codeine, or placebo. Results showed that neither codeine nor dextromethorphan were superior to placebo in treating night cough in children
Weippl 1984	Compared common cold symptom alleviation in children using a dextromethorphan-based syrup (SCH 399) and an expectorant containing antihistamine. Treatment with SCH 399 was found to be more effective
Yoder 2006	Assessed efficacy of dextromethorphan, diphenhydramine, and placebo in treating nocturnal cough in children due to acute upper respiratory tract infection

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Search strategies

CENTRAL
Topic search
#1 MeSH descriptor Cough explode all trees
#2 cough*
#3 MeSH descriptor Bronchitis explode all trees
#4 bronchit*
#5 (#1 OR #2 OR #3 OR #4)
#6 MeSH descriptor Honey explode all trees
#7 honey*
#8 lozenge*
#9 pastille*
#10 troche*
#11 MeSH descriptor Benzocaine explode all trees
#12 MeSH descriptor Menthol explode all trees
#13 MeSH descriptor Eucalyptus explode all trees
#14 MeSH descriptor Dextromethorphan explode all trees
#15 benzocaine*
#16 menthol*
#17 eucalypt*
#18 dextromethorphan*
#19 (#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18)
#20 (#5 AND #19)

MEDLINE
Topic search
1. cough/
2. cough$.mp.
3. exp Bronchitis/
4. bronchit$.mp.
5. or/1-4
6. Honey/
7. honey$.mp.
8. lozenge$.mp.
9. pastille$.mp.
10. troche$.mp.
11. Benzocaine/
12. Menthol/
13. eucalyptus/
14. Dextromethorphan/
15. benzocaine$.mp.
16. menthol$.mp.

17. eucalypt$.mp.
18. dextromethorphan$.mp.
19. or/6-18
20. 19 and 5

RCT filter
1. (clinical trial or controlled clinical trial or randomised controlled trial).pt.
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

EMBASE

Topic search
1. exp Coughing/
2. cough$.mp.
3. exp Bronchitis/
4. bronchit$.mp.
5. or/1-4
6. Honey/
7. honey$.mp.
8. lozenge/
9. lozenge$.mp.
10. pastille$.mp.
11. troche$.mp.
12. Benzocaine/
13. Menthol/
14. Eucalyptus/
15. Dextromethorphan/
16. benzocaine$.mp.
17. menthol$.mp.
18. eucalypt$.mp.
19. dextromethorphan$.mp.
20. or/6-19
21. 20 and 5

RCT filter
1. Randomized Controlled Trial/
2. Controlled Study/
3. randomisation/
4. Double Blind Procedure/
5. Single Blind Procedure/
6. Clinical Trial/
7. Crossover Procedure/
8. follow up/
9. exp prospective study/

10. or/1-9
11. (clinica$ adj3 trial$).mp.
12. ((singl$ or doubl$ or trebl$ or tripl$) adj5 (mask$ or blind$ or method$)).mp.
13. exp Placebo/
14. placebo$.mp.
15. random$.mp.
16. (latin adj3 square$).mp.
17. exp Comparative Study/
18. ((control$ or prospectiv$ or volunteer$) adj3 (trial$ or method$ or stud$)).mp.
19. (crossover$ or cross-over$).mp.
20. or/11-19
21. 10 or 20
22. exp ANIMAL/
23. Nonhuman/
24. Human/
25. 22 or 23
26. 25 not 24
27. 21 not 26

WHAT'S NEW

Last assessed as up-to-date: 27 October 2010.

Date	Event	Description
13 January 2011	New search has been performed	New literature search run, no new studies found

HISTORY

Protocol first published: Issue 1, 2009

Review first published: Issue 2, 2009

Date	Event	Description
15 September 2009	Amended	Contact author details changed.
27 June 2009	Amended	Reference corrected. Gilbert 2008 was used instead of Paul 2007 which was the original paper. Gilbert 2008 referred to Paul 2007's study

CONTRIBUTIONS OF AUTHORS

SM and AC wrote the protocol based on previous protocols. Both also wrote the review.

DECLARATIONS OF INTEREST

None of the authors have any conflict of interest.

SOURCES OF SUPPORT

Internal sources

- Cochrane Airways Scholarship, Australia.

Support for SM

- Royal Children's Hospital Foundation, Australia.

Research support for AC

External sources

- NHMRC, Australia.
- Queensland Smart State Clinical Fellowship, Australia.

Support for AC

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Not applicable

INDEX TERMS

Medical Subject Headings (MeSH)

*Honey; Antitussive Agents [*therapeutic use]; Chronic Disease; Cough [therapy]; Tablets

MeSH check words

Child; Humans