



# OTC Cough and Cold Medicines in Children

Efficacy information

July 2009

# Review criteria

- What medicines?
  - Expectorants / mucolytics
  - Cough suppressants (antitussives)
  - Antihistamines
  - Decongestants (oral, topical)
- What outcomes
  - Symptom relief (and time period)
- What age groups
  - Less than 6 years; 6 to 12 years

# Limitations

- Hierarchy of evidence
  - Systematic review ± meta-analysis
  - Randomised controlled trials
    - Bias – lack of blinding, lack of power (number of participants), lack of objective diagnosis, objective outcomes, source
  - Cohort / case controlled
  - Before / after or longitudinal studies
- Method
  - Pharmaceutical company data (including unpublished)
  - Primary literature (check studies / missing papers)

# Expectorants / mucolytic

- Bromhexine (Bisolvon™) - mucolytic
  - For conditions with abnormal mucus secretion and impaired mucus transport (breaks up the phlegm)
- Primary information source - Boehringer
  - 28 studies, 1441 exposures
  - Mixed conditions – including asthma, pneumonias
  - Mixed formulations – in 9 studies no longer available
  - Small studies – 25 of the studies had less than 55 participants
  - 23 of the 28 studies were non-randomised, longitudinal
  - Treatment period 5 to 30 days (mean ~ 10)

# Bromhexine

- Published studies – 6 were open, uncontrolled (longitudinal)
- RCT – Tarantino et al (1988)
  - 3 to 12 years old; 8 days treatment
  - Acute sinus inflammation (included whooping cough, measles complications etc)
  - All patients received amoxicillin
  - Used 5- Likert scale for nasal secretions, rhinitis score
  - Outcome statistically favored bromhexine – but baseline characteristics did not appear balanced.

# Guaifenesin

- Less than 12 years old
  - Taylor et al. 1993                      n = 49
    - Guaifenesin + dextromethophan vs Guaifenesin + codeine vs placebo
    - **No significant difference**

# Expectorants / mucolytics

## Conclusion

Inadequate evidence of benefit in children less than 12 years old from good randomised trials in children with common cold / cough

# Antihistamines

- Brompheniramine
  - Information source – CHPA, primary literature, systematic review
  - Less than 6 years old
    - Hutton et al. 1991 (URTI) n = 96
      - Brompheniramine + phenylephrine vs placebo vs NT
      - **No significant difference**
    - Clemons et al. 1997 (URTI) n = 59
      - Brompheniramine + phenylpropanolamine vs placebo
      - **No significant difference** (though more children asleep at 2 hours with brompheniramine)
  - 6 to 12 years – no studies



# Antihistamines

- Chlorpheniramine
  - Less than 6 years old
    - Sakchainanont et al. 1990 (rhinorrhoea ± cough)
      - Chlorpheniramine vs clematine vs placebo
      - All groups improved
      - **No significant difference**
  - 6 – 12 years old – no studies

# Antihistamines

- Diphenhydramine
  - 2 to 16.5 years (Median 4.5 years)
    - Paul et al. 2004 (URTI + cough) n = 100
      - Diphenhydramine vs dextromethorphan vs placebo
      - **No significant difference**
    - Yoder et al. 2006 (older subgroup – median 7.5 years)
      - **No significant difference**

# Antihistamines

- Pyribenzamine

- 9 to 16 year olds

- Fisher et al. 1959 (common cold) n = 74
      - Pyribenzamine vs placebo
      - **No significant difference**

# Antihistamines

- Doxylamine
  - Less than 12 years old – no studies

# Antihistamines – Systematic reviews

Antihistamines for common cold. De Sutter A, Lemiengre M, Campbell H.

- Antihistamines in monotherapy - in children as well as in adults - do not alleviate to a clinical extent nasal congestion, rhinorrhoea and sneezing, or subjective improvement of the common cold. First generation antihistamines also cause more side-effects than placebo, in particular they increase sedation in cold sufferers. *Combinations of antihistamines with decongestives are not effective in small children. In older children and adults most trials show a beneficial effect on general recovery as well as on nasal symptoms. However, it is not clear whether these effects are clinically significant.*

# Antihistamines – Systematic reviews

Antihistamines for prolonged non-specific cough in children.  
Change A, Peake J, McElrea M

- This review has significant limitations. However, our finding of uncertain efficacy of anti-histamines for chronic cough are similar to that for acute cough in children. In contrast to recommendations in adults with chronic cough, anti-histamines cannot be recommended as empirical therapy for children with chronic cough. If anti-histamines were to be trialled in these children, current data suggest a clinical response (time to response) occurs within two weeks of therapy. However the use of anti-histamines in children with non-specific cough has to be balanced against the well known risk of adverse events especially in very young children.

# Antihistamines

## Conclusion

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# Decongestants

- Phenylephrine

- Less than 6 years old

- Hutton et al. 1991 (URTI) n = 96

- Brompheniramine + phenylephrine vs placebo vs NT

- **No significant difference**

- 6 to 12 years – no studies



# Decongestants

- Pseudoephedrine

- 2 to 16 years old

- Gallargo et al. 1994                      n = 35

- Pseudoephedrine vs pseudoephedrine + naproxen vs placebo
      - Pseudoephedrine + naproxen had shorter duration of symptoms but
      - **No significant difference** between pseudoephedrine and placebo

# Decongestants – systematic reviews

Nasal decongestants for the common cold. Taverner D, Latte G.

- There is insufficient data on the use of these medications in children and therefore they are not recommended for use in children younger than 12 years of age with the common cold.

# Decongestants

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# Decongestants + antihistamines

Decongestants and antihistamines for acute otitis media. Coleman C, Moore M

- Given lack of benefit and increased risk of side effects, these data do not support the use of decongestant treatment in children with AOM. There was a small statistical benefit from combination medication use but the clinical significance is minimal and study design may be biasing the results. Thus, the routine use of antihistamines for treating AOM in children cannot be recommended.

Antihistamines and / or decongestants for OME. Griffin G, Flynn C, et al.

- Because the pooled data demonstrate no benefit and some harm from the use of antihistamines or decongestants alone or in combination in the management of OME, we recommend against their use.

Antihistamines for common cold. De Sutter A, Lemiengre M, Campbell H.

- Combinations of antihistamines with decongestives are not effective in small children. In older children and adults most trials show a beneficial effect on general recovery as well as on nasal symptoms. However, it is not clear whether these effects are clinically significant.

# Cough suppressants

- Dextromethorphan

- Less than 12 years old

- Taylor et al. 1993 n = 49
      - Guaifenesin + dextromethorphan vs guaifenesin + codeine vs placebo
      - **No significant difference**
    - Korppi et al. 1991 n = 78
      - Dextromethorphan vs dextromethorphan + salbutamol vs placebo
      - **No significant difference**
    - Reece et al. 1966 (inpatients) n = 22 (3 groups)
      - Phenylpropanolamine + pheniramine + dextromethorphan + ammonium chloride vs phenylpropanolamine + dextromethorphan + glyceryl guaicolate + 5% alcohol vs placebo
      - **F1 and F2 reduce cough** – but numbers small and variable baseline severity
    - Reece et al. 1966 (outpatients) n = 43 (3 groups)
      - Phenylpropanolamine + pheniramine + dextromethorphan + ammonium chloride vs phenylpropanolamine + dextromethorphan + glyceryl guaicolate + 5% alcohol vs placebo
      - **F1 and F2 reduce cough** – but numbers small and variable baseline

# Cough suppressants

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# Cough suppressants – systematic reviews

Should we advise parents to administer over the counter cough medicines for acute cough?  
Systematic review of randomised controlled trials. Schroeder K, Fahey T.

- OTC cough medicines do not appear more effective than placebo in relieving symptoms of acute cough. Even if statistically significant, effect sizes were small and of doubtful clinical relevance. The number of trials in each category was small, and the results of this systematic review have to be interpreted with caution. Based on the available evidence from a small number of studies, we cannot recommend OTC cough medicines as a first line treatment for children with acute cough.

Over-the-counter medications for acute cough in children and adults in ambulatory settings. Smith S, Schroeder K, Fahey T

- There is no good evidence for or against the effectiveness of OTC medicines in acute cough. The results of this review have to be interpreted with caution due to differences in study characteristics and quality. Studies often showed conflicting results with uncertainty regarding clinical relevance. Higher quality evidence is needed to determine the effectiveness of self-care treatments for acute cough.

# Cough suppressants

## Conclusion

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# Miscellaneous

- Topical nasal decongestants - Xylometazoline (Otrivin™)
  - 4 x RCTs
    - 2 positive (10 to 75 years, for allergic rhinitis and included sodium chromoglycate; 12 to 75 years for tympanic membrane perforation)
    - 2 NSD – both had adjunctive amoxicillin and were for chronic maxillary sinusitis
  - 8 studies but no placebos
- Topical nasal anticholinergics - Ipratropium (Atrovent™)
  - Cochrane: There is currently no evidence to support the use of inhaled anticholinergics for symptomatic control of non-specific cough in children.
- Nasal saline
  - Cochrane: The use of topical saline could be included as a treatment adjunct for the symptoms of chronic rhinosinusitis.
- Honey and lozenges
  - Cochrane: 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 1 year of age).

