Antihistamines and/or decongestants for otitis media with effusion (OME) in children (Review)

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TABLE OF CONTENTS

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ABSTRACT

Background
Otitis media with effusion (OME) is common and may cause hearing loss with associated developmental delay. Treatment remains controversial. The effectiveness of antihistamines, decongestants and antihistamine/decongestant combinations in promoting the resolution of effusions has been assessed by randomized controlled trials.

Objectives
The objective of this review is to determine whether antihistamine, decongestant, or combination therapy is effective in treating children who present with OME.

Search strategy
The Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, Issue 1 2006), EMBASE (1974 to 2006), MEDLINE (1951 to 2006) and a gray literature database were searched using a search strategy created by an experienced medical librarian. The date of the last search was March 2006. Reference lists from included studies and relevant reviews were searched by hand; pharmaceutical manufacturers of antihistamines and decongestants and first authors of included studies were contacted to identify other potentially relevant studies.

Selection criteria
Randomized controlled trials (RCTs) using antihistamines, decongestants or antihistamine/decongestant combinations as treatment for OME in children were selected. We excluded trials that randomized on the basis of acute otitis media (AOM) even though OME was also studied in follow up.

Data collection and analysis
Data were extracted from the published reports by two authors independently using standardized data extraction forms and methods. The methodological quality of the included studies was independently assessed by two authors. Dichotomous results were expressed as a relative risk with 95% confidence intervals using a fixed-effect model when homogeneous and a random-effects model when heterogeneous. Nearly all outcomes analysed were homogeneous. Continuous results were discussed qualitatively. Statistical analysis was conducted using RevMan software.

Main results
No statistical or clinical benefit was found for any of the interventions or outcomes studied. However, treated study subjects experienced 11% more side effects than untreated subjects (number needed to treat to harm = 9).

Authors' conclusions
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.

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PLAIN LANGUAGE SUMMARY

Antihistamines and/or decongestants do not help and may harm when used for symptoms of otitis media with effusion ('glue ear').

Otitis media with effusion (OME), also known as glue ear or serous otitis media, is a condition in which there is fluid persisting in the middle ear. Many treatments have been suggested. This review summarizes the studies using antihistamines, decongestants or a combination of antihistamines and decongestants and finds no benefit for any of the short or long-term outcomes including resolution of the fluid, hearing problems, or the necessity of additional referral to specialists. Further, using these medications causes significant side effects, such as gastro-intestinal upset, irritability, drowsiness or dizziness in approximately 10% of patients. Therefore antihistamines, decongestants or antihistamine/decongestant combinations are not recommended treatments for OME. Watchful waiting is the best approach with consideration of referral for evaluation by an ENT consultant if symptoms persist beyond 12 weeks.

BACKGROUND

This is one of a number of reviews prepared within the Cochrane Ear, Nose and Throat Disorders Group on management options for patients with otitis media with effusion.

Symptoms, prevalence and aetiology

Otitis media with effusion (OME), or 'glue ear', is characterized by an accumulation of fluid in the middle ear, in the absence of acute inflammation. It is very common in children, especially between the ages of one and three years and in seasons where the prevalence of upper respiratory tract infections ('colds') is high, with an incidence of ten to thirty percent. It occurs frequently even up to the age of seven, with a prevalence of three to eight percent (Fiellau 1977; Fiellau 1983; Lous 1981; Teele 1989). Otitis media with effusion is the commonest cause of acquired hearing loss in childhood. The reason why it develops is uncertain, but low-grade infection, poor Eustachian tube function and adenoidal infection or hypertrophy have all been implicated (Bluestone 1995). Otitis media with effusion usually resolves spontaneously within a few months (Fiellau 1979; Rosenfeld 1999).

Acutely, OME may be associated with earache (otalgia), hearing loss and/or balance difficulty. Long-term complications are reported to include hearing loss and linguistic, developmental or social consequences, especially if the OME is bilateral and of long duration (Fiellau 1983; Golz 1998; Grace 1990; Lous 1995). However a report for the Agency for Health Research and Quality did not find evidence to support an effect of early-life OME on language development or cognitive verbal intelligence (Shekelle 2003). The same report did find evidence to support a link between early-life OME and increased risk of conductive hearing loss. Some children have nearly normal hearing despite the presence of fluid within the middle ear.

Diagnosis

The best technique for diagnosing OME is pneumatic otoscopy, with a sensitivity of 94% and a specificity of 80% based on a meta-analysis of eight different methods of diagnosis (Takata 2003). OME is may also be present when tympanometry results in a flat curve (relative gradient less than 0.1, type B), when mobility of the tympanic membrane is absent or reduced, or fluid or air bubbles are evident behind the eardrum. The presence of a significant (10 dB) air-bone gap correlates well with the presence of fluid in the middle ear. Persistence of OME in this review will be determined by pneumatic otoscopy or a combination of the aforementioned techniques.

Management options

Many patients with OME require no specific treatment. Commonly proposed medical treatment options include the use of decongestants, mucolytics, steroids, antihistamines, antibiotics and autoinflation. Surgical treatment options include grommet insertion (ventilation tubes), myringotomy (tympanocentesis, i.e. surgical incision of the eardrum, with or without aspiration of fluid from the middle ear cavity) and adenoidectomy. Antibiotics, grommets and intranasal steroids for OME have already been addressed in Cochrane reviews; decongestants alone or in combination with antihistamines were studied in a published meta-analysis (Witmer 1998) but only two randomized controlled trials were found and the analysis had significant methodological flaws. Wide international variation in clinical practice exists and the optimal treatment strategy remains controversial although a recent guideline (AAFP 2004) recommended watchful waiting for three months and recommended against antihistamines and/or decongestants. Rosenfeld and Bluestone (Rosenfeld 1999) recommended modification of risk factors such as avoidance of tobacco smoke, use of breastfeeding and choice of small group (< 5 children) day-care when possible to assist in the management and prevention of OME.

Antihistamines and/or decongestants

Antihistamines and decongestants are relatively safe and inexpensive and are commonly used separately or in combination in the management of OME. Theoretically, antihistamines may reduce the congestion of mucous membranes and decrease obstruction of tubes lined by mucous membrane, such as the Eustachian tube. An open Eustachian tube would allow the middle ear pressure to equalize to ambient air pressure. It may also allow drainage of fluid from the middle ear. If mucous membrane congestion is caused by allergy then anti-allergy medications such as antihistamines may

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work to reduce congestion and similarly improve Eustachian tube dysfunction. Some recent evidence suggests that viral or bacterial organisms contribute to middle ear inflammation and the release of histamines as well as other inflammatory mediators such as leukotrienes (Chonmaitree 2003). Decongestants are vasoconstrictors and should reduce mucous membrane swelling and enhance Eustachian tube function. However the evidence to support the use of antihistamines or decongestants in the treatment of OME is underwhelming. This review will analyze the best evidence to date.

OBJECTIVES

The objective of this review was to determine whether antihistamine, decongestant, or combination therapy is effective in treating children who present with OME.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Studies eligible for inclusion were randomized controlled trials. Methods of randomization were not used to exclude studies but were considered in the quality assessment

Types of participants

We included studies evaluating children (age 18 or under) who had a diagnosis of OME. We chose specifically not to evaluate acute otitis media, patients with anatomical deformity, or patients with other chronic immunocompromised states. When studies included mixed populations, but contained extractable data for a population that met our criteria, the study was included.

Types of intervention

The intervention of interest was the use of oral or nasal decongestant and/or antihistamine as compared to no medication or placebo. Our study specifically did not address the use of oral or nasal steroid for OME; these interventions are addressed in a separate Cochrane review (Thomas 2006).

Types of outcome measures

We anticipated a large number of possible outcomes to be reported in the trials, and thus adopted the following strategy of another Cochrane review group (Smucny 2004). After the primary search strategy was completed, we reviewed abstracts for possible inclusion. One author then reviewed all articles considered for inclusion, extracting a list of measured outcomes. This list was given to the other investigators, blinded to the number of studies that reported any given outcome. From that list, the primary outcomes of interest were selected. These then became the outcome criteria for inclusion in the review. Our primary interest was in outcomes of importance to patients. The general categories included:

a) resolution of symptoms or signs (however measured);
b) duration of effusion;
c) duration of hearing loss as defined by pure tone audiometric loss of over 20 dB;
d) reduction of complications of OME;
e) decreased necessity for tympanostomy or tympanocentesis; and
f) medication side effects or complications.

Upon review of all included studies, however, it became clear that the only outcome measured consistently was resolution of the effusion. This, therefore, became our primary (that is, main) outcome.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Ear, Nose and Throat Disorders Group methods used in reviews.

A research librarian familiar with Cochrane methods formulated a sensitive search strategy. We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, Issue 1 2006), EMBASE (1974 to 2006), MEDLINE (1951 to 2006). The date of the last search was March 2006. Ongoing monthly updates of our saved search strategy have been conducted in MEDLINE since the initial search and have found no new studies.

Next, bibliographies of all included trials and relevant reviews were searched by hand to identify additional studies. Our reference librarian searched a gray literature database using the search terms noted above.

Finally, a letter was sent to all first authors of included papers and to pharmaceutical companies that manufacture decongestants or antihistamines requesting data and references for any published and unpublished applicable trials.

Our search strategy was as follows:

1. (antihistam$ or anti-histamin$ or (anti adj histamin$)).ab,ti,sh.
2. exp Histamine antagonists/
3. (terfenadine or seldane).mp. or 50679-08-8.rn. [mp=title, abstract, registry number word, mesh subject heading]
4. (astemizole or hismanal).mp. or 68844-77-9.rn. [mp=title, abstract, registry number word, mesh subject heading]
5. diphenhydramine.mp. or (147-24-0 or 88637-37-0).rn. [mp=title, abstract, registry number word, mesh subject heading]
6. (chlorpheniramine or dexbrompheniramine).mp. or (113-92-8 or 2391-03-9 or 132-21-8).rn. [mp=title, abstract, registry number word, mesh subject heading]
7. (chlorphenamine or doxylamine).mp. or (132-22-9 or 562-10-7 or 469-21-9).rn. [mp=title, abstract, registry number word, mesh subject heading]

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8. brompheniramine.mp. or (980-71-2 or 86-22-6).rn. [mp=title, abstract, registry number word, mesh subject heading]
9. triprolidine.mp. or (6138-79-0 or 550-70-9 or 486-12-4).rn. [mp=title, abstract, registry number word, mesh subject heading]
10. carbinoxamine.mp. or (3505-38-2 or 486-16-8).rn. [mp=title, abstract, registry number word, mesh subject heading]
11. cetirizine.mp. or (83881-52-1 or 83881-51-0).rn. [mp=title, abstract, registry number word, mesh subject heading]
12. (fexofenadine or loratadine).mp. or (138452-21-8 or 83799-24-0 or 79794-75-5).rn. [mp=title, abstract, registry number word, mesh subject heading]
13. pheniramine.mp. or (132-20-7 or 86-21-5).rn. [mp=title, abstract, registry number word, mesh subject heading]
14. (pyrilamine or mepyramine).mp. or (59-33-6 or 91-84-9).rn. [mp=title, abstract, registry number word, mesh subject heading]
15. acrivastine.mp. or 87848-99-5.rn. [mp=title, abstract, registry number word, mesh subject heading]
16. azatadine.mp. or (3978-86-7 or 3964-81-6).rn. [mp=title, abstract, registry number word, mesh subject heading]
17. clemastine.mp. or (15686-51-8 or 14976-57-9).rn. [mp=title, abstract, registry number word, mesh subject heading]
18. hydroxyzine.mp. or (2192-20-3 or 68-88-2).rn. [mp=title, abstract, registry number word, mesh subject heading]
19. exp nasal decongestants/ or decongestants.mp.
20. vasoconstrictor agents, nasal/
21. exp Vasoconstrictor agents/
22. 21 and nasal.mp. [mp=title, abstract, registry number word, mesh subject heading]
23. pseudoephedrine.mp. or (345-78-8 or 90-82-4).rn. [mp=title, abstract, registry number word, mesh subject heading]
24. phenylpropanolamine.mp. or (154-41-6 or 14838-15-4).rn. [mp=title, abstract, registry number word, mesh subject heading]
25. phenylephrine.mp. or (61-76-7 or 59-42-7).rn. [mp=title, abstract, registry number word, mesh subject heading]
26. oxymetazoline.mp. or (2315-02-8 or 1491-59-4).rn. [mp=title, abstract, registry number word, mesh subject heading]
27. propylhexedrine.mp. or 101-40-6.rn. [mp=title, abstract, registry number word, mesh subject heading]
28. xylometazoline.mp. or (1218-35-5 or 526-36-3).rn. [mp=title, abstract, registry number word, mesh subject heading]
29. naphazoline.mp. or (550-99-2 or 835-31-4).rn. [mp=title, abstract, registry number word, mesh subject heading]
30. otitis media/
31. limit 30 to yr=1960-1978
32. (serous or secretory or adhesive or exudative or mucous or mucoid or seromucoid or suppurative).mp. [mp=title, abstract, registry number word, mesh subject heading]
33. 31 and 32
34. (Otitis adj media adj2 (serous or secretory or adhesive or exudative or mucous or mucoid or seromucoid or suppurative)).mp.
35. otitis media with effusion.mp. [mp=title, abstract, registry number word, mesh subject heading]
36. (otitis adj media adj2 effusion).mp. [mp=title, abstract, registry number word, mesh subject heading]
37. 30 and (serous or secretory or adhesive or exudative or mucous or mucoid or seromucoid or suppurative).ti.
38. 33 or 34 or 35 or 36 or 37
39. 38 and (1 or 2 or 3 or 4 or 5 or 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 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29)

The search strategy was combined with a filter for identifying randomised controlled trials, controlled clinical trials and systematic reviews/meta-analyses (see Table 01).

METHODS OF THE REVIEW

Data extraction

Two authors independently reviewed all the titles and abstracts and determined which studies met the inclusion criteria. Articles chosen by either author were retrieved and the full inclusion criteria were applied. We chose not to blind authors to study authors and journals (Berlin 1997; Jadad 1996). At least two authors independently extracted and recorded data from included studies into a standardized article abstraction form. Disagreements were settled by consensus including a third reviewer when necessary.

Quality assessment

Two reviewers then graded the quality of each included study using the method of Mohar (Mohar 1995). Quality score depended on the randomization process (one point for mentioning randomization and one added point for describing the method of randomization), follow up (one point for describing all losses to follow up) and blinding (one point for mentioning blinding and one added point for describing a reasonable blinding process) for a maximum of five points. Allocation concealment was also assessed as acceptable or not acceptable. Disagreements were discussed and resolved through consensus. Quality scores and method of allocation concealment were used for sensitivity analysis.

Data analysis

Our primary analysis compared outcomes for four groups of patients: those who received antihistamine versus placebo, those who received decongestant versus placebo, those who received antihistamine/decongestant combination versus placebo and those who received any medication (antihistamine, decongestant or antihistamine/decongestant combination) versus placebo.

Anticipating some heterogeneity, specific subanalyses were planned for the following factors for the primary outcome:

- Setting (primary versus tertiary care)
- Age of study participants
- Patient's history of allergies

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- Oral versus nasal decongestant
- Patient's history of recent acute otitis media
- Type of decongestant (specific medications)
- Type of antihistamine
- Method to diagnose resolution of OME
- Timing of dichotomous outcomes (i.e. follow up at two weeks versus six weeks versus 12 or more weeks)
- Study validity score
- Year of publication

Because we found a limited number of studies and because there was minimal heterogeneity, the value of these subanalyses and those planned for diagnostic criteria were not meaningful and thus they were not conducted. Only subanalyses based on study quality were warranted. See Results and Discussion for related qualitative comments.

Continuous measures were not included in the meta-analysis but were described in words. For dichotomous data, relative risk was calculated with confidence intervals using the fixed-effect method, unless heterogeneity was found, in which case results were discussed in the text. Approximate chi-square tests for homogeneity were used to assess comparability of included data.

DESCRIPTION OF STUDIES

Our comprehensive search resulted in the selection of 70 studies based on title alone, of which 42 were selected for review of abstracts. Of these, 16 met our final inclusion criteria and were included in the review. There was full agreement on the final selection of included studies. For more information please see the tables of 'Characteristics of included and excluded studies'. A total of 1737 patients, nearly all of whom were under the age of 18, participated in the studies.

Nine studies took place in ENT clinics and five in community-based clinics. Fifteen studies involving 1516 patients provided dichotomous outcomes and were included in the statistical meta-analyses. One of the studies (Olson 1978) provided continuous outcomes and could not be included in the statistical meta-analyses. The author of this study was contacted but no longer had the original data for re-calculation to provide dichotomous results. Two other studies (Fraser 1977; Khan 1981) did not provide sufficient individual patient data to allow inclusion of their results in the meta-analysis. All three studies gave a simple statement of their results.

Though five studies reported outcomes using ears as the unit of measure rather than persons, we were able to convert the data into a usable, consistent format using a design effect method (Perera 2006). All but one study was in English; the single Swedish study was translated into English and the data were included here.

Two pairs of studies reported on the same populations; duplicated data were not included, but where studies reported different outcomes in different manuscripts, data were pooled as appropriate.

All articles used tympanometry (the closest thing to a 'gold standard' test for OME) in their methods of diagnosis except for three (Edstrom 1977; Haugeto 1981; Saunte 1978). Edstrom used clinical examination only (dullness of the tympanic membrane and immobility on pneumatic otoscopy) and Haugeto and Saunte used clinical (pneumatic otoscopy) and audiometric assessments.

Six studies provided data on the primary outcome (lack of cure at or before one month) and a further six studied our secondary outcome (lack of cure at one to three months). Two articles reported on the late outcome of lack of cure after three months and seven studies reported on other outcomes including hearing loss and school performance.

Six articles provided data on side effects of interventions and controls and eight studies considered complications such as surgery, recurrent OME or acute otitis media.

METHODOLOGICAL QUALITY

Eight papers had a quality score of three or more and seven had a score of two or less. Adequacy of allocation concealment was determined separately and only two of 15 papers demonstrated appropriate concealment of allocation to intervention or control groups. Only two of the included studies used intention-to-treat analysis.

RESULTS

OME persistence

None of the included studies provided an assessment of symptoms other than hearing loss. We therefore chose OME persistence as our primary outcome. As OME is often asymptomatic and because most studies provided this as their primary outcome, we chose to do the same. Outcomes were measured at one month or less, at one to three months (secondary outcome) and after three months (late outcome).

Six of the 16 included studies (all of which had a quality score of three or more) reported dichotomous results for the primary outcome: cure or no cure at one month or less. Pooling data for any medication combination resulted in a relative risk (RR) of 0.99 with a 95% confidence interval (CI) from 0.92 to 1.05 (Analysis 04:01). These studies were statistically homogenous. In fact, the meta-analysis results for all interventions and outcomes except one were homogeneous (i.e. not heterogeneous) using a P value for heterogeneity of 0.10 (Barker 2005).

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Separating out the various interventions had little effect. For decongestant alone the RR for the primary outcome was 1.06 (95% CI 0.92 to 1.22) (Analysis 02:01) and for antihistamine/decongestant combinations the RR was 0.97 (95% CI 0.89 to 1.04) (Analysis 03:01), both non-significant, statistically and clinically.

The results of studies that could not be combined in the meta-analysis are consistent with the summary findings. Olson 1978 found that decongestants alone were not effective for the short-term resolution of OME; in fact, some of the analyses in this study statistically favored the placebo group! Khan 1981 found that, for the antihistamine/decongestant combination the primary outcome (cure or no cure of OME at one month or less), there was no statistical difference between intervention and control.

For the outcome of delayed persistence of OME (one to three months), pooling data for any medication combination found no statistical benefit (RR 1.04, 95% CI 0.89 to 1.21) (Analysis 4.02). For decongestant alone the RR was 1.05 with the 95% CI from 0.85 to 1.30 (Analysis 2.02). For the antihistamine/decongestant combination there was also no estimated benefit (RR 1.09, 95% CI 0.85 to 1.40) (Analysis 3.02).

Our main outcome for antihistamines alone (due to lack of other evidence) was the measure of delayed persistence of OME with RR 0.94 and 95% CI 0.65 to 1.36 (Analysis 1.02) or, more usefully, RD (Actual Risk Difference) of -0.03 with 95% CI -0.19 to 0.13. This confidence interval is somewhat wider than the previous three examples because of a smaller sample size. None of the studies included in this review evaluated side effects for antihistamines so we used an alternative resource, the Lexidrug program online (Lexidrug 2006) (accessed June 27, 2006). We looked at the side effect profile of three commonly used antihistamines with a low side effect frequency: cetirizine, chlorpheniramine and loratadine. All three had two or more side effects with a frequency of more than 10% with many other side effects in the frequency range from 1% to 10%. This is in agreement with our review which showed a general frequency of side effects of approximately 10% for antihistamine/decongestant combinations or decongestants alone.

A study by Fraser 1977, whose data we were unable to extract for meta-analysis, found no benefit for OME resolution at one to three months in either the antihistamine/decongestant or decongestant arms versus placebo.

In summary, for our two main outcome measures, no clinical benefit was found for any of the interventions studied and there was sufficient power in the meta-analysis to have detected any clinically significant benefit.

Late outcome (cure or no cure after three months) was studied only for the antihistamine/decongestant combination and was found to favour control by a small but statistically non-significant amount (RR 1.24, 95% CI 0.72 to 2.13) (Analysis 03:03). The wider confidence intervals indicate less power to show a statistically significant outcome but the trend is clearly toward harm.

Complications (recurrent OME or acute otitis media)

Recurrent OME was evaluated as a complication by two studies for antihistamine/decongestant versus control and the outcome was found to be statistically non-significant (RR 1.30, 95% CI 0.80 to 2.11) (Analysis 03:09:04).

Acute otitis media (AOM) was studied as another complication of OME in three studies; one each for antihistamine alone, decongestant alone and antihistamine/decongestant combination and for each the results were not statistically significant (antihistamine alone (RR 0.89, 95% CI 0.46 to 1.73) (Analysis 01:02); decongestant alone (RR 0.55, 95% CI 0.23 to 1.31) (Analysis 02:06) and antihistamine/decongestant combination (RR 0.76, 95% CI 0.46 to 1.26) (Analysis 03:10)). Because of the small size of the studied population for this outcome, the confidence intervals are fairly wide indicating only fair power to detect a difference between treatment and control.

Other outcomes

Other measured outcomes were: hearing loss (early: four studies and late: one study), school performance (one study) and surgery (tympanostomy: three studies).

No treatment lessened hearing loss at one month follow up (four studies) (Analysis 4.05) and the trend was toward harm (RR 1.08, 95% CI 0.93 to 1.27). At late follow up (one study) (Analysis 4.06) the trend was again toward harm (RR 1.50, 95% CI 0.63 to 3.56).

For school performance (studied only for the intervention of antihistamine/decongestant) the RR was 0.81 (95% CI 0.35 to 1.86) (Analysis 3.07).

For surgery after any medication, decongestant alone or antihistamine/decongestant combination, results were not statistically significant. The relative risk and confidence intervals for any medication were RR 0.96, 95% CI 0.69 to 1.32 (Analysis 04:08). For decongestant alone the result was RR 1.07, 95% CI 0.71 to 1.62 (Analysis 02:05). The antihistamine/decongestant analysis for this outcome (RR 0.54, 95% CI 0.09 to 3.41) (Analysis 03:08) was the only outcome to have been found to be heterogeneous (P = 0.06 for heterogeneity) therefore we shall describe the studies rather than trying to interpret an inappropriate pooling of results). This analysis looked at the two included studies that measured the outcome of surgical complications for the intervention of antihistamine/decongestant combination. One of these studies was clearly an outlier (Saunte 1978) (see Analysis 4.01). It was a very small study (n = 21) with few outcomes and was the only study to show any significant benefit for several of our measured outcomes. The positive results from this study were always overwhelmed by the other studies in its comparison group. The other study in Analysis 3.08 was slightly larger and showed no hint of benefit from the intervention. In summary, this intervention (antihistamine/decongestant combination) shows no clinically significant benefit

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for the outcome of surgical complications but the power to detect such a benefit is only fair because of the small study sizes.

Medication side effects

Pooling the data from the six studies that evaluated medication side effects found a rate of medication standard error (SE) of 17% in the treated group, versus 6% in the placebo group. This was both statistically significant (RR 2.70, 95% CI 1.87 to 3.88) (Analysis 04:04) and clinically meaningful. The number needed to treat to harm = 9, based on an Actual Risk Reduction of 11%.

Subanalyses

Validity

Subanalyses were performed on the basis of quality of study. Those studies with a quality score of three or more and those with a quality score of less than three had similar statistically non-significant results except when the study by Saunte 1978 was the lone comparator. Allocation concealment also did not influence the findings as studies with adequate concealment had the same statistically non-significant results except when the study by Saunte 1978 stood alone in the comparison. This study was small, used a different method to diagnose OME and found benefit where other studies did not (see Discussion below). Quality subanalyses were not included in the meta-analysis because they added no important information.

DISCUSSION

One study (Saunte 1978) is an outlier (Analysis 4.01). This, at first glance, seems not to make sense as this study had a high quality score for methodology and had adequate allocation concealment. Reading the study, however (see table of 'Characteristics of included studies') shows that this study was one of only three that did not include tympanometry as one of the methods of diagnosis of OME, and the number of study subjects was very small (N = 21). The small size of this trial might lead some authors to discard it on this basis alone (Bandolier 2000).

This meta-analysis and systematic review found no benefit from any treatment combination - antihistamine, decongestant or antihistamine/decongestant combination - for any of the measured patient oriented outcomes for OME. It did find, however, an increased rate of medication side effects (number needed to treat to harm = 9). There was a paucity of included studies comparing antihistamines to controls but we did review three studies (Bhambhani 1983; Klein 1980; Chonmaitree 2003) that were excluded because the researchers randomized by acute otitis media (rather than by OME) and then followed the groups for prevention and treatment of OME. All of these studies found no benefit for antihistamines in the prevention or treatment of OME.

One limitation of our analysis is the relatively small number of studies found. However we were unlikely to miss studies given our comprehensive search, and we found many more than the previous systematic review on this topic. Furthermore, the studies were so consistent in their findings that even if we missed a study, the summary results are unlikely to be overturned. Another limitation of our review is that the included articles had some methodological flaws. They varied in duration and thoroughness of follow up, had poor allocation concealment, unclear randomization and blinding processes and lack of intention-to-treat analysis in most studies. In general, all of these design flaws tend to overestimate the benefit of treatment (Bandolier 2000). Since we did not find benefit from any of the interventions, the faults of the included studies strengthen our conclusion.

Strengths of this review are the comprehensive search strategy, the rigorous protocol that was used, the general homogeneity of studies with regard to diagnosis, quality and interventions and the homogeneity and consistency of the outcomes. Subanalysis by quality showed that both good quality and poor quality studies resulted in no benefit for any of the interventions. This also strengthens the conclusions of the review.

It is possible that these medications may provide some benefit in specific situations such as for allergic-related OME and for OME related to upper respiratory infection. This cannot be determined from our meta-analysis that lumps them together but the consistency of the lack of benefit makes this possibility unlikely.

AUTHORS' CONCLUSIONS

Implications for practice

Because we found no benefit for any of the studied interventions for any of the outcomes measured and we found harm from the side effects of the interventions, we recommend that practitioners not use antihistamines, decongestants or antihistamine/decongestant combinations to treat OME in children. This recommendation is consistent with the American Academy of Family Physicians, American Academy of Otolaryngology - Head and Neck Surgery and American Academy of Pediatrics joint guideline on the management of OME.

Implications for research

This review of the use of antihistamines, decongestants or antihistamine/decongestant combination does not show any significant benefit but does show harm from the interventions assessed. The results are surprisingly consistent. It appears highly unlikely that further research studies of these interventions for the treatment of OME would change the outcomes, and harm may be caused by the interventions, therefore we feel that further research on this question is not justified. It is possible that, though there was no suggestion of it in any of the studied articles, antihistamines might be useful specifically for allergic OME or decongestants might be helpful for OME related to upper respiratory infection or post-

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acute otitis media. These are possible, though not likely fruitful, areas for future research.

POTENTIAL CONFLICT OF INTEREST

None known.

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TABLES

Characteristics of included studies

Study	**Cantekin 1983**
Methods	Quality score: 3/5 based on Jadad scoring (Randomization: 1+0; Blinding: 1+1; Withdrawals: 0). Follow up was 87% and the RCT was conducted over 3 years, from 1978-81. Intention-to-treat analysis: yes
Participants	553 pediatric ENT patients were referred from outpatient clinics. Diagnosis was based on an algorithm involving otoscopy, tympanometry and middle ear muscle reflex testing. Exclusion criteria included: congenital craniofacial malformation, Down's Syndrome, history of tonsillectomy, adenoidectomy, or tympanostomy (myringotomy) tubes, structural middle ear abnormality, underlying hearing loss, severe upper airway obstruction, acute otitis media, purulent rhinitis, any sinusitis, or history of antihistamine or decongestant use in the preceding 30 days.
Interventions	Antihistamine (chlorpheniramine) and decongestant (pseudoephedrine) combination versus placebo.
Outcomes	The primary outcome was effusion or no effusion at 4 weeks. Other outcomes measured were hearing, medication side effects and the complication of recurrent OME
Notes	

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Characteristics of included studies (*Continued*)

Allocation concealment	B – Unclear

Study	**Cantekin 1991**
Methods	Quality score: 3/5 (Randomization: 1+0; Blinding: 1+1; Withdrawals: 0). Intention-to-treat analysis: no. Follow up was 89%. RCT was conducted over 3 years from 1981-84.
Participants	318 children aged 7 months to 12 years were recruited from community practices and a hospital ambulatory care centre. Diagnosis was based on an algorithm using otoscopy and tympanometry. Exclusion criteria included: congenital craniofacial malformation, systemic illness, history of tonsillectomy, adenoidectomy, insertion of tubes (tympanostomy), structural middle ear abnormality, hearing loss ...
Interventions	Antihistamine (chlorpheniramine) and decongestant (pseudoephedrine) combination versus placebo.
Outcomes	The primary outcome was effusion or no effusion at 4 weeks with a secondary outcome measured at 12 weeks. Hearing improvement or no improvement was measured at 4 weeks and the complication of acute otitis media was assessed. Side effects of medications were counted.
Notes	
Allocation concealment	B – Unclear

Study	**Dusdieker 1985**
Methods	Quality score: 4/5 (Randomization: 1+0; Blinding: 1+1; Withdrawals: 1). Intention-to-treat analysis: no. Follow up was 89%.
Participants	66 children aged 6 months to 10 years were recruited from a pediatric outpatient clinic. All had completed antibiotic treatment before enrollment. Diagnosis was based on pneumatic otoscopy and tympanometry. Exclusion criteria included: history of cleft lip or palate, chronic disease, immunodeficiency disease, recent use of corticosteroids or known hearing loss > 25 dB bilaterally or > 35 dB unilaterally.
Interventions	Antihistamine (chlorpheniramine), decongestant (pseudoephedrine) and placebo
Outcomes	Our primary outcome was not measured (cure at or before 4 weeks), but a secondary outcome of effusion or no effusion at 12 weeks was measured as was the complication of Acute Otitis Media (AOM).
Notes	Antihistamine arm of the study
Allocation concealment	B – Unclear

Study	**Dusdieker 1985a**
Methods	See Notes
Participants	
Interventions	
Outcomes	
Notes	Same study as Dusdieker 1985 but different arm - decongestant arm
Allocation concealment	D – Not used

Study	**Edstrom 1977**
Methods	Quality score: 1/5 (Randomization: 0; Blinding: 1+0; Withdrawals: 0).

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	Intention-to-treat analysis: no.
	Follow up was 78%. The trial took place in 1974.
Participants	94 children mainly less than 10 years were seen in an ENT clinic.
	Diagnosis was based on pneumatic otoscopy.
	Exclusion criteria: none reported.
Interventions	Antihistamine (cinnarizine) and placebo.
Outcomes	The only outcome measured was the secondary outcome of effusion or no effusion at less than 12 weeks (7 weeks here).
Notes	
Allocation concealment	B – Unclear

Study	**Fabian 1986**
Methods	Quality score: 3/5 (Randomization: 1; Blinding: 1+0; Withdrawals: 1).
	Intention-to-treat analysis: yes.
	Follow up 100%
Participants	172 children aged 6 months to 15 years were recruited from ENT clinics in Sweden.
	Diagnosis was based on pneumatic otoscopy and tympanometry.
	Exclusion criteria included: need for acute tympanocentesis, chronic illness, refusal to participate, difficult child to examine, previous side effects to one drug or the other.
Interventions	Decongestant (oxymetazoline nasal drops or phenylpropanolamine orally) versus no treatment.
Outcomes	The primary outcome of effusion or no effusion at 4 weeks was measured as was the secondary outcome of cure or no cure at 4-8 weeks, all significant side effects and the complication of surgery (tympanostomy).
Notes	
Allocation concealment	B – Unclear

Study	**Fraser 1977**
Methods	Quality score: 1/5 (Randomization: 1+0; Blinding: 0; Withdrawals: 0).
	Intention-to-treat analysis: unable to determine.
	Follow up was 96%.
Participants	85 children aged 3-12 years with bilateral OME were recruited.
	Diagnosis was based on an algorithm using otoscopy and tympanometry.
	Exclusion criteria: none given.
Interventions	Decongestant (ephedrine nasal drops) or antihistamine/decongestant combination (brompheniramine/ phenylpropanolamine) versus autoinflation (control).
Outcomes	No individual patient data were given. The authors gave a simple statement that outcomes from all three interventions were the same.
Notes	
Allocation concealment	C – Inadequate

Study	**Haugeto 1981**
Methods	Quality score: 3/5 (Randomization: 1; Blinding: 1+1; Withdrawals: 0).

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Characteristics of included studies (*Continued*)

	Intention-to-treat analysis: no. Follow up was 94%.
Participants	61 children aged 1-14 years were seen in an ENT Department in Norway. Diagnosis was based on pneumatic otoscopy, otomicroscopy, tympanometry and audiometry. Exclusion criterion: age less than one year.
Interventions	Decongestant (phenylpropanolamine) or decongestant/antihistamine combination (phenylpropanolamine/brompheniramine) versus placebo.
Outcomes	The primary outcome of effusion or not at 4 weeks was measured as was improvement or no improvement in hearing at 4 weeks.
Notes	For 'Any Medication' comparison, this will be decongestant arm only
Allocation concealment	B – Unclear

Study	**Haugeto 1981a**
Methods	See Notes
Participants	
Interventions	
Outcomes	
Notes	Same study as Haugeto 1981 but different arm, antihistamine/decongestant arm.
Allocation concealment	D – Not used

Study	**Hayden 1984**
Methods	Quality score: 4/5 (Randomization: 1+0; Blinding: 1+1; Withdrawals: 1). Intention-to-treat analysis: no. Follow up was 50% and the duration of the study was 4 years from 1978-82.
Participants	67 children aged 9 months to 10 years were recruited from private pediatrics offices approximately 2 weeks after treatment for AOM. Diagnosis was based on either clinical criteria (pneumatic otoscopy) or tympanometry. We used only tympanometry data. Exclusion criteria: none given.
Interventions	Decongestant (phenylephrine) given intranasally versus intranasal placebo.
Outcomes	The primary outcome of effusion or not at 4 weeks was measured.
Notes	
Allocation concealment	B – Unclear

Study	**Hughes 1984**
Methods	Quality score: 3/5 (Randomization: 1+0; Blinding: 1+1; Withdrawals: 0). Intention-to-treat analysis: no. Follow up was 88%.
Participants	42 children (no age range given) from GP practices were referred to a single ENT specialist. Diagnosis was based on clinical examination and tympanometry. Exclusion criteria: previous surgery to ears, nose or throat and abnormal palatal function.

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Characteristics of included studies (*Continued*)

Interventions	Antihistamine/decongestant combination (triprolidine/pseudoephedrine) versus placebo
Outcomes	Our primary outcome (effusion or not at 4 weeks or less) was not measured. Secondary (1-3 months) and Late (greater than 3 months) were measured as was the outcome of surgery (tympanostomy).
Notes	
Allocation concealment	B – Unclear

Study	**Khan 1981**
Methods	Quality score: 2/5 (Randomization: 1; Blinding: 1; Withdrawals: 0). Intention-to-treat analysis: unable to determine. Follow up was 97%.
Participants	58 children aged 5-14 years were recruited from an ENT clinic. Diagnosis was based on a combination of history, otoscopy and audiology. Exclusion criterion: presence of AOM.
Interventions	Antihistamine/decongestant combination (brompheniramine/phenylephrine and phenylpropanolamine) versus placebo.
Outcomes	No individual patient data are available. The outcome measured was hearing loss at 4 weeks. The authors stated that no significant difference in hearing was found between the antihistamine/decongestant combination and the placebo group. All children got tympanostomies.
Notes	
Allocation concealment	B – Unclear

Study	**Lesser 1986**
Methods	Quality score: 2/5 (Randomization: 1; Blinding: 0; Withdrawals: 1). Intention-to-treat analysis: no. Follow up 95%. Study duration from Sept. 1984 to Jan. 1985.
Participants	39 children aged 3-12 years with OME after tympanostomy and (adenoidectomy or tonsillectomy) were recruited from an ENT practice. Diagnosis was based on a thick effusion at tympanostomy at entry to the study and on, at outcome, an algorithm that included tympanometry, audiography and otoscopy. Exclusion criteria included: previous surgery for OME and use of mucolytics, antihistamines or decongestants in the preceding 72 days.
Interventions	Antihistamine/decongestant combination (brompheniramine/phenylephrine and phenylpropanolamine) versus no treatment.
Outcomes	Our primary outcome of effusion or not at 4 weeks was not measured. A secondary outcome of effusion or not at 6 weeks (by counting ears) was measured as was the side effect of nosebleed.
Notes	
Allocation concealment	B – Unclear

Study	**Mandel 1987**
Methods	
Participants	
Interventions	
Outcomes	

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Characteristics of included studies (*Continued*)

Notes	This is a report of the same study as Cantekin 1991 so the outcomes will not be reported separately.
Allocation concealment	B – Unclear

Study	**O'Shea 1980**
Methods	Quality score: 2/5 (Randomization: 0: Blinding: 1+1; Withdrawals: 0). Intention-to-treat analysis: no. Follow up was 91%. The study took place between March and December 1977.
Participants	83 children aged 3-9 years with their first episode of OME were recruited from Pediatrics and ENT practices in Rhode Island. Diagnosis was based on a combination of otoscopy, audiometry and tympanometry. Exclusion criteria included: oral temperature greater than 37.8C and ear or nose deformity.
Interventions	Antihistamine/decongestant combination (diphenhydrinate/pseudoephedrine) versus placebo.
Outcomes	Our primary outcome of effusion or not at 4 weeks was not measured. A secondary outcome was measured by patient-ear-visit at 3 months. Hearing at 3 months was measured for improvement (by at least 20 dB) or no improvement. Adverse effects of sedation, hyperactivity or any of the above were measured after 1 month.
Notes	
Allocation concealment	B – Unclear

Study	**O'Shea 1982**
Methods	This study was a report of late follow up of the previous study so the methods were the same.
Participants	Participants were the same as above.
Interventions	Interventions were the same as above.
Outcomes	A late outcome of effusion or no effusion was measured by ears at 1 year. Improvement in hearing and school performance were also measured at 1 year. The complication of recurrence of OME at 1 year was measured.
Notes	Late follow-up of O'Shea 1980.
Allocation concealment	B – Unclear

Study	**Olson 1978**
Methods	Quality score: 2/5 (Randomization: 1; Blinding: 1; Withdrawals: 0). Intention-to-treat analysis: unable to determine. Follow up was 67%.
Participants	78 children over 6 months of age were recruited from a community based paediatric practice in upstate New York after a recent diagnosis of AOM treated with antibiotics and decongestant. Diagnosis was based on tympanometry. Exclusion criterion was presence of ear grommets (ventilation tubes). A history of previous OME and of allergies was recorded and used to generate outcomes.
Interventions	Decongestant (pseudoephedrine) versus placebo.
Outcomes	No individual patient data were given for our primary outcome. The authors stated that in all comparisons measured, patients who received oral decongestant consistently did worse than those on placebo although the difference did not always reach statistical significance.
Notes	See outcomes
Allocation concealment	A – Adequate

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Study	Saunte 1978
Methods	Quality score: 3/5 (Randomization: 1; Blinding 1+1; Withdrawals: 0). Intention-to-treat analysis: no Follow up was 68%.
Participants	21 children aged 1-12 were recruited from an ENT clinic. A history of allergies was noted. Diagnosis was based on audiometry and pneumatic otoscopy. Exclusion criteria included: no AOM within 2 weeks of OME and normal hearing prior to OME.
Interventions	Antihistamine/decongestant (brompheniramine/phenylpropanolamine) versus placebo.
Outcomes	The primary outcome of effusion or not at 4 weeks was measured as was hearing. The surgical complication of tympanostomy was measured and side effects were assessed.
Notes	
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
Altman 1998	ALLOCATION: Randomized, double blind. PARTICIPANTS: Patients undergoing myringotomy - not confined to Otitis Media with Effusion (OME).
Bhambhani 1983	ALLOCATION: Randomized by AOM, not OME.
Brown 1985	ALLOCATION: Review, not a trial.
Brownoff 1998	ALLOCATION: Randomized, double blind. PARTICIPANTS: Did not have OME, this was a prevention study.
Cantekin 1980	ALLOCATION: Not randomized.
Chonmaitree 2003	ALLOCATION: Randomisation by AOM, not OME.
Collins 1983	ALLOCATION: Randomized, not blinded. PARTICIPANTS: Had OME, were awaiting adenoidectomy. INTERVENTION: Antihistamine/decongestant, sodium cromoglycate, control. OUTCOME: Mean free histamine content in middle ear fluid. Excluded because no patient oriented outcome was measured and none of our primary or secondary outcomes was measured.
Gates 1986	ALLOCATION: Treatment group only - no control.

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Grundfast 1981	ALLOCATION: Review, not a trial.
Kjellman 1978	ALLOCATION: Did not study otitis media with effusion, this was a prevention study.
Klein 1980	ALLOCATION: Randomized, double blind but randomized by AOM, not OME.
Kraemer 1984	ALLOCATION: Not a randomized controlled trial.
Lildholdt 1982	ALLOCATION: Randomized, double blind. PARTICIPANTS: Did not have OME, had only a history of treated OME.
Malm 1985	ALLOCATION: Review, not a trial.
Marshall 1984	ALLOCATION: Review, not a trial.
McCormick 2003	ALLOCATION: Randomized by AOM, not OME.
Moller 1980	ALLOCATION: No randomization. PARTICIPANTS: All children had cleft palate.
Moran 1982	ALLOCATION: Randomized and multiply blinded. PARTICIPANTS: Patients had AOM with effusion, not OME.
Ogino 1992	ALLOCATION: No mention of randomization.
Otten 1990	ALLOCATION: Randomized but not blinded. PARTICIPANTS: Children with URTI and OME. INTERVENTION: Combination treatment of antibiotic with decongestant. Excluded because we could separate out the decongestant effect.
Sorri 1982	ALLOCATION: Not randomized.
Suzuki 1999	ALLOCATION: Randomized. PARTICIPANTS: Included adults, could not separate out children.
Theoharides 1994	ALLOCATION: Randomized. PARTICIPANTS: Children with OME. INTERVENTION:

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Characteristics of excluded studies (*Continued*)

	Non-feasible intervention-direct instillation of antihistamine into the middle ear through a grommet.
van Heerbeek 2002	ALLOCATION: Randomized and double blinded. PARTICIPANTS: Children with OME. INTERVENTION: Nasal decongestant or placebo. OUTCOME: Eustachian tube function at 15 minutes after Tx. Excluded because no patient oriented outcomes were measured and none of our primary or secondary outcomes was measured.

ADDITIONAL TABLES

Table 01. Search filter

Filter

40. limit 39 to (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or meta analysis or multicenter study or randomized controlled trial)
41. clinical trial.pt.
42. exp Clinical trials/
43. ((clinical or control$ or compar$) adj (study or studies or trial$)).ti,ab,sh.
44. multicenter study.pt.
45. (multicenter$ or multicentre$ or multi-centre$ or multi-center$).ti,ab,sh.
46. random$.ti,ab,sh. or randomized controlled trial.pt.
47. (blind$ or mask$ or placebo$).ti,ab,sh.
48. (single-blind$ or double-blind$ or triple-blind$).ti,ab,sh.
49. Double-blind method/ or Meta-analysis/ or Random allocation/ or Research design/
50. 39 and (41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49)
51. meta-analy$.mp. [mp=title, abstract, registry number word, mesh subject heading]
52. metaanaly$.mp. [mp=title, abstract, registry number word, mesh subject heading]
53. meta-analysis.pt.
54. meta-analysis/
55. overview$.ti,ab.
56. (quantitativ$ adj (review or overview)).tw.
57. (systematic$ adj (review or overview)).tw.
58. (methodologic$ adj (review or overview)).tw.
59. (integrative research review or research integration).mp. [mp=title, abstract, registry number word, mesh subject heading]
60. (quantitativ$ adj synthes$).mp. [mp=title, abstract, registry number word, mesh subject heading]
61. 39 and (51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60)
62. (40 or 50 or 61) not animal.mp. [mp=title, abstract, registry number word, mesh subject heading]
63. 40 or 50 or 61
64. limit 63 to human
65. 62 or 64
66. from 65 keep 1-43

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ANALYSES

Comparison 01. Antihistamine versus control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Secondary outcome: cure or no cure at 1-3 months	2	140	Relative Risk (Fixed) 95% CI	0.94 [0.65, 1.36]
02 Complication: AOM	1	46	Relative Risk (Fixed) 95% CI	0.89 [0.46, 1.73]

Comparison 02. Decongestant versus control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Primary outcome: cure or no cure at or before 1 month	3	276	Relative Risk (Fixed) 95% CI	1.06 [0.92, 1.22]
02 Secondary outcome: cure or no cure at 1-3 months	2	216	Relative Risk (Fixed) 95% CI	1.05 [0.85, 1.30]
03 Side effect: any significant side effects at or before one month	1	172	Relative Risk (Fixed) 95% CI	11.05 [0.66, 185.38]
04 Outcome: hearing on or about 1 month	1	15	Relative Risk (Fixed) 95% CI	0.88 [0.16, 4.68]
05 Outcome: surgery (tympanostomy (myringotomy))	1	172	Relative Risk (Fixed) 95% CI	1.07 [0.71, 1.62]
06 Complication: AOM	1	44	Relative Risk (Fixed) 95% CI	0.55 [0.23, 1.31]

Comparison 03. Antihistamine/decongestant combination versus control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Primary outcome: cure or no cure at or before 1 month	4	901	Relative Risk (Fixed) 95% CI	0.97 [0.89, 1.04]
02 Secondary outcome: cure or no cure at 1-3 months	3	158	Relative Risk (Fixed) 95% CI	1.09 [0.85, 1.40]
03 Late outcome: cure or no cure after 3 months	2	119	Relative Risk (Fixed) 95% CI	1.24 [0.72, 2.13]
04 Side effect: any significant side effects at or before one month	5	972	Relative Risk (Fixed) 95% CI	2.54 [1.76, 3.67]
05 Outcome: hearing at or less than 3 months	3	343	Relative Risk (Fixed) 95% CI	1.09 [0.93, 1.27]
06 Late outcome: hearing at 1 year	1	48	Relative Risk (Fixed) 95% CI	1.50 [0.63, 3.56]
07 Late outcome: school performance at 1 year	1	42	Relative Risk (Fixed) 95% CI	0.81 [0.35, 1.86]
08 Outcome: surgery (tympanostomy (myringotomy))	2	57	Relative Risk (Random) 95% CI	0.54 [0.09, 3.41]
09 Complication: recurrent OME	4	284	Relative Risk (Fixed) 95% CI	1.30 [0.92, 1.83]
10 Complication: AOM	2	636	Relative Risk (Fixed) 95% CI	0.76 [0.46, 1.26]

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Comparison 04. Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Primary outcome: cure or no cure at or before 1 month	7	1177	Relative Risk (Fixed) 95% CI	0.99 [0.92, 1.05]
02 Secondary outcome: cure or no cure at 1-3 months	7	514	Relative Risk (Fixed) 95% CI	1.04 [0.89, 1.21]
03 Late outcome: cure or no cure after 3 months	2	119	Relative Risk (Fixed) 95% CI	1.24 [0.72, 2.13]
04 Side effect: any significant side effects at or before 1 month	6	1144	Relative Risk (Fixed) 95% CI	2.70 [1.87, 3.88]
05 Outcome: hearing on or about 1 month	4	358	Relative Risk (Fixed) 95% CI	1.08 [0.93, 1.27]
06 Late outcome: hearing at 1 year	1	48	Relative Risk (Fixed) 95% CI	1.50 [0.63, 3.56]
07 Late outcome: school performance at 1 year	1	42	Relative Risk (Fixed) 95% CI	0.81 [0.35, 1.86]
08 Outcome: surgery (tympanostomy (myringotomy))	3	229	Relative Risk (Fixed) 95% CI	0.96 [0.69, 1.32]
09 Complication: recurrent OME	2	142	Relative Risk (Fixed) 95% CI	1.30 [0.80, 2.11]
10 Complication: AOM	3	408	Relative Risk (Fixed) 95% CI	0.74 [0.48, 1.14]

INDEX TERMS

Medical Subject Headings (MeSH)

Drug Therapy, Combination; Histamine H1 Antagonists [adverse effects; *therapeutic use]; Nasal Decongestants [adverse effects; *therapeutic use]; Otitis Media with Effusion [*drug therapy]; Randomized Controlled Trials

MeSH check words

Child; Humans

COVER SHEET

Title	Antihistamines and/or decongestants for otitis media with effusion (OME) in children
Authors	Griffin GH, Flynn C, Bailey RE, Schultz JK
Contribution of author(s)	GH Griffin: Primary review manager and author. CA Flynn: Consultant, editor and co-author. RE Bailey: Co-author. JK Schultz: Co-author.
Issue protocol first published	2002/1
Review first published	2006/4
Date of most recent amendment	22 August 2006
Date of most recent SUBSTANTIVE amendment	22 August 2006
What's New	Information not supplied by author

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Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Glenn Griffin Quinte West Medical Centre 80 Catherine Street Trenton Ontario ON K8V 6N8 CANADA E-mail: ghgriffin@hotmail.com Tel: +1 613 394 4620 Fax: +1 613 394 7079
DOI	10.1002/14651858.CD003423.pub2
Cochrane Library number	CD003423
Editorial group	Cochrane Ear, Nose and Throat Disorders Group
Editorial group code	HM-ENT

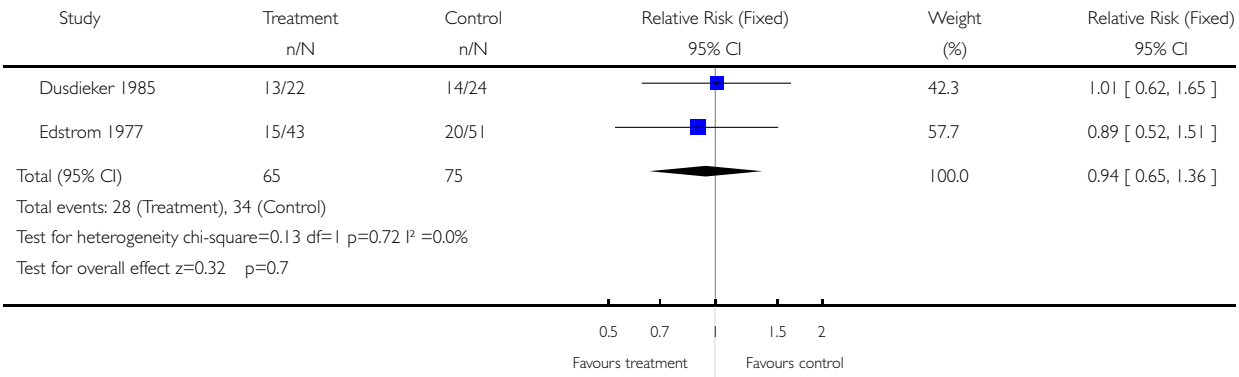
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Antihistamine versus control, Outcome 01 Secondary outcome: cure or no cure at 1-3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 01 Antihistamine versus control

Outcome: 01 Secondary outcome: cure or no cure at 1-3 months



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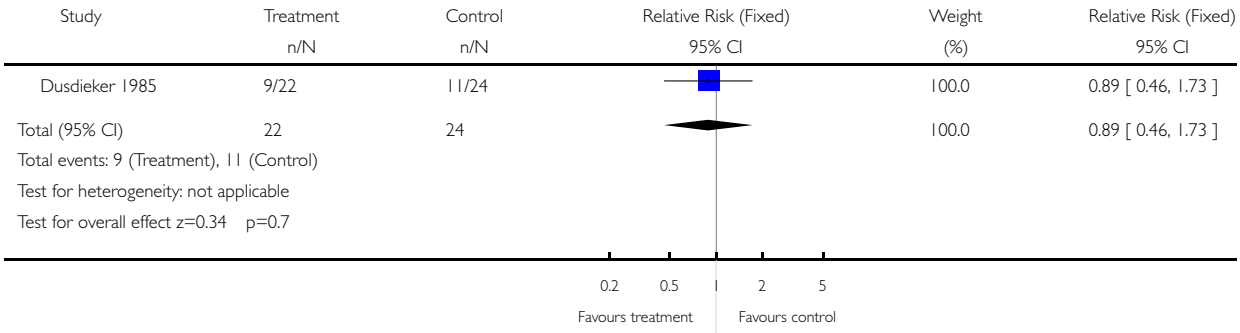
Analysis 01.02. Comparison 01 Antihistamine versus control, Outcome 02 Complication: AOM

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 01 Antihistamine versus control

Outcome: 02 Complication: AOM

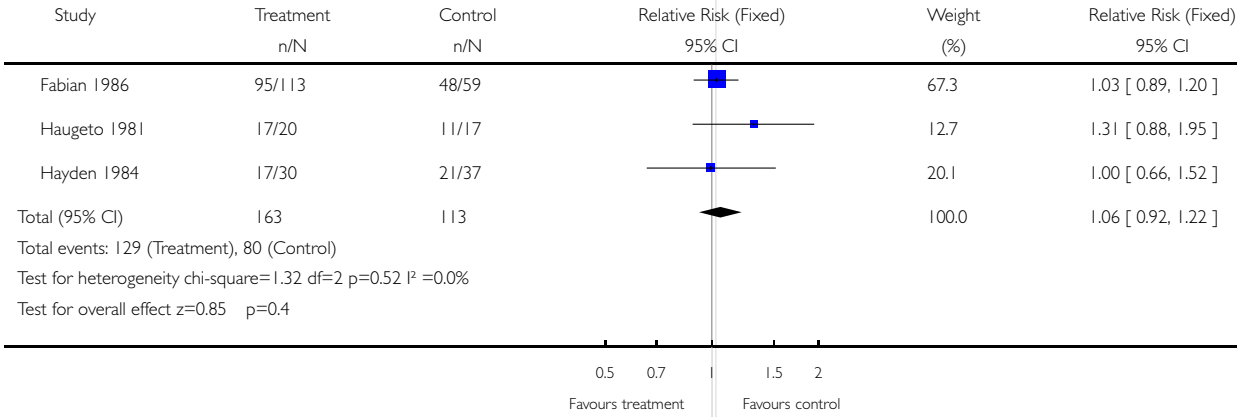


Analysis 02.01. Comparison 02 Decongestant versus control, Outcome 01 Primary outcome: cure or no cure at or before 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 01 Primary outcome: cure or no cure at or before 1 month



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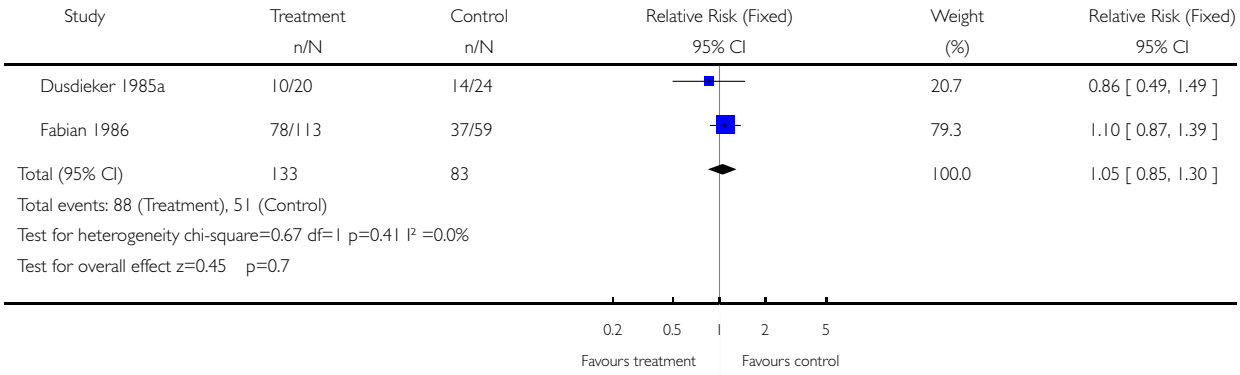
Analysis 02.02. Comparison 02 Decongestant versus control, Outcome 02 Secondary outcome: cure or no cure at 1-3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 02 Secondary outcome: cure or no cure at 1-3 months

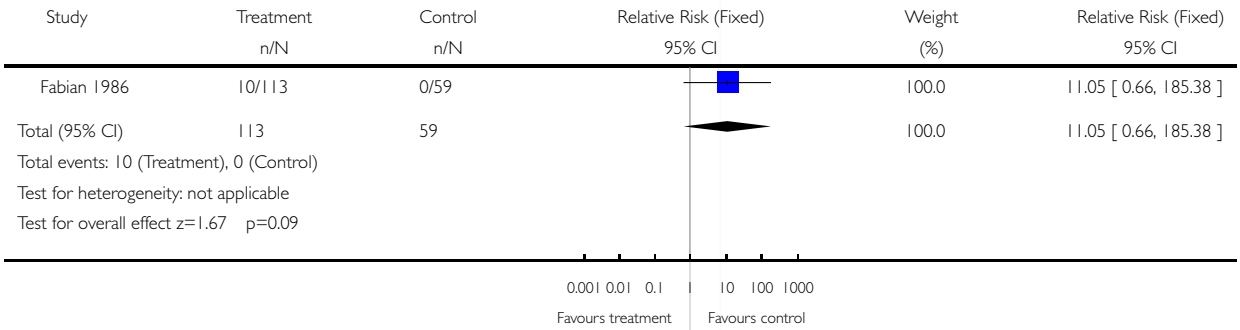


Analysis 02.03. Comparison 02 Decongestant versus control, Outcome 03 Side effect: any significant side effects at or before one month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 03 Side effect: any significant side effects at or before one month



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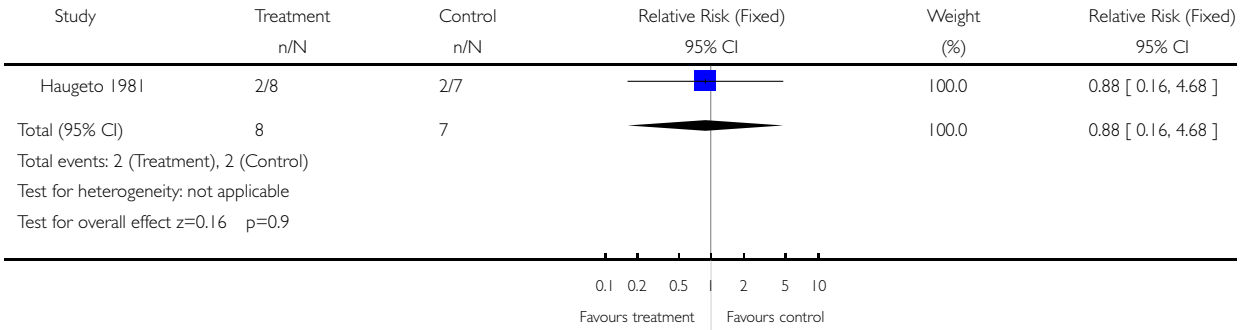
Analysis 02.04. Comparison 02 Decongestant versus control, Outcome 04 Outcome: hearing on or about 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 04 Outcome: hearing on or about 1 month

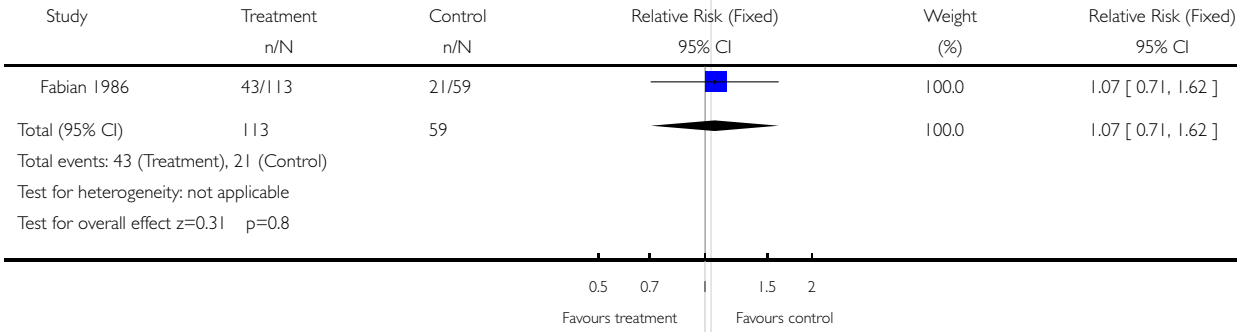


Analysis 02.05. Comparison 02 Decongestant versus control, Outcome 05 Outcome: surgery (tympanostomy (myringotomy))

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 05 Outcome: surgery (tympanostomy (myringotomy))



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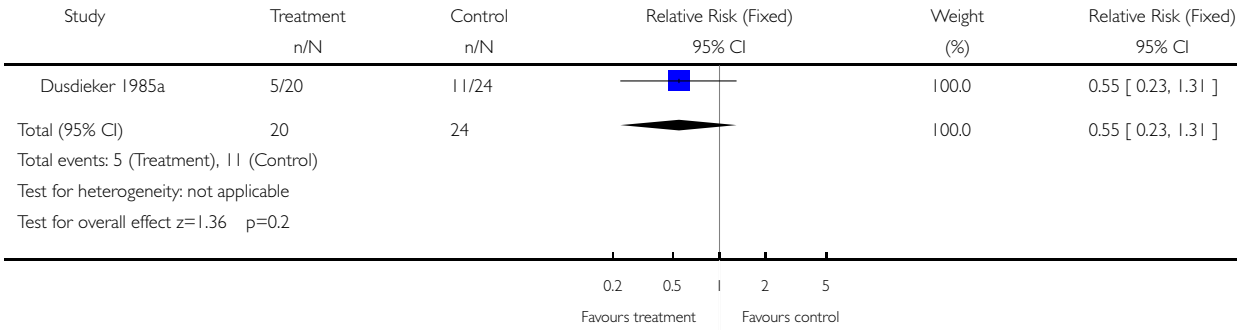
Analysis 02.06. Comparison 02 Decongestant versus control, Outcome 06 Complication: AOM

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 02 Decongestant versus control

Outcome: 06 Complication: AOM

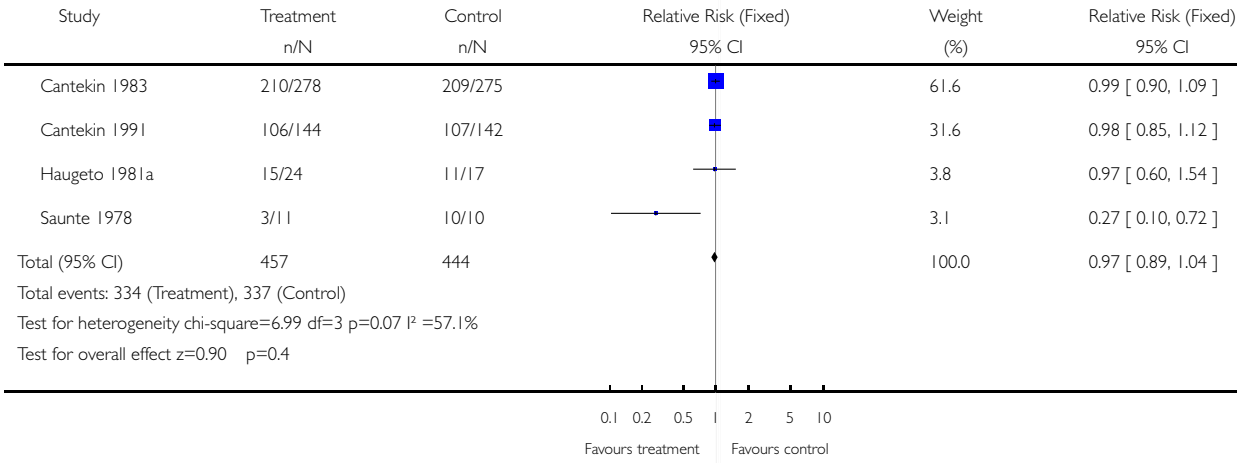


Analysis 03.01. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 01 Primary outcome: cure or no cure at or before 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 01 Primary outcome: cure or no cure at or before 1 month



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Analysis 03.02. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 02 Secondary outcome: cure or no cure at 1-3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 02 Secondary outcome: cure or no cure at 1-3 months

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Hughes 1984	13/20	10/16		24.3	1.04 [0.63, 1.71]
Lesser 1986	9/21	8/18		18.8	0.96 [0.47, 1.97]
O'Shea 1980	29/40	27/43		56.9	1.15 [0.86, 1.56]
Total (95% CI)	81	77		100.0	1.09 [0.85, 1.40]

Total events: 51 (Treatment), 45 (Control)

Test for heterogeneity chi-square=0.29 df=2 p=0.87 I^2 =0.0%

Test for overall effect z=0.69 p=0.5

Analysis 03.03. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 03 Late outcome: cure or no cure after 3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 03 Late outcome: cure or no cure after 3 months

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Hughes 1984	8/26	6/16		45.5	0.82 [0.35, 1.93]
O'Shea 1980	14/38	9/39		54.5	1.60 [0.79, 3.24]
Total (95% CI)	64	55		100.0	1.24 [0.72, 2.13]

Total events: 22 (Treatment), 15 (Control)

Test for heterogeneity chi-square=1.38 df=1 p=0.24 I^2 =27.8%

Test for overall effect z=0.79 p=0.4

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Analysis 03.04. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 04 Side effect: any significant side effects at or before one month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 04 Side effect: any significant side effects at or before one month

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1983	51/278	20/275		56.6	2.52 [1.55, 4.12]
Cantekin 1991	23/158	11/160		30.7	2.12 [1.07, 4.20]
Lesser 1986	1/13	0/12		1.5	2.79 [0.12, 62.48]
O'Shea 1980	12/27	3/28		8.3	4.15 [1.31, 13.09]
Saunte 1978	3/11	1/10		2.9	2.73 [0.34, 22.16]
Total (95% CI)	487	485		100.0	2.54 [1.76, 3.67]
Total events: 90 (Treatment), 35 (Control)					
Test for heterogeneity chi-square=0.98 df=4 p=0.91 I^2 =0.0%					
Test for overall effect z=5.00 p<0.00001					

Analysis 03.05. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 05 Outcome: hearing at or less than 3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 05 Outcome: hearing at or less than 3 months

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1991	102/140	88/134		85.1	1.11 [0.95, 1.30]
Haugeto 1981a	2/7	2/7		1.9	1.00 [0.19, 5.24]
O'Shea 1980	13/27	14/28		13.0	0.96 [0.56, 1.65]
Total (95% CI)	174	169		100.0	1.09 [0.93, 1.27]
Total events: 117 (Treatment), 104 (Control)					
Test for heterogeneity chi-square=0.26 df=2 p=0.88 I^2 =0.0%					
Test for overall effect z=1.07 p=0.3					

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Analysis 03.06. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 06 Late outcome: hearing at 1 year

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 06 Late outcome: hearing at 1 year

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
O'Shea 1982	9/24	6/24		100.0	1.50 [0.63, 3.56]
Total (95% CI)	24	24		100.0	1.50 [0.63, 3.56]
Total events: 9 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.92 p=0.4					

Analysis 03.07. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 07 Late outcome: school performance at 1 year

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 07 Late outcome: school performance at 1 year

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
O'Shea 1982	6/19	9/23		100.0	0.81 [0.35, 1.86]
Total (95% CI)	19	23		100.0	0.81 [0.35, 1.86]
Total events: 6 (Treatment), 9 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.50 p=0.6					

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Analysis 03.08. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 08 Outcome: surgery (tympanostomy (myringotomy))

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 08 Outcome: surgery (tympanostomy (myringotomy))

Study	Treatment n/N	Control n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
Hughes 1984	13/20	10/16		62.5	1.04 [0.63, 1.71]
Saunte 1978	1/11	5/10		37.5	0.18 [0.03, 1.30]
Total (95% CI)	31	26		100.0	0.54 [0.09, 3.41]
Total events: 14 (Treatment), 15 (Control)					
Test for heterogeneity chi-square=3.51 df=1 p=0.06 I^2 =71.5%					
Test for overall effect z=0.65 p=0.5					

Analysis 03.09. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 09 Complication: recurrent OME

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 09 Complication: recurrent OME

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Quality score 3 or greater					
Cantekin 1983	20/47	12/47		30.0	1.67 [0.92, 3.01]
Subtotal (95% CI)	47	47		30.0	1.67 [0.92, 3.01]
Total events: 20 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.70 p=0.09					
02 Quality score less than 3					
O'Shea 1982	6/24	8/24		20.0	0.75 [0.31, 1.83]
Subtotal (95% CI)	24	24		20.0	0.75 [0.31, 1.83]
Total events: 6 (Treatment), 8 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					
03 Allocation concealment adequate					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					

(*Continued . . .*)

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(. . . *Continued*)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for overall effect: not applicable					
04 Allocation concealment not adequate					
Cantekin 1983	20/47	12/47		30.0	1.67 [0.92, 3.01]
O'Shea 1982	6/24	8/24		20.0	0.75 [0.31, 1.83]
Subtotal (95% CI)	71	71		50.0	1.30 [0.80, 2.11]
Total events: 26 (Treatment), 20 (Control)					
Test for heterogeneity chi-square=2.13 df=1 p=0.14 I^2 =53.1%					
Test for overall effect z=1.06 p=0.3					
Total (95% CI)	142	142		100.0	1.30 [0.92, 1.83]
Total events: 52 (Treatment), 40 (Control)					
Test for heterogeneity chi-square=4.26 df=3 p=0.23 I^2 =29.7%					
Test for overall effect z=1.50 p=0.1					

Analysis 03.10. Comparison 03 Antihistamine/decongestant combination versus control, Outcome 10 Complication: AOM

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 03 Antihistamine/decongestant combination versus control

Outcome: 10 Complication: AOM

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Quality score 3 or greater					
Cantekin 1991	12/158	16/160		50.0	0.76 [0.37, 1.55]
Subtotal (95% CI)	158	160		50.0	0.76 [0.37, 1.55]
Total events: 12 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.75 p=0.5					
02 Quality score less than 3					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 Allocation concealment adequate					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					

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Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
04 Allocation concealment not adequate					
Cantekin 1991	12/158	16/160		50.0	0.76 [0.37, 1.55]
Subtotal (95% CI)	158	160		50.0	0.76 [0.37, 1.55]
Total events: 12 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.75 p=0.5					
Total (95% CI)	316	320		100.0	0.76 [0.46, 1.26]
Total events: 24 (Treatment), 32 (Control)					
Test for heterogeneity chi-square=0.00 df=1 p=1.00 I^2 =0.0%					
Test for overall effect z=1.07 p=0.3					

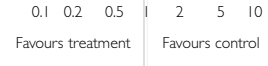
Analysis 04.01. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 01 Primary outcome: cure or no cure at or before 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 01 Primary outcome: cure or no cure at or before 1 month

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1983	210/278	209/275		48.3	0.99 [0.90, 1.09]
Cantekin 1991	106/144	107/142		24.8	0.98 [0.85, 1.12]
Fabian 1986	95/113	48/59		14.5	1.03 [0.89, 1.20]
Haugeto 1981	17/20	11/17		2.7	1.31 [0.88, 1.95]
Haugeto 1981a	15/24	11/17		3.0	0.97 [0.60, 1.54]
Hayden 1984	17/30	21/37		4.3	1.00 [0.66, 1.52]
Saunte 1978	3/11	10/10		2.4	0.27 [0.10, 0.72]
Total (95% CI)	620	557		100.0	0.99 [0.92, 1.05]
Total events: 463 (Treatment), 417 (Control)					
Test for heterogeneity chi-square=9.27 df=6 p=0.16 I^2 =35.3%					
Test for overall effect z=0.41 p=0.7					



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Analysis 04.02. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 02 Secondary outcome: cure or no cure at 1-3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 02 Secondary outcome: cure or no cure at 1-3 months

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dusdieker 1985	13/22	14/24		9.6	1.01 [0.62, 1.65]
Dusdieker 1985a	10/20	14/24		9.2	0.86 [0.49, 1.49]
Edstrom 1977	15/43	20/51		13.2	0.89 [0.52, 1.51]
Fabian 1986	78/113	37/59		35.0	1.10 [0.87, 1.39]
Hughes 1984	13/20	10/16		8.0	1.04 [0.63, 1.71]
Lesser 1986	9/21	8/18		6.2	0.96 [0.47, 1.97]
O'Shea 1980	29/40	27/43		18.8	1.15 [0.86, 1.56]
Total (95% CI)	279	235		100.0	1.04 [0.89, 1.21]
Total events: 167 (Treatment), 130 (Control)					
Test for heterogeneity chi-square=1.56 df=6 p=0.96 I^2 =0.0%					
Test for overall effect z=0.50 p=0.6					

Analysis 04.03. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 03 Late outcome: cure or no cure after 3 months

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 03 Late outcome: cure or no cure after 3 months

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Hughes 1984	8/26	6/16		45.5	0.82 [0.35, 1.93]
O'Shea 1982	14/38	9/39		54.5	1.60 [0.79, 3.24]
Total (95% CI)	64	55		100.0	1.24 [0.72, 2.13]
Total events: 22 (Treatment), 15 (Control)					
Test for heterogeneity chi-square=1.38 df=1 p=0.24 I^2 =27.8%					
Test for overall effect z=0.79 p=0.4					

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Analysis 04.04. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 04 Side effect: any significant side effects at or before 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 04 Side effect: any significant side effects at or before 1 month

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1983	51/278	20/275		55.5	2.52 [1.55, 4.12]
Cantekin 1991	23/158	11/160		30.2	2.12 [1.07, 4.20]
Fabian 1986	10/113	0/59		1.8	11.05 [0.66, 185.38]
Lesser 1986	1/13	0/12		1.4	2.79 [0.12, 62.48]
O'Shea 1980	12/27	3/28		8.1	4.15 [1.31, 13.09]
Saunte 1978	3/11	1/10		2.9	2.73 [0.34, 22.16]
Total (95% CI)	600	544		100.0	2.70 [1.87, 3.88]
Total events: 100 (Treatment), 35 (Control)					
Test for heterogeneity chi-square=2.05 df=5 p=0.84 I^2 =0.0%					
Test for overall effect z=5.34 p<0.00001					

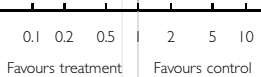
Analysis 04.05. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 05 Outcome: hearing on or about 1 month

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 05 Outcome: hearing on or about 1 month

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1991	102/140	88/134		83.4	1.11 [0.95, 1.30]
Haugeto 1981	2/7	2/7		1.9	1.00 [0.19, 5.24]
Haugeto 1981a	2/8	2/7		2.0	0.88 [0.16, 4.68]
O'Shea 1980	13/27	14/28		12.8	0.96 [0.56, 1.65]
Total (95% CI)	182	176		100.0	1.08 [0.93, 1.27]
Total events: 119 (Treatment), 106 (Control)					
Test for heterogeneity chi-square=0.34 df=3 p=0.95 I^2 =0.0%					
Test for overall effect z=1.02 p=0.3					



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Analysis 04.06. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 06 Late outcome: hearing at 1 year

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 06 Late outcome: hearing at 1 year

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
O'Shea 1982	9/24	6/24		100.0	1.50 [0.63, 3.56]
Total (95% CI)	24	24		100.0	1.50 [0.63, 3.56]
Total events: 9 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.92 p=0.4					

Analysis 04.07. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 07 Late outcome: school performance at 1 year

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 07 Late outcome: school performance at 1 year

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
O'Shea 1982	6/19	9/23		100.0	0.81 [0.35, 1.86]
Total (95% CI)	19	23		100.0	0.81 [0.35, 1.86]
Total events: 6 (Treatment), 9 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.50 p=0.6					

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Analysis 04.08. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 08 Outcome: surgery (tympanostomy (myringotomy))

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 08 Outcome: surgery (tympanostomy (myringotomy))

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Fabian 1986	43/113	21/59		62.8	1.07 [0.71, 1.62]
Hughes 1984	13/20	10/16		25.3	1.04 [0.63, 1.71]
Saunte 1978	1/11	5/10		11.9	0.18 [0.03, 1.30]
Total (95% CI)	144	85		100.0	0.96 [0.69, 1.32]
Total events: 57 (Treatment), 36 (Control)					
Test for heterogeneity chi-square=3.12 df=2 p=0.21 I^2 =35.8%					
Test for overall effect z=0.27 p=0.8					

Analysis 04.09. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 09 Complication: recurrent OME

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 09 Complication: recurrent OME

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cantekin 1983	20/47	12/47		60.0	1.67 [0.92, 3.01]
O'Shea 1982	6/24	8/24		40.0	0.75 [0.31, 1.83]
Total (95% CI)	71	71		100.0	1.30 [0.80, 2.11]
Total events: 26 (Treatment), 20 (Control)					
Test for heterogeneity chi-square=2.13 df=1 p=0.14 I^2 =53.1%					
Test for overall effect z=1.06 p=0.3					

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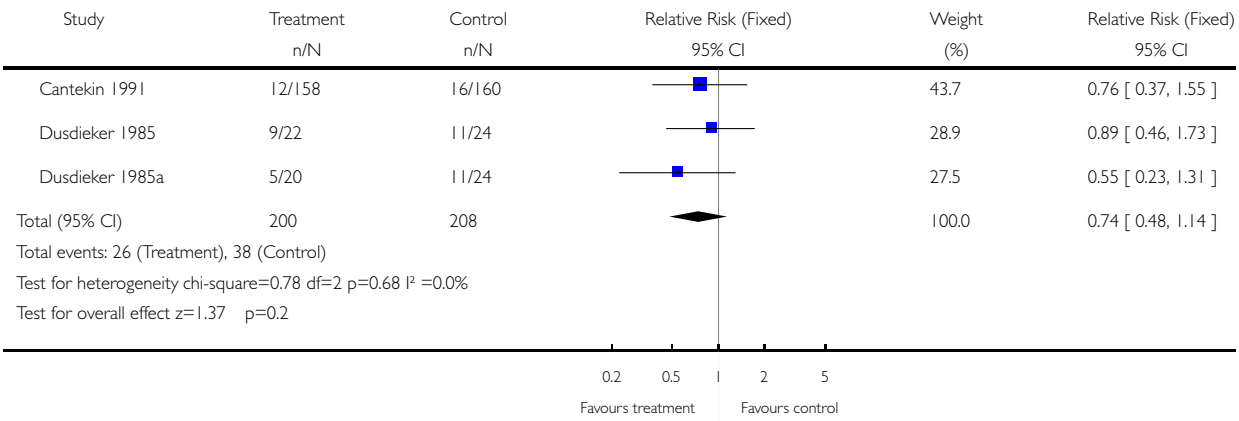
Analysis 04.10. Comparison 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control, Outcome 10 Complication: AOM

Review: Antihistamines and/or decongestants for otitis media with effusion (OME) in children

Comparison: 04 Any medication: antihistamine, decongestant or antihistamine/decongestant combination versus control

Outcome: 10 Complication: AOM



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