SINUS X ANTIBIOTICS = ESTRATÉGIA DE BUSCA

PUBMED – 24/10/2008.

DOENÇA	**TOTAL DE ESTUDOS**
("Sinusitis"[Mesh]) OR (Sinusitis)OR (Sinusitides) OR ("Rhinitis"[Mesh]) OR (Rhinitis) OR (Rhinitides) OR ("Paranasal Sinus Diseases"[Mesh]) OR (Paranasal Sinus Diseases) OR (Disease, Paranasal Sinus) OR (Diseases, Paranasal Sinus) OR (Paranasal Sinus Disease) OR (Sinus Disease, Paranasal) OR (Sinus Diseases, Paranasal) OR ("Nasopharyngitis"[Mesh]) OR (Nasopharyngitis) OR (Nasopharyngitides) OR ("Common Cold"[Mesh]) OR (Common Cold) OR (Cold, Common) OR (Colds, Common) OR (Common Colds) OR (Coryza, Acute) OR (Acute Coryza) OR (rhinorrhoea OR rhinorrhea) OR (Rhinosinusitis) OR (Persistent Nasal Discharge) OR (Nasal Discharge)	**57696**
INTERVENÇÃO • ("Anti-Bacterial Agents"[Mesh])OR (Anti-Bacterial Agents**)** OR (Agents, Anti-Bacterial) OR (Anti Bacterial Agents) OR (Antibacterial Agents) OR (Agents, Antibacterial) OR (Antibiotics) OR (Bacteriocidal Agents) OR (Agents, Bacteriocidal) OR (Bacteriocides) OR (Anti-Mycobacterial Agents) OR (Agents, Anti-Mycobacterial) OR (Anti Mycobacterial Agents) OR (Antimycobacterial Agents) OR (Agents, Antimycobacterial) OR (Antibiotics or antibiotic) OR ("Anti-Infective Agents"[Mesh]) OR(Anti-Infective Agents) OR (Agents, Anti-Infective) OR (Anti Infective Agents) OR (Antiinfective Agents) OR (Agents, Antiinfective) OR (Microbicides) OR (Antimicrobial Agents) OR (Agents, Antimicrobial) OR (Anti-Microbial Agents) OR (Agents, Anti-Microbial) OR (Anti Microbial Agents) OR • ("Amoxicillin"[Mesh]) OR (Amoxycillin) OR (Amoxicilline) OR (Hydroxyampicillin) OR (Amoxicillin, (R*)-isomer) OR (Amoxil) OR (BRL-2333) OR (BRL 2333) OR (BRL2333) OR (Clamoxyl) OR (Penamox) OR (Clamoxyl G.A.) OR (G.A., Clamoxyl) OR (Pfizer Brand of Amoxicillin Sodium Salt) OR (SmithKline Beecham Brand of Amoxicillin Sodium Salt) OR (Clamoxyl parenteral) OR (parenteral, Clamoxyl) OR (Amoxicillin monosodium salt) OR (Trimox) OR (Wymox) OR (Actimoxi) OR (Clariana Brand of Amoxicillin) OR (Amoxicillin Clariana Brand) OR (Amoxicillin monopotassium salt) OR (Amoxicillin trihydrate) OR (trihydrate, Amoxicillin) OR (Polymox)	

- ("Ampicillin"[Mesh]) OR (Ampicillin) OR(Aminobenzylpenicillin) OR (Penicillin, Aminobenzyl) OR (Aminobenzyl Penicillin) OR (Ampicillin Sodium) OR (Sodium, Ampicillin) OR (Ampicillin Trihydrate) OR (Trihydrate, Ampicillin) OR (Ukapen) OR (Omnipen) OR (Pentrexyl) OR (Polycillin) OR (Amcill) OR (KS-R1) OR (KS R1) OR (KSR1)

- ("Azithromycin"[Mesh])OR (**Azithromycin)OR** (Azythromycin) OR (Azithromycin Monohydrate) OR (Monohydrate, Azithromycin) OR (CP-62993) OR (CP 62993) OR (CP62993) OR (Zithromax) OR (Azitrocin) OR (Bayer Brand of Azithromycin Dihydrate) OR (Pfizer Brand of Azithromycin) OR (Azithromycin Pfizer Brand) OR (Pfizer Brand of Azithromycin Dihydrate) OR (Ultreon) OR (Zitromax) OR (Azadose) OR (Mack Brand of Azithromycin Dihydrate) OR (Sumamed) OR (Toraseptol) OR (Lesvi Brand of Azithromycin Dihydrate) OR (Vinzam) OR (Funk Brand of Azithromycin Dihydrate) OR (Zentavion) OR (Vita Brand of Azithromycin Dihydrate) OR (Azithromycin Dihydrate) OR (Dihydrate, Azithromycin) OR (Goxal) OR (Pharmacia Brand of Azithromycin Dihydrate)

- ("Cefaclor"[Mesh]) OR (Ceflacor) OR (S-6472) OR (S 6472) OR (S6472) OR (Lilly 99638) OR (Ceclor) OR (Keclor)

- ("Penicillins"[Mesh]) OR (Penicillins) OR (Antibiotics, Penicillin) OR (Penicillin Antibiotics) OR (Penicillin)

- ("Sulfamethoxazole"[Mesh])OR (**Sulfamethoxazole) OR** (Sulfisomezole) OR (Sulphamethoxazole) OR (Sulfamethylisoxazole) OR (Gantanol)

- ("Sulfisoxazole"[Mesh]) OR (Sulfisoxazole) OR (Sulfasoxizole) OR (Sulfadimethyloxazole) OR (Sulfafurazole) OR (Neoxazoi) OR (Sulfafurazol FNA) OR (FNA Brand of Sulfisoxazole) OR (Sulfisoxazole Diolamine) OR (Diolamine, Sulfisoxazole) OR (V-Sul) OR (V Sul) OR (Vangard Brand of Sulfisoxazole) OR (Sulfisoxazole, Monolithium Salt) OR (Monolithium Salt Sulfisoxazole) OR (Sulfisoxazole, Monosodium Salt) OR (Monosodium Salt Sulfisoxazole) OR (Sulfisoxazole, Monosodium, Monomesylate Salt) OR (Sulfisoxazole, Triammonium Salt) OR (Triammonium Salt Sulfisoxazole) OR (TL-azole) OR (TL azole) OR (Zenith Brand of Sulfisoxazole) OR (Gantrisin) OR (Gantrisin Pediatric) OR (Pediatric, Gantrisin) OR (Roche Brand of Sulfisoxazole Diolamine) OR (Roche Brand of Sulfisoxazole) OR (Sulfisoxazole Roche Brand) OR (Roche Brand of Sulfisoxazole Acetate) OR (Sulfisoxazole, Ammonium Salt) OR (Ammonium

Salt Sulfisoxazole)	
TIPO DE ESTUDO - RCT ((randomized controlled trial [pt]) OR (controlled clinical trial [pt]) OR (randomized [tiab]) OR (placebo [tiab]) OR (drug therapy [sh]) OR (randomly [tiab]) OR (trial [tiab]) OR (groups [tiab])) AND (humans [mh])	
LIMITE CRIANÇA	
PERÍODO 2002 A 2008 25/10/2008	

All MeSH Categories
Diseases Category
Respiratory Tract Diseases
Nose Diseases
Paranasal Sinus Diseases
Sinusitis
Ethmoid Sinusitis
Frontal Sinusitis
Maxillary Sinusitis
Sphenoid Sinusitis

All MeSH Categories
Diseases Category
Respiratory Tract Diseases
Nose Diseases
Rhinitis
Rhinitis, Allergic, Perennial
Rhinitis, Allergic, Seasonal
Rhinitis, Atrophic
Rhinitis, Vasomotor

All MeSH Categories
Diseases Category
Respiratory Tract Diseases
Nose Diseases
Paranasal Sinus Diseases
Paranasal Sinus Neoplasms
Maxillary Sinus Neoplasms
Sinusitis
Ethmoid Sinusitis
Frontal Sinusitis
Maxillary Sinusitis
Sphenoid Sinusitis

All MeSH Categories
Diseases Category
Stomatognathic Diseases
Pharyngeal Diseases
Nasopharyngeal Diseases
Nasopharyngitis

All MeSH Categories
Diseases Category
Otorhinolaryngologic Diseases
Pharyngeal Diseases
Nasopharyngeal Diseases
Nasopharyngitis

LILACS

DOENÇA	**TOTAL DE ESTUDOS**
(Sinusite) OR (Ex C08.460.692.752) OR (Ex C08.730.749) OR (Ex C09.603.692.752) OR (Rinite) OR (Ex C08.460.799) OR (Ex C08.730.674) OR (Ex C09.603.799) OR (Doenças dos Seios Paranasais) OR (Ex C08.460.692) OR (Ex C09.603.692) OR (Nasofaringite) OR (Ex C07.550.350.700) OR (Ex C09.775.350.700) OR (Resfriado Comum) OR (Resfriado (Constipação)) OR (Coriza Aguda) OR (Ex C02.782.687.207) OR (Ex C08.730.162) OR (("Sinusitis"[Mesh]) OR (Sinusitis)OR (Sinusitides) OR ("Rhinitis"[Mesh]) OR (Rhinitis) OR (Rhinitides) OR ("Paranasal Sinus Diseases"[Mesh]) OR (Paranasal Sinus Diseases) OR (Disease, Paranasal Sinus) OR (Diseases, Paranasal Sinus) OR (Paranasal Sinus Disease) OR (Sinus Disease, Paranasal) OR (Sinus Diseases, Paranasal) OR ("Nasopharyngitis"[Mesh]) OR (Nasopharyngitis) OR (Nasopharyngitides) OR ("Common Cold"[Mesh]) OR (Common Cold) OR (Cold, Common) OR (Colds, Common) OR (Common Colds) OR (Coryza, Acute) OR (Acute Coryza) OR (rhinorrhoea OR rhinorrhea) OR (Rhinosinusitis) OR (Persistent Nasal Discharge) OR (Nasal Discharge)	**57696**
INTERVENÇÃO • ("Anti-Bacterial Agents"[Mesh])OR (Anti-Bacterial Agents**)** OR (Agents, Anti-Bacterial) OR (Anti Bacterial Agents) OR (Antibacterial Agents) OR (Agents, Antibacterial) OR (Antibiotics) OR (Bacteriocidal Agents) OR (Agents, Bacteriocidal) OR (Bacteriocides) OR (Anti-Mycobacterial Agents) OR (Agents, Anti-Mycobacterial) OR (Anti Mycobacterial Agents) OR	

(Antimycobacterial Agents) OR (Agents, Antimycobacterial) OR (Antibiotics or antibiotic) OR ("Anti-Infective Agents"[Mesh]) OR(Anti-Infective Agents) OR (Agents, Anti-Infective) OR (Anti Infective Agents) OR (Antiinfective Agents) OR (Agents, Antiinfective) OR (Microbicides) OR (Antimicrobial Agents) OR (Agents, Antimicrobial) OR (Anti-Microbial Agents) OR (Agents, Anti-Microbial) OR (Anti Microbial Agents) OR

- ("Amoxicillin"[Mesh]) OR (Amoxycillin) OR (Amoxicilline) OR (Hydroxyampicillin) OR (Amoxicillin, (R*)-isomer) OR (Amoxil) OR (BRL-2333) OR (BRL 2333) OR (BRL2333) OR (Clamoxyl) OR (Penamox) OR (Clamoxyl G.A.) OR (G.A., Clamoxyl) OR (Pfizer Brand of Amoxicillin Sodium Salt) OR (SmithKline Beecham Brand of Amoxicillin Sodium Salt) OR (Clamoxyl parenteral) OR (parenteral, Clamoxyl) OR (Amoxicillin monosodium salt) OR (Trimox) OR (Wymox) OR (Actimoxi) OR (Clariana Brand of Amoxicillin) OR (Amoxicillin Clariana Brand) OR (Amoxicillin monopotassium salt) OR (Amoxicillin trihydrate) OR (trihydrate, Amoxicillin) OR (Polymox)

- ("Ampicillin"[Mesh]) OR (Ampicillin) OR(Aminobenzylpenicillin) OR (Penicillin, Aminobenzyl) OR (Aminobenzyl Penicillin) OR (Ampicillin Sodium) OR (Sodium, Ampicillin) OR (Ampicillin Trihydrate) OR (Trihydrate, Ampicillin) OR (Ukapen) OR (Omnipen) OR (Pentrexyl) OR (Polycillin) OR (Amcill) OR (KS-R1) OR (KS R1) OR (KSR1)

- ("Azithromycin"[Mesh])OR (**Azithromycin)OR** (Azythromycin) OR (Azithromycin Monohydrate) OR (Monohydrate, Azithromycin) OR (CP-62993) OR (CP 62993) OR (CP62993) OR (Zithromax) OR (Azitrocin) OR (Bayer Brand of Azithromycin Dihydrate) OR (Pfizer Brand of Azithromycin) OR (Azithromycin Pfizer Brand) OR (Pfizer Brand of Azithromycin Dihydrate) OR (Ultreon) OR (Zitromax) OR (Azadose) OR (Mack Brand of Azithromycin Dihydrate) OR (Sumamed) OR (Toraseptol) OR (Lesvi Brand of Azithromycin Dihydrate) OR (Vinzam) OR (Funk Brand of Azithromycin Dihydrate) OR (Zentavion) OR (Vita Brand of Azithromycin Dihydrate) OR (Azithromycin Dihydrate) OR (Dihydrate, Azithromycin) OR (Goxal) OR (Pharmacia Brand of Azithromycin Dihydrate)

- ("Cefaclor"[Mesh]) OR (Ceflacor) OR (S-6472) OR (S 6472) OR (S6472) OR (Lilly 99638) OR (Ceclor) OR (Keclor)

• ("Penicillins"[Mesh]) OR (Penicillins) OR (Antibiotics, Penicillin) OR (Penicillin Antibiotics) OR (Penicillin) • ("Sulfamethoxazole"[Mesh])OR (**Sulfamethoxazole) OR** (Sulfisomezole) OR (Sulphamethoxazole) OR (Sulfamethylisoxazole) OR (Gantanol) • ("Sulfisoxazole"[Mesh]) OR (Sulfisoxazole) OR (Sulfasoxizole) OR (Sulfadimethyloxazole) OR (Sulfafurazole) OR (Neoxazoi) OR (Sulfafurazol FNA) OR (FNA Brand of Sulfisoxazole) OR (Sulfisoxazole Diolamine) OR (Diolamine, Sulfisoxazole) OR (V-Sul) OR (V Sul) OR (Vangard Brand of Sulfisoxazole) OR (Sulfisoxazole, Monolithium Salt) OR (Monolithium Salt Sulfisoxazole) OR (Sulfisoxazole, Monosodium Salt) OR (Monosodium Salt Sulfisoxazole) OR (Sulfisoxazole, Monosodium, Monomesylate Salt) OR (Sulfisoxazole, Triammonium Salt) OR (Triammonium Salt Sulfisoxazole) OR (TL-azole) OR (TL azole) OR (Zenith Brand of Sulfisoxazole) OR (Gantrisin) OR (Gantrisin Pediatric) OR (Pediatric, Gantrisin) OR (Roche Brand of Sulfisoxazole Diolamine) OR (Roche Brand of Sulfisoxazole) OR (Sulfisoxazole Roche Brand) OR (Roche Brand of Sulfisoxazole Acetate) OR (Sulfisoxazole, Ammonium Salt) OR (Ammonium Salt Sulfisoxazole)	
TIPO DE ESTUDO - RCT ((randomized controlled trial [pt]) OR (controlled clinical trial [pt]) OR (randomized [tiab]) OR (placebo [tiab]) OR (drug therapy [sh]) OR (randomly [tiab]) OR (trial [tiab]) OR (groups [tiab])) AND (humans [mh])	
LIMITE CRIANÇA	
PERÍODO 2002 A 2008 25/10/2008	

```
(sinusitis [MeSH] OR

 sinusitis [Text Word] OR rhinitis [MeSH] OR rhinitis [Text Word]

 OR paranasal sinus diseases [MeSH] OR paranasal sinus diseases
```

[Text Word] OR nasopharyngitis [MeSH] OR nasopharyngitis [Text Word] OR common cold [MeSH] OR common cold [Text Word] OR rhinorrhoea [Text Word] OR rhinorrhea [Text Word] OR nasal discharge [Text Word])

AND (antibiotics [MESH] OR antibiotics [Text Word] OR antibiotic [Text Word] OR anti-infective agents [MeSH] OR amoxicillin* [text word] OR amoxycillin* [text word] OR ampicillin [text word] OR azithromycin [text word] OR cefaclor [text word] OR penicillin [text word] OR sulphamethoxazole [text word] OR sulfisoxazole [text word]).

LILACS

Antibiotics for persistent nasal discharge (rhinosinusitis) in children

Morris P, Leach A

This review should be cited as: Morris P, Leach A. Antibiotics for persistent nasal discharge (rhinosinusitis) in children (Cochrane Review). In: The Cochrane Library, Issue 4, 2002. Oxford: Update Software.

A substantive amendment to this systematic review was last made on 27 February 2002. Cochrane reviews are regularly checked and updated if necessary.

Background: Nasal discharge (rhinosinusitis) is extremely common in children. It is the result of inflammation of the mucosa of the upper respiratory tract, and is usually due to either infection or allergy.

Objectives: To determine the effectiveness of antibiotics versus placebo or standard therapy in treating children with persistent nasal discharge (rhinosinusitis) for at least 10 days.

Search strategy: The Cochrane Controlled Trials Register, MEDLINE, EMBASE, and the references of relevant articles were searched. Authors and pharmaceutical companies were contacted. Date of most recent searches: February 2002.

Selection criteria: All randomised controlled trials that compared antibiotics versus placebo or standard therapy. Trials which included the use of other medications were included if all participants were allowed equal access to such medications or if the additional or alternative therapies were regarded as ineffective. Trials that only combined or compared antibiotics with surgery, or sinus puncture and lavage, were not included in the review.

Data collection and analysis: Data were extracted by a single reviewer for the following eight outcomes: overall clinical failure (primary outcome), failure to cure, failure to improve, clinical improvement, time to resolution, complications, side-effects and bacteriologic failure. For the dichotomous outcome variables of each individual study, proportional and absolute risk reductions were calculated using a modified

intention-to-treat analysis. The summary weighted risk ratio and 95% confidence interval (fixed effects model) were calculated using the inverse of the variance of each study result for weighting (Cochrane statistical package, REVMAN version 4.1).

Main results: A total of six studies involving 562 children compared antibiotics with placebo or standard therapy. Only the primary outcome (overall clinical failure) was reported in all studies. Around 40% of all randomised children did not have a clinical success documented when reviewed two to six weeks after randomisation. The control event rate varied from to 22 to 71% (mean 46%). The risk ratio estimated using a fixed effects model was 0.75 (95% CI 0.61 to 0.92). There was no evidence of statistical heterogeneity. Side effects occurred in 4 of 189 control group children (four studies). More children treated with antibiotics had side effects (17 of 330), but this difference was not statistically significant (RR 1.75, 95% CI 0.63 to 4.82).

Reviewers' conclusions: For children with persistent nasal discharge or older children with radiographically confirmed sinusitis, the available evidence suggests that antibiotics given for 10 days will reduce the probability of persistence in the short to medium-term. The benefits appear to be modest and around eight children must be treated in order to achieve one additional cure (NNT 8, 95% CI 5 to 29). No long term benefits have been documented. These conclusions are based on a small number of small randomised controlled trials and may require revision as
randomised controlled trials and may require revision as
additional data become available.

Background

Nasal discharge is extremely common in children. It is the result of inflammation of the mucosa of the upper respiratory tract, and is usually due to either infection or allergy (Wald 1991). It can be a presenting feature of **rhinitis, sinusitis, rhinosinusitis, nasopharyngitis** and the common cold. Clinical assessment and diagnostic tests routinely available to general practitioners cannot always distinguish between these conditions in children. Changes consistent with sinusitis in adults with the common cold suggest that making clear distinctions between these conditions may be artificial (Gwaltney 1994). An international consensus panel has proposed that rhinosinusitis be the preferred diagnosis for childhood illnesses where nasal discharge is a prominent feature (Clement 1998). Acute episodes may last up to 12 weeks before complete resolution of symptoms occurs. Illnesses that persist beyond 12 weeks are termed chronic.

A literature search on rhinosinusitis (see topic search strategy) using the Cochrane Library (Issue 1, 2002) and the MEDLINE database (PubMed [Feb 2002]; Shojania 2001) identified published systematic reviews of the following interventions: antibiotics (Williams 2000; Ioannidis 2001; Benninger 2000; de Ferranti 1998; de Bock 1997), house dust mite avoidance (Sheikh 2001), immunotherapy (Ross 2000), and intranasal corticosteroids versus antihistamines (Weiner 1998). Reviews of antibiotics were concerned with acute rhinosinusitis. All the other reviews were limited to studies where participants had a clinical diagnosis of allergic rhinitis.

Most infections that cause nasal discharge are viral and follow a

characteristic clinical course (Cherry 1992). Initially the discharge is clear and constitutional symptoms (fever, headache, cough, sore throat etc) are common. After one to three days the discharge becomes muco-purulent or purulent, though the child's overall condition often improves. The discharge usually resolves spontaneously and the total duration of illness is about seven days. A small proportion of these episodes will be associated with symptomatic bacterial infections of the middle ear and paranasal sinuses.

Bacterial infections of the respiratory mucosa are not well understood. While antibiotics are frequently prescribed for otitis media, sinusitis and bronchitis, the benefits appear modest (Glasziou 2000; Takata 2001; Rosenfeld 2001; de Bock 1997; de Ferranti 1998; Williams 2000; Benninger 2000; Ioannidis 2001; Wald 2001; Smucny 2000). The common bacterial respiratory pathogens are considered part of the normal flora of the nasopharynx (Ingvarrson 1982), and accurate identification of bacterial disease is difficult. While antibiotics are not an effective treatment for the common cold, they may provide some symptomatic relief in the subgroup that are also infected with Streptococcus pneumoniae, Haemophilus influenzae, or Moraxella catarrhalis (Heald 1993; Kaiser 1996; Kaiser 2001).

In France, early treatment with antibiotics is recommended for children with purulent nasal discharge (Narcy 1991). In the United States, on the other hand, antibiotics are only recommended when the discharge has persisted at least 10 days. In these children secondary bacterial infection and sinusitis are presumed to be present (Wald 1986; Wald 1991). Despite this, a recent survey of

340 paediatricians and family medicine practitioners found that only 19% would withhold antibiotics from an infant with scant, greenish mucopurulent nasal secretions. Even fewer (6%), were willing to wait 7-10 days before providing antibiotics if the infant attended day care (Schwartz 1997). While the presence of 'purulence' has been shown to be an important predictor of antibiotic prescribing in respiratory infections (Watson 1999; Little 2000), its meaning is unclear. Viral infections may be associated with opaque secretions (Winther 1984), and large numbers of

numbers of neutrophils (pus cells) may be present when the discharge is clear.

Chronic nasal discharge is much more common in developing countries. In these high risk populations, diseases of the respiratory mucosa are reminiscent of the poorer urban communities in Britain 40 years ago (Miller 1960). Even profuse purulent nasal discharge is relatively asymptomatic and may be accepted as a normal part of childhood by other family members. This discharge can persist for years. The only follow up study of children with therapy-resistant purulent rhinitis found that the condition resolved spontaneously in nearly all children at an average age of seven years (Otten 1992). Several investigators have highlighted the association between high rates of persistent nasal discharge and bacterial respiratory diseases like otitis media, bronchitis, pneumonia and bronchiectasis (Williams 1959; Miller 1960; Shann 1984; Gratten 1986; Montgomery 1990; Leach 1994; Torzillo 1995). Therefore, the potential impact that an effective treatment might have in reducing exposure and transmission of pathogenic bacteria makes this a relevant clinical question even in countries with

limited resources.

Randomised controlled trials involving children with presumed viral upper respiratory tract infections have also examined the potential of antibiotics to prevent secondary bacterial infection. Most studies failed to demonstrate any benefit (Gadomski 1993). This review examines whether antibiotics improve outcomes for children with persistent nasal discharge (rhinosinusitis). Very few studies have addressed this problem (Ioannidis 2001); probably in part due to the fact that many clinicians already accept that antibiotics are an effective treatment in these circumstances. It is unclear if this belief is supported by evidence from randomised controlled trials.

Objectives

To determine the effectiveness of antibiotics in treating children with persistent nasal discharge (rhinosinusitis) for at least 10 days.

Criteria for considering studies for this review

Types of studies

All randomised controlled trials comparing antibiotics with a placebo medication or standard therapy.

Types of participants

All trials which included children under 18 years of age with

nasal discharge that had persisted for at least 10 days. Trials that included children with an underlying immunodeficiency or anatomical defect were analysed separately. Nasal discharge had to be the primary condition requiring medical intervention. Studies that only enrolled children with radiological signs of sinusitis were included if the investigators could provide the outcome details for the relevant children, or if more than 80% of children in the study had nasal discharge. The decision to include studies, where a diagnosis of sinusitis had been confirmed, was made because nasal discharge is the most frequent presenting complaint in these children and there is consensus that rhinitis and sinusitis cannot be differentiated on clinical grounds alone. For example, almost 90% of children between two and six years (and 70% of those older than six years) with persistent nasal discharge will have x-ray changes consistent with sinusitis (Wald 1986).

Types of intervention

All randomised controlled comparisons of antibiotics (effective against Streptococcus pneumoniae and non-capsular Haemophilus influenzae) versus placebo medication or standard therapy (decongestants or nasal saline drops) in the management of persistent nasal discharge. Trials that only compared or combined antibiotics with surgery, or sinus puncture and lavage, were not included in the review. Trials which included the use of other medications were included if all participants were allowed equal access to such medications or if the additional or alternative therapies were regarded as ineffective. Trials only comparing two or more antibiotics without a non-antibiotic comparison group were not included in the

not included in the review.

Types of outcome measures

Attempts were made to obtain data on at least one of the following outcome measures:

Primary outcome

a) proportions of participants with nasal discharge at follow up, or those with no substantial improvement if failure to cure rates are not available (overall clinical failure);

Secondary outcomes

a) proportions of participants with nasal discharge at follow up (failure to cure);
b) proportions of participants who were not improved at follow-up (failure to improve);
c) mean difference in symptoms and signs (mean clinical improvement);
d) mean time to resolution of nasal discharge (mean time to clinical cure);
e) proportions of participants with progression or extension of disease resulting in additional medical therapy (complications);
f) proportions of participants who had to cease treatment due to side effects (side effects);
g) proportions with persistent carriage of pathogenic bacteria- Streptococcus pneumoniae, Haemophilus influenzae or Moraxella catarrhalis (bacteriologic failure).

The proportions of participants were categorised as overall

clinical failure, failure to cure, failure to improve, and the mean clinical improvement, were determined using the following hierarchy of assessment measures:

i) Symptoms and/or signs- assessed by clinician;

ii) Symptoms and/or signs- assessed by participant or particpant's carer;

iii) Radiological assessment alone.

Search strategy for identification of studies

See: Collaborative Review Group search strategy

The following topic search strategy was used to identify the relevant randomised controlled trials: (sinusitis [MeSH] OR sinusitis [Text Word] OR rhinitis [MeSH] OR rhinitis [Text Word] OR paranasal sinus diseases [MeSH] OR paranasal sinus diseases [Text Word] OR nasopharyngitis [MeSH] OR nasopharyngitis [Text Word] OR common cold [MeSH] OR common cold [Text Word] OR rhinorrhoea [Text Word] OR rhinorrhea [Text Word] OR nasal discharge [Text Word]) AND (antibiotics [MESH] OR antibiotics [Text Word] OR antibiotic [Text Word] OR anti-infective agents [MeSH] OR amoxicillin* [text word] OR amoxycillin* [text word] OR ampicillin [text word] OR azithromycin [text word] OR cefaclor [text word] OR penicillin [text word] OR sulphamethoxazole [text word] OR sulfisoxazole [text word]).

Trials were identified from the following sources:

1. The Cochrane Controlled Trials Register (which includes the ARI Collaborative Review Group Specialised Trials Register).

2. MEDLINE 1999-2002 accessed via PubMed and combined with the following terms to identify randomised controlled trials: clinical

trial [ptyp] OR "clinical trial*"[text word] OR random*[text word] OR "double-blind"[text word] OR "double blind"[text word] OR "single-blind"[text word] OR "single blind"[text word] OR placebo*[text word] .

3. OLDMEDLINE accessed via the National Library of Medicine Gateway and combined with the following terms to identify randomised controlled trials: random: OR "double-blind" OR "double blind" OR "single-blind" OR "single blind" OR placebo: OR "clinical trial:" OR "drug therapy".

4. EMBASE 1997-2002 accessed via Science Direct and combined with the following terms to identify randomised controlled trials: clinical trial! OR random! OR "double-blind" OR "double blind" OR "single-blind" OR "single blind" OR placebo!

5. The list of references in relevant publications.

6. Written communication with the authors of trials included in the review.

7. Written communication with major pharmaceutical companies (with offices in Australia) that manufacture antibiotics.

Methods of the review

Trials that satisfied the inclusion criteria were reviewed and the following information recorded: study setting, source of funding, patient recruitment details (including number of eligible children), inclusion and exclusion criteria, randomisation and allocation

allocation concealment method, numbers of participants randomised, blinding (masking) of participants, care providers and outcome assessors, dose and type of antibiotic therapy, duration of therapy, co-interventions, numbers of patients not followed up,

reasons for withdrawals from study protocol (clinical, side effects, refusal and other), details on side effects of therapy, and whether intention-to-treat analyses were possible from the data. Further information was requested from the authors where required.

Studies included in the review had four components of quality assessed:

1. Allocation concealment. Trials scored as: Grade A: Adequate concealment, Grade B: Unclear, Grade C: Clearly inadequate concealment. (Grade A = high quality).
2. Blinding. Trials scored as: Grade A: Participant and care provider and outcome assessor blinded, Grade B: Outcome assessor blinded, Grade C: Unclear, Grade D: No blinding of outcome assessor (Grade A, B = high quality).
3. Reporting of participants by allocated group. Trials scored as: Grade A: The progress of all randomised children in each group described, Grade B: Unclear or no mention of withdrawals or dropouts, Grade C: The progress of all randomised children in each group clearly not described. (Grade A = high quality).
4. Follow-up of randomised participants. Trials scored as: Grade A: Outcomes measured in >90% (where withdrawals due to complications and side-effects are categorised as treatment failures), Grade B: Outcomes measured in 80 to 90%, Grade C: Unclear, Grade D: Outcomes measured in <80%. (Grade A = high quality).

While only the allocation concealment quality assessment is displayed in the meta-analysis figures, all assessments are included in the 'Characteristics of included studies' table. Additional reviewers will allow the inter-reviewer reliability for

the identification of high quality studies for each component to be measured using the Kappa statistic.

For the dichotomous outcome variables of each individual study, proportional and absolute risk reductions were calculated using a modified intention-to-treat analysis. This analysis assumed that children of known allocation status who were not available for outcome assessment had not improved (and probably represents a conservative estimate of effect). An initial qualitative comparison of all the individually analysed studies examined whether pooling of results (meta-analysis) was reasonable. This took into account differences in study populations, interventions, outcome assessment and estimated effect size.

The results from studies that met the inclusion criteria and reported any of the outcomes of interest were included in the subsequent meta-analysis. The summary weighted risk ratio and 95% confidence interval (fixed effects model) were calculated using the inverse of the variance of each study result for weighting (Cochrane statistical package, REVMAN version 4.1). The numbers needed to treat (NNT) were calculated using the summary odds ratio and the average control event rate described in the relevant studies. Time to clinical cure and clinical improvement were to be treated as normally distributed continuous variables (if feasible) so the mean difference in outcomes could be estimated. If studies used different scoring systems to document clinical improvement, attempts to estimate the standardised mean difference were made. Any heterogeneity between the study results was described and tested to see if it reached statistical significance using a chi-square test ($P < 0.1$ was considered to be consistent with

statistical heterogeneity). The 95% confidence interval estimated using a random effects model was included whenever statistical heterogeneity was present.

A priori subgroup analysis was planned for: i) children less than 8 years of age; ii) children with persistent 'purulent ' nasal discharge (see 'What's New' notes in coversheet for details of changes to protocol). Sensitivity analyses were planned to assess the impact on the overall outcomes of the following
the impact on the overall outcomes of the following potentially important factors: a) study quality; b) study size; c) variation in the inclusion criteria; d) differences in the medications used in the intervention and comparison groups; and e) analysis limited to participants managed 'per protocol' (treatment and follow up as planned) rather than 'intention-to-treat'.

Description of studies

See Table of characteristics of included studies.
The six studies included within this review have important differences in their study populations, the interventions being compared, and methods of outcome assessment. Four of the studies enrolled children who met the current definition of acute rhinosinusitis (Wald 1986; Wald 1991; Dolhman 1993; Garbutt 2001), one study enrolled children with chronic rhinosinusitis (Otten 1988), and one study included children with both acute and chronic disease (Rachelefsky 1982). Four of the five larger studies required x-ray confirmation of sinusitis. This represents an important limitation to this review. Only the most recently published study (Garbutt 2001) and a small study specificaly

restricted to younger children did not include x-rays . Two of the studies only enrolled participants with purulent nasal discharge (Otten 1988; Wald 1991). The appearance of discharge was not described in the other studies. One study excluded children with a history of atopic disease (Wald 1986), while this was one of the inclusion criteria in two of the other studies (Rachelefsky 1982; Dolhman 1993).

Only three of the studies compared antibiotics with a placebo intervention of similar appearance. One study used saline nasal drops as their placebo intervention. The other studies compared antibiotics versus decongestants and antibiotics plus decongestants versus decongestants. Several of the studies had two or more antibiotic arms: amoxycillin, erythromycin and trimethoprim-sulphamethoxazole; amoxycillin and amoxycillin-clavulanate; amoxycillin, amoxycillin, amoxycillin-clavulanate and trimethoprim-sulphamethoxazole. Dosage was generally equivalent to 30 to 40mg/kg/day of amoxycillin and length of treatment was 10 to 14 days with the exception of one study where antibiotics continued for three or six weeks (Dolhman 1993). One study also randomised children to sinus lavage (Otten 1988). Only the children randomised to medical interventions (antibiotics or normal saline nasal drops) were included in this review.

All outcomes were assessed at 2-6 weeks, so only short to medium-term effects were described. The decision to include studies comparing antibiotic versus decongestants (Rachelefsky 1982) and antibiotic plus decongestants versus decongestants (Dolhman 1993) was based on the belief that although decongestants

may provide temporary symptomatic relief, they do not alter the overall clinical course.

Methodological quality

All six studies appeared to randomly allocate participants to antibiotics or control interventions. Unfortunately, other factors that may affect the validity of the results were not well described. Only two studies (Dolhman 1993; Garbutt 2001) described the method of randomisation. Allocation concealment was poorly reported and only three studies described methods that would ensure this was achieved (Wald 1986; Dolhman 1993; Garbutt 2001). Three studies (Wald 1986; Wald 1991; Garbutt 2001) used a placebo of similar appearance to the active treatment but only two of these specifically stated that the outcome assessor was blinded (Wald 1986; Garbutt 2001). While the other three studies reported a 'double-blind' assessment of outcome, it was not clear how this was achieved given the obvious differences between antibiotic and control therapies. Four studies did not report the progress of all randomised children by allocated group (Rachelefsky 1982; Wald 1986; Dolhman 1993; Garbutt 2001). However, allocation status and outcome data were described for more than 95% of participants except in one study where 15% of randomised
except in one study where 15% of randomised children were not accounted for (Garbutt 2001). In this review, withdrawals due to complications or side effects and participants lost to follow up were categorised as treatment failures. This had a major impact on the intrepretation of the results of one of the studies (Dolhman 1993) which was reported as evidence of no effect. This conclusion relied on the exclusion of 12 of 31 children in the comparison

group (39%). Five of these children developed severe respiratory infections and required additional antibiotic treatment.

Results

A total of six studies involving 562 children compared antibiotics with placebo or standard therapy. Only data for the primary outcome (overall clinical failure) were reported in all studies. The estimated effect size was consistent with a treatment benefit in four studies. In the single study of children with chronic purulent rhinosinusitis (Otten 1988), and in the most recently published study of acute rhinosinusitis (Garbutt 2001), antibiotics did not appear to provide any benefit (although the 95% confidence intervals included the summary estimate of effect). There was no evidence of statistical heterogeneity in the analysis of the primary outcome (P = 0.27). The decision to pool the results of all the studies was made on the basis of the biological plausibility and apparent consistency of effect. This decision will be reviewed as data from future studies become available. The other analyses where outcomes data were presented graphically (failure to cure, failure to improve, mean improvement, complications, and side effects) represent a a non-random sample of all studies and should be interpreted cautiously.

Primary Outcome

i) OVERALL CLINICAL FAILURE

All six studies involving 562 children reported data that could be used for this outcome. A total of 214 randomised children (38%) did not have have documented cure (5 studies) or clinical improvement (1 study, Garbutt 2001). The control event rate varied

from 22 to 71% (mean 48%). The risk ratio estimated using a fixed effects model was 0.75 (95% CI 0.61 to 0.92). These estimates are equivalent to a number needed to treat (NNT) of 8 (95% CI 5 to 29).

Two studies reported additional information that supported a beneficial effect of antibiotics (not included within this review). The larger Pittsburgh study excluded 28 children who had group A streptococcus isolated on throat swab (Wald 1986). When culture results were available, 14/18 children on antibiotic had improved compared with 1/10 on placebo (RR 0.25, 95% CI 0.1 to 0.6; P = 0.001, Fisher exact test). The Los Angeles study also included a crossover design where children where clinical failures were randomised to additional therapy (Rachelefsky 1982). Children who received additional treatment with amoxycillin or trimethoprim-sulphamethoxazole were more likely to be cured than those who received erythromycin or decongestants.

Seconday Outcomes

i) FAILURE TO CURE

Five studies involving 401 children reported this outcome (Rachelefsky 1982; Wald 1986; Otten 1988; Wald 1991; Wald 1991). A total of 181 randomised children did not have a clinical cure documented (45%). The control event rate varied from to 47 to 71% (mean 56%). The risk ratio estimated using a fixed effects model was 0.72 (95% CI 0.59 to 0.89). These estimates are equivalent to a number needed to treat (NNT) of 6 (95% CI 4 to 20).

ii) FAILURE TO IMPROVE

Three studies involving 350 children reported this outcome (Rachelefsky 1982; Wald 1986; Garbutt 2001). The risk ratio

estimated using a fixed effects model was 0.53 (95% CI 0.38 to 0.74).

iii) MEAN CLINICAL IMPROVEMENT

Two studies provided the mean difference in clinical score (Dolhman 1993; Garbutt 2001). In both studies, there was a slightly greater mean difference in the antibiotic groups than the control group. Neither difference was statistically significant. In one of these studies (Dolhman 1993), the standard deviation of the difference was not reported and so these data have not been

the difference was not reported and so these data have not been

entered into the table of comparisons.

iv) MEAN TIME TO RESOLUTION

No studies reported this outcome.

v) COMPLICATIONS

Two studies involving 284 children reported this outcome (Rachelefsky 1982; Garbutt 2001). In both trials, fewer children in the antibiotic groups required additional antibiotics for a worsening of their clinical status. This difference was statistically significant (RR 0.34, 95% CI 0.14 to 0.84; fixed effects model). If it is assumed that no complications occurred in the four studies that did not report this outcome, the size of the relative effect is unchanged but the size of the risk difference is reduced from 8% to 4% and is no longer statistically significant.

vi) SIDE EFFECTS

Four studies involving 469 children reported this outcome

(Rachelefsky 1982; Wald 1986; Dolhman 1993; Garbutt 2001). In these trials between one and four per cent of additional children in the antibiotic groups experienced either diarrhoea or allergic reactions sufficient to result in their withdrawal from the study. In one study the treatment allocation of two children who experienced allergic reactions was not described (Rachelefsky 1982). It was assumed they were in the antibiotic groups. The estimated effect size was consistent in all studies. The risk ratio calcuated using the fixed effects model was 1.75 (95% CI 0.63 to 4.82). This difference was not statistically significant.

vii) BACTERIOLOGIC FAILURE

No studies reported this outcome.

SUB-GROUP ANALYSES

i) AGE LESS THAN EIGHT YEARS

Only one small study (Wald 1991) was limited to children under the age of eight years. The other studies did not report outcomes according to age. At present, there is insufficient evidence to determine whether age increases or decreases the effectiveness of antibiotics in children with persistent disease.

ii) PURULENT NASAL DISCHARGE

Two studies (Otten 1988, Wald 1991) only included children with purulent nasal discharge. The other studies did not report outcomes according to presence or absence of 'purulence'. At present, there is insufficient evidence to determine whether the appearance of nasal discharge increases or decreases the effectiveness of antibiotics in children with persistent disease. Since the Danish study (Otten 1988) was the only trial not to

demonstrate any benefit of antibiotic treatment, this factor may be important. However there were several other important differences between this study and the others (see below).

SENSITIVITY ANALYSES

The proposed sensitivity analyses were only conducted for the primary outcome of overall clinical failure. Meta-analyses conducted with eligible studies removed according to quality citeria, sample size, and the type of comparison therapy, did not substantially alter the estimated effect size and overall conclusions. Using the 'per protocol' results from the individual studies did not make any difference to the combined estimate of effect size.

The different inclusion criteria used in the studies may be important. The only study that did not require x-ray confirmation of sinusitis did not describe a benefit of antibiotics (Garbutt 2001). Only one study specifically recruited children with chronic rhinosinusitis and also failed to demonstrate any benefit of antibiotics (Otten 1988). However, the Los Angeles study included children with a mean duration of symptoms of 18 weeks (Rachelefsky 1982) and in these children antibiotics were beneficial. Interestingly, a past history of atopy did not appear to be important. The two studies that recruited children from paediatric allergy clinics (Rachelefsky 1982, Dolhman 1993) had similar results to the Pittsburgh study (Wald 1986) where children with allergic rhinitis were excluded. Nasal smear results were also reported in the two studies of atopic children. There was no increase in the relative proportion of eosinophils present in the nasal discharge at the time of treatment. This is consistent with

an infectious rather than allergic aetiology. The Los Angeles study also reported nasal smear

study also reported nasal smear results after treatment and documented an increase in the proportion of eosinophils following resolution of rhinosinusitis (Rachelefsky 1982).

Several different antibiotics were used in the included studies (see description of studies). In the only study that included an erythromycin arm (Rachelefsky 1982), this antibiotic considerably was less effective than amoxycillin (risk ratio for clinical failure for amoxycillin versus erythromycin RR = 0.2, 95% CI 0.05 to 0.8, P = 0.016, Fisher exact test). There was no evidence to support substanial differences in outcome for children randomised to amoxycillin, amoxycillin-clavulanate compared with trimethroprim-sulphamethoxazole. Restriction of the analysis to only included children randomised to beta-lactam antibiotics (amoxycillin and amoxycillin-clavulanate) slightly increased the estimated effect size, but did not alter the overall conclusions.

Time of outcome assessment may also be important in determining effect size. The Danish study (Otten 1988) was the only one where all children were assesssed at six weeks rather than at two to three weeks. However, their clinical assessment of most children at two weeks also failed to document any benefit of antibiotics and so cannot explain the lack of any effect described in this study.

Summary of analyses

MetaView: Tables and Figures

The figures and graphs in Cochrane Reviews display the Peto Odds Ratio and the Weighted Mean Difference by default. These are not always the methods used by reviewers when combining data in their review. You should check the text of the review for a description of the statistical methods used.

Discussion

STRENGTH OF EVIDENCE

The evidence contained within this review is consistent with antibiotics increasing the rates of clinical cure or improvement in children with persistent nasal discharge. This is based on the results of six small randomised controlled trials. The estimated effect size is modest (RR = 0.75, 95% CI 0.61 to 0.92). If these studies are valid and there is no publication bias, the probability that antibiotics appeared effective by chance alone is remote. However, an effect of this size could be explained by bias. There is empirical evidence that lack of allocation concealment and double-blinding can both result in exaggerated estimates of effect size (Schultz 1995). These aspects of study design were poorly described. Publication bias is also possible but there are currently too few studies available to determine if this is likely.

APPLICABILITY

All studies were conducted in developed countries. Most enrolled children with a spectrum of clinical disorders (rather than persistent nasal discharge alone) and required radiographic confirmation of sinusitis. The control event rate for clinical failure was fairly consistent across the studies (range: 22 to

71%). Whether this is similar to that seen in children outside of clinical trials is not clear due to the lack of longitudinal observational studies in this area. This review did provide not any strong evidence that severity of disease or duration of discharge will affect outcome. However both of these factors may be important. This review does not support the use of antibiotics in children with nasal discharge of less than 10 days duration.

OTHER RELEVANT INFORMATION

There is some anecdotal evidence that the prevalence of chronic nasal discharge in young children has decreased since the 1940s (Miller 1960). This issue has not been addressed in well-designed studies. The introduction of antibiotics after World War Two and improvements in housing standards and hygiene practices may have contributed to this decline in rates of disease. A role for antibiotics is also supported by an international consensus panel of experts who have recommended that antibiotics are appropriate therapy for children with rhinosinusitis (Clement 1998). A Cochrane Review of antibiotics for maxillary sinusitis in adults Cochrane Review of antibiotics for maxillary sinusitis in adults described a similar beneficial effect as seen in the studies of children (Williams 1999). A Cochrane Review of antibiotics for the common cold (not including studies of purulent nasal discharge) did not find antibiotics to be of benefit (Arroll 2000). This is consistent with the view that antibiotics are only of substantial benefit in those who already have a bacterial infection.

TRADE OFFS

It would appear that the modest benefit of antibiotics must be weighed up against the cost and inconvenience of therapy and the

risk of occasional side effects. Although the increase in side effects was not statistically significant in this review, there is additional evidence from another Cochrane Review that side effects will occur in around six per cent of children with respiratory infections who are treated with antibiotics (Glasziou 1999). Antibiotics may also influence the prevalence of antibiotic resistance within the community. This was not evaluated in these studies and this hypothesis has not been tested in large randomised controlled trials. Increasing antibiotic resistance may also limit the potential benefits of this therapy. The most dramatic increase in pneumococcal penicillin resistance has occurred in the last ten years, and the only study published since 1993 did not describe a benefit of antibiotic treatment. However, this study also reported relatively high clinical improvement rates in both the antibiotics groups and the control group.

Reviewers' conclusions

Implications for practice

Parents should be advised that, for children with persistent nasal discharge or older children with radiographically confirmed sinusitis, the available evidence suggests antibiotics given for 10 days will reduce the probability of persistence in the short to medium-term. The benefits appear to be modest and around eight children must be treated in order to achieve one additional cure. No long term benefits have been documented. These conclusions are based on a small number of small randomised controlled trials and may require revision as additional data become available.

Antibiotics are not without risk and in these studies around one additional child experienced diarrhoea or an allergic reaction for every 30 treated. This difference was not statistically significant. Unnecessary antibiotic prescribing may also contribute to increasing rates of antibiotic resistance. Parents or children who place greatest value on early resolution of symptoms and who are willing to risk the possible side effects associated with this intervention are most likely to choose antibiotic therapy.

Implications for research

Despite increasing concern about inappropriate antibiotic prescibing for nasal discharge, there is a paucity of randomised controlled trials evaluating the benefits and harms associated with this intervention. There is an urgent need for large simple trials comparing the effects of antibiotics with placebo in children with persistent nasal discharge (greater than 10 days). Since x-rays are not routinely done in the primary care setting, radiographic confirmation of sinusitis should not be an inclusion criterion. Children should be stratified according to the duration of symptoms (acute versus chronic rhinosinusitis) and appearance of the discharge (transparent versus opaque). Outcomes should be assessed at the completion of the intervention and again three to six months later. Time to resolution of discharge should also be documented. Additional research is also needed to examine the impact of antibiotics on the bacteria infecting the nasopharynx and sinuses. Any subsequent increases in antibiotic resistance should be described.

Acknowledgements

This review is dedicated to the investigators and participants of the original relevant randomised controlled trials. It was completed with the help of a Glaxo sponsored educationl grant from the Australian Cochrane Centre. Thanks to: John Mathews (Menzies the Australian Cochrane Centre. Thanks to: John Mathews (Menzies School of Health Research, Darwin, Australia) for supervision and advice; Dave Sackett for explaining medical decision-making; John Williams (Cochrane Reviewer) for helpful comments; Ron D'Souza; the Cochrane Acute Respiratory Infections Collaborative Review Group for ongoing assistance and financial support for workshop attendance; Heather McIntosh and the Australasian Cochrane Centre for training in systematic review methodology; and the National Health and Medical Research Council of Australia for funding (Aboriginal Health Scholarship 958508).

Potential conflict of interest

None known.

Notes

The Acute Respiratory Infections Group would like to thank Amy Zelmer for reading and commenting on this review.

Characteristics of included studies

Table: Characteristics of included studies

Characteristics of excluded studies

Study : Jeppesen 1972

Only reported outcomes in terms of sinuses affected rather than by particpant. Majority of particpants also had sinus lavage.

Study : Lexomboom 1971

Symptoms (including subgroup with nasal discharge) present less than 10 days.

Study : Otten 1994

Compared antibiotics with sinus lavage.

Study : Reinert 1991

Nasal discharge was not persistent (present >10days) at time of treatment.

Study : Taylor 1977

Details of subgroup of children with nasal discharge not described.

Study : Todd 1984

Duration of nasal discharge not described.

Study : Wald 1984

Only compared two antibiotic groups.

References

References to studies included in this review

Dolhman 1993 {published data only}

Dohlman-AW; Hemstreet-MP; Odrezin-GT; Bartolucci-AA. Subacute sinusitis: are antimicrobials necessary? J Allergy Clin Immunol 1993;91(5):1015-1023.

Garbutt 2001 {published data only}

Garbutt JM, Goldstein M, Gellman E, Shannon W, Littenberg B. A randomized, placebo-controlled trial of antimicrobial treatment for children with clinically diagnosed acute sinusitis. Pediatrics 2001;107(4):619-625.

Otten 1988 {published data only}

Otten FW, Grote JJ. Treatment of chronic maxillary sinusitis in children. Int J Ped Otorhinolaryngol 1988;15:269-278.

Otten-FW; Grote-JJ. Otitis media with effusion and chronic upper respiratory tract infection in children: a randomized, placebo-controlled clinical study. Laryngoscope 1990 Jun;100(6):627-33.

Rachelefsky 1982 {published data only}

Rachelefsky GS, Katz RM, Siegal SC. Chronic sinusitis in children with respiratory alergy: the role of antimicrobials. J Allergy Clin Immunol 1982;69(4):382-387.

Wald 1986 {published data only}

* Wald ER, Chiponis D, Ledesma-Medina J. Comparative effectiveness of amoxycillin and amoxycillin-clavulanate potassium in acute paranasal sinus infections in children: a double blind, placebo-controlled trial. Pediatrics 1986;77:795-800.

Wald 1991 {published data only}

* Wald-ER. Purulent nasal discharge. Pediatr Infect Dis J 1991 Apr;10(4):329-33.

* indicates the major publication for the study

References to studies excluded from this review

Jeppesen 1972

Jeppesen-F; Illum-P. Pivampicillin (Pondocillin) in the treatment of maxillary sinusitis. Acta Otolaryngol Stockh 1972;74(5):375-382.

Lexomboom 1971

Lexomboom U, Duangmani C, Kusalasai V et al. Evaluation of orally administered antibiotics for treatment of upper respiratory infections in Thai children. J Pediatrics 1971;78(5):772-778.

Otten 1994

* Otten-HW; Antvelink-JB; Ruyter-de-Wildt-H; Rietema-SJ; Siemelink-RJ; Hordijk-GJ. Is antibiotic treatment of chronic sinusitis effective in children? Clin Otolaryngol 1994 Jun;19(3):215-7.

Reinert 1991

* Reinert-P; Narcy-P; Paliwoda-A; Rouffiac-E. Evaluation de l'association pivalate de tixocortol-neomycine versus placebo (excipient) dans la rhinopharyngite aigue de l'enfant [Evaluation of tixocortol pivalate-neomycin combination versus ++a placebo excipient in acute rhinopharyngitis in children]. Ann Pediatr Paris 1991 Sep;38(7):503-8.

Taylor 1977

Taylor-B; Abbott-GD; Kerr-MM; Fergusson-DM. Amoxycillin and co-trimoxazole in presumed viral respiratory infections of childhood: placebo-controlled trial. BMJ 1977;2:552-554.

Todd 1984

Todd-JK; Todd-N; Damato-J; Todd-WA. Bacteriology and treatment of purulent nasopharyngitis: a double blind, placebo-controlled evaluation. Ped Inf Dis J 1984;3(3):226-232.

Wald 1984

Wald ER, Reilly JS, Casselbrant M, et al. Treatment of acute maxillary sinusitis in childhood: A comparative study of

amoxicillin and cefaclor. J Pediatrics 1984;104(2):297-302.

Additional references

Arroll 2000

Arroll B, Kenealy T. Antibiotics for the common cold. Cochrane Database Syst Rev 2000;(2):CD000247.

Benninger 2000

Benninger MS, Sedory Holzer SE, Lau J. Diagnosis and treatment of uncomplicated acute bacterial rhinosinusitis: summary of the Agency for Health Care Policy and Research evidence-based report. Otolaryngol Head Neck Surg 2000;122(1):1-7.

Cherry 1992

Cherry JD. In: Feigan RD and Cherry JD (eds), Textbook of Pediatric Infectious Diseases. 3rd Edition. WB Saunders, 1992.

Clement 1998

Clement P, Bluestone CD, Gordts F et al. Management of rhinosinusitis in children. Consensus meeting, Brussels, Belgium, September 13, 1996. Arch Otolaryngol Head Neck Surg 1998;124:31-34.

Cole 1986

Cole PJ. Inflammation: a two-edged sword- the model of bronchiectasis. Eur J Respir Dis 1986;69(Suppl 147):6-15.

de Bock 1997

de Bock GH, Dekker FW, Stolk J, Springer MP, Kievit J, van Houwelingen JC. Antimicrobial treatment in acute maxillary sinusitis: a meta-analysis. J Clin Epidemiol 1997;50(8):881-890.

de Ferranti 1998

de Ferranti SD, Ioannidis JP, Lau J, Anninger WV, Barza M. Are amoxycillin and folate inhibitors as effective as other antibiotics for acute sinusitis? A meta-analysis. BMJ 9-5-1998;317(7159):632-637.

Gadomski 1993

Gadomski A. Potential interventions for preventing pneumonia among young children: lack of effect of antibiotic treatment for upper respiratory infections. Pediatr Inf Dis J 1993;12:115-20.

Glasziou 2000

Glasziou PP, Del Mar CB, Hayem M, Sanders SL. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev 2000;(4):CD000219.

Gratten 1986

Gratten M, Gratten H, Poli A et al. Colonisation of Haemophilus influenzae and Streptococcus pneumoniae in the upper respiratory tract of infants in Papua New Guinea: primary acquisition, duration of carriage, and relationship to carriage in mothers. duration of carriage, and relationship to carriage in mothers. Biol Neonate 1986;50:114-20.

Gwaltney 1994

Gwaltney JM, Phillips CD, Miller RD, Riker D. Computed tomographic study of the common cold. N Eng J Med 1994;330:25-30.

Heald 1993

Heald A, Auckenthaler R, Borst F et al. Adult bacterial nasopharyngitis: a clinical entity. J Gen Intern Med 1993;8:667-73.

Ingvarrson 1982

Ingvarrson L, Lundgren K, Ursing J. The bacterial flora of the nsaopharynx in healthy children. Acta Otolaryngol Suppl (Stockh) 1982;386:94-6.

Ioannidis 2001

Ioannidis JP, Lau J. Technical report: evidence for the diagnosis and treatment of acute uncomplicated sinusitis in children: a systematic overview. Pediatrics 2001;108(3):E57.

Kaiser 1996

Kaiser L, Lew D, Hirschel B, Auckenthaler R, Morabia A, Heald A, Benedict P, Terrier F, Wunderli W, Matter L, Germann D, Voegeli J, Stalder H. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. Lancet 1996;347:1507-10.

Kaiser 2001

Kaiser L, Morabia A, Stalder H, Ricchetti A, Auckenthaler R, Terrier F, Hirschel B, Khaw N, Lacroix JS, Lew D. Role of nasopharyngeal culture in antibiotic prescription for patients with common cold or acute sinusitis. Eur J Clin Microbiol Infect Dis 2001;20(7):445-451.

Leach 1994

Leach AJ, Boswell JB, Asche V, Nienhuys TG, Mathews JD. Bacterial colonisation of the nasopharynx predicts very early onset and persistence of otitis media in Australian Aboriginal infants. Ped Infect Dis J 1994;13:983-9.

Little 2000

Little DR, Mann BL, Godbout CJ. How family physicians distinguish acute sinusitis from upper respiratory tract infections: a retrospective analysis. J Am Board Fam Pract 2000;13(2):101-106.

Miller 1960

Miller FJW et al. Growing up in Newcastle-on-Tyne. London: Oxford University Press, 1960.

Montgomery 1990

Montgomery JM, Lehmann D, Smith T, Michael A, Joseph B, Lupiwa T, Coakley C, Spooner V, Best B, Riley ID, Alpers MP. Bacterial colonisation of the upper respiratory tract andits association with acute lower respiratory tract infections in highland children of Papua New Guinea. Rev Infect Dis 1990;12(S8):S1006-16.

Narcy 1991

Narcy P. Rhinopharyngites: strategies therapeutiques. Concours Med 1991;113:803-806.

Otten 1992

Otten-FW; Van-Aarem-A; Grote-JJ. Long-term follow-up of chronic therapy resistant purulent rhinitis in children. Clin-Otolaryngol 1992 Feb;17(1):32-3.

Rosenfeld 2001

Rosenfeld RM, Casselbrant ML, Hannley MT. Implications of the AHRQ evidence report on acute otitis media. Otolaryngol Head Neck Surg 2001;125(5):440-448.

Ross 2000

Ross RN, Nelson HS, Finegold I. Effectiveness of specific immunotherapy in the treatment of allergic rhinitis: an analysis of randomized, prospective, single- or double-blind, placebo-controlled studies. Clin Ther 2000;22(3):342-350.

Schultz 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA 1995;273(5):408-12.

Schwartz 1997

Schwartz RH, Freij BJ, Ziai M, Sheridan MJ. Antimicrobial prescribing for acute purulent rhinitis in children: a survey of pediatricians and family practitioners. Pediatr Infect Dis J 1997;16:185-90.

Shann 1984

Shann F, Gratten M, Germer S, Linnemann V, et al. Aetiology of pneumonia in children in Goroka Hospital, Papua New Guinea. Lancet 1984;2:537-41.

Sheikh 2001

Sheikh A, Hurwitz B. House dust mite avoidance measures for
Sheikh A, Hurwitz B. House dust mite avoidance measures for

perennial allergic rhinitis (Cochrane Review). Cochrane Database Syst Rev 2001;4:CD001563.:CD001563.

Shojania 2001

Shojania KG, Bero LA. Taking advantage of the explosion of systematic reviews: an efficient MEDLINE search strategy. Eff Clin Pract 2001;4(4):157-162.

Smucny 2000

Smucny J, Fahey T, Becker L, Glazier R, McIsaac W. Antibiotics for acute bronchitis. Cochrane Database Syst Rev 2000;(4):CD000245.

Takata 2001

Takata GS, Chan LS, Shekelle P, Morton SC, Mason W, Marcy SM. Evidence assessment of management of acute otitis media: I. The role of antibiotics in treatment of uncomplicated acute otitis media. Pediatrics 2001;108(2):239-247.

Todd 1984

Todd-JK; Todd-N; Damato-J; Todd-WA. Bacteriology and treatment of purulent nasopharyngitis: a double blind, placebo-controlled evaluation. Pediatr Infect Dis J 1984 May-Jun;3(3):226-32.

Torzillo 1995

Torzillo PJ, Hanna JN, Morey F et al. Invasive pneumococcal

disease in central Australia. Med J Aust 1995;162:182-186.

Wald 2001

Wald ER, Bordley WC, Darrow DH, Grimm KT, et al. Clinical practice guideline: management of sinusitis. Pediatrics 2001;108(3):798-808.

Watson 1999

Watson RL, Dowell SF, Jayaraman M, Keyserling H, Kolczak M, Schwartz B. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice, and parent beliefs. Pediatrics 1999;104(6):1251-1257.

Weiner 1998

Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. BMJ 1998;317(7173):1624-1629.

Williams 1959

Williams HE and O'Reilly RN. Bronchiectasis in children. Its multiple clinical and pathological aspects. Arch Dis Child 1959;34:192-201.

Williams 2000

Williams JW, Jr., Aguilar C, Makela M, Cornell J, Holleman DR, Chiquette E, Simel DL. Antibiotics for acute maxillary sinusitis. Cochrane Database Syst Rev 2000;(2):CD000243.

Winther 1984

Winther-B; Brofeldt-S; Gronborg-H; Mygind-N; Pedersen-M; Vejlsgaard-R. Study of bacteria in the nasal cavity and nasopharynx during naturally acquired common colds. Acta Otolaryngol Stockh 1984 Sep-Oct;98(3-4):315-20.

Coversheet

Title

Antibiotics for persistent nasal discharge (rhinosinusitis) in children

Reviewer(s)

Morris P, Leach A

Contribution of Reviewer(s)

Peter Morris designed the review, searched the literature, identified the relevant studies, and analysed the results.

Issue protocol first published: 1998 Issue 2

Issue review first published: 2000 Issue 3

Date of last minor amendment: 28 August 2002

Date of last substantive amendment: 27 February 2002

Most recent changes: The updated review (Issue 4, 2002) contained several substantial changes to the previous version:
1. A single primary outcome measure was selected and the hierarchy of assessment measures was made explicit.
2. The quality assessment tool was ammended and "reporting of participants by allocated group" was added.
3. The search strategy was ammended to make it more efficient and more easily repeatable.
4. An additional trial was identified and contributed data to five of the eight outcomes (Garbutt 2002).
The overall conclusions were unchanged.

The first published review (Issue 3, 2000) contained several substantial changes to the published protocol:
1. The term "rhinosinusitis" was included as the medical diagnosis that best describes children with persistent nasal discharge. This was done to bring the review into line with current international consensus recommendations.
2. The age of eligible children was extended to 18 years.
2. The age of eligible children was extended to 18 years. Children less than 8 years of age will be analysed as an a priori sub-group as data become available. This was done because older children were included in most trials and individual patient data were not available. A similar Cochrane review is available for adults greater than 18 years.

3. Children with both purulent and non-purulent persistent nasal discharge were included in the review. Children with persistent purulent nasal will be analysed as an a priori sub-group as data become available. This was done because the methods used to distinguish between purulent and non-purlent discharge were not clear and individual patient data were not available.
4. The proceedings of the ICAAC meetings were not hand searched due to the cost involved. The years 1992, 1996 and 1997 were available to the author and did not include any additional trials.
5. The possibilty of observer bias is being addressed by the recruitment of a second reviewer. Data extraction will be done while "blinded" to the study details and findings of the first author.

Date new studies sought but none found: Information not supplied by reviewer

Date new studies found but not yet included/excluded: Information not supplied by reviewer

Date new studies found and included/excluded: Information not supplied by reviewer

Date reviewers' conclusions section amended: Information not supplied by reviewer

Contact address:

Dr Peter Morris
Ear Health and Education Unit

Menzies School of Health Research

Royal Darwin Hospital

PO Box 41096

Darwin

Northern Territory

AUSTRALIA

0811

Telephone: 08 89228196 extension: 28371

Facsimile: 08 89225187

E-mail: peterm@menzies.edu.au

For information on the editorial group see: Cochrane Acute Respiratory Infections Group

External sources of support to the review

The National Health and Medical Research Council (Aboriginal Health Scholarship) AUSTRALIA

Acute Respiratory Infection Cochrane Review Group AUSTRALIA

Internal sources of support to the review

Menzies School of Health Research AUSTRALIA

Synopsis

Antibiotics can sometimes stop persistent runny noses in children, but there is no evidence of long term benefit.

Runny noses (rhinosinusitis) are very common in children. The runny nose is a symptom of inflamed membranes in the upper air passages and is usually caused by infection or allergy. Most episodes occur as part of the common cold and usually children have begun to improve within 10 days of onset, although in a few

children the runny nose is persistent. This review of trials found that 10 days of antibiotics can sometimes stop persistent runny noses. However, there is not enough evidence of any long term benefit, and adverse effects from antibiotics are common.

Keywords

Adolescence; Antibiotics [*therapeutic use]; Child; Human; Randomized Controlled Trials; Rhinitis [*drug therapy]; Sinusitis [*drug therapy]; Treatment Outcome

CRG Code: HM-ARI

Cochrane Library number: CD001094

----- END OF DOCUMENT -----