Clinical review

Clinical evidence
Acute otitis media

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This review of the effects of treatment for otitis media and of the effects of preventive interventions is one of over 60 chapters included in the first issue of *Clinical Evidence*, which is published by the BMJ Publishing Group. Future issues of *Clinical Evidence* will cover myringotomy; a separate chapter in issue 1 contains information on otitis media with effusion.

Background

Definition: Otitis media is inflammation in the middle ear. Subcategories include acute otitis media, otitis media with effusion (also known as "glue ear"), recurrent acute otitis media, and chronic suppurative otitis media. Acute otitis media presents with systemic and local signs and has a rapid onset. The persistence of an effusion beyond three months without signs of infection defines otitis media with effusion, whereas chronic suppurative otitis media is characterised by continuing inflammation in the middle ear giving rise to otorrhoea and a perforated tympanic membrane.

Incidence/prevalence: Acute otitis media is a common condition with a high morbidity and low mortality. In the United Kingdom about 30% of children aged under 3 years visit their general practitioner with acute otitis media each year, and 97% receive antimicrobial treatment. About 1 in 10 children will have an episode of acute otitis media by 3 months of age. It is the most common reason for outpatient antimicrobial treatment in the United States.[1]

Aetiology: The most common bacterial causes for acute otitis media are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. The incidence of penicillin resistant *S pneumoniae* has risen, but rates vary between countries. The most important risk factors for poor outcome are young age and attendance at day care centres such as nursery schools. Others include white race, male sex, and history of enlarged adenoids, tonsillitis, and asthma. Other factors that may make a poor outcome more likely include multiple previous episodes, bottle feeding, a history of ear infections in parents or siblings, and use of a soother or pacifier. The evidence for the effect of environmental tobacco smoke is controversial.[1]

Prognosis: In about 80% of children the condition resolves without antibiotic treatment in about three days. Complications are rare but include hearing loss, mastoiditis, meningitis, and recurrent attacks.[1]

Treating acute otitis media

Likely to be beneficial:
- Non-steroidal anti-inflammatory drugs

Trade off between benefits and harms:
- Antibiotics

Unknown effectiveness:
- Paracetamol

Preventing recurrent otitis media

Likely to be beneficial:
- Long term antibiotic prophylaxis

Aims: To reduce the severity and duration of pain and other symptoms, to prevent complications, and to minimise adverse effects of treatment.

Outcomes: Pain control, which can be assessed by proxy measures in infants such as parental observation of distress or crying and use of analgesics; incidence of complications such as deafness (usually divided into short term and long term hearing loss), recurrent attacks of otitis media, mastoiditis, and meningitis; resolution of otoscopic appearances; incidence of adverse effects of treatment.

Methods: Search of the Cochrane Library, Medline, and Embase, using validated search string, July 1998. We gave priority to relevant systematic reviews. When more than one was found both were included for comparison. Where systematic reviews were unavailable, randomised controlled trials (preferably double blind) were used.

Question: What are the effects of treatments?

Option: Analgesia

We found limited evidence from one RCT that non-steroidal anti-inflammatory drugs are more effective than placebo in relieving pain.[2] The trial found no significant difference between paracetamol and placebo, but the dosing regimen may not have been optimal and the trial may have been too small.

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Benefits

We found no systematic review. We found one double blind multicentre RCT comparing thrice daily treatment with ibuprofen, paracetamol, or placebo for 48 hours in 219 children aged 1-6 years with otoscopically proved acute otitis media.[2] All children received antibiotic treatment with ceflacor. The proportions of children still experiencing pain by the second day were 7% with non-steroidal anti-inflammatory drugs, 10% with paracetamol, and 25% with placebo. Ibuprofen was significantly more effective than placebo ($P < 0.01$) but paracetamol was not (P value not given).There was no significant difference between placebo and active treatments for other outcomes (appearance of the tympanic membrane, rectal temperature, and parental assessment).

Harms

All treatments were equally well tolerated.

Comment

The trial may have been too small to detect a significant difference between paracetamol and placebo. The lack of significant difference may also be explained by the use of a three times daily regimen, since paracetamol is usually given four times daily. The evidence from this trial may be further limited because the assessment of the child's pain relief was based on parental observation, using a scale of 0 or 1.

Option: Antibiotics

Evidence from systematic reviews of RCTs is conflicting. The more recent and inclusive review suggests that antibiotics reduce the proportion of children still in pain at 2-7 days and reduce the risk of developing contralateral acute otitis media, but that they have no immediate beneficial effect in terms of reduced pain within 24 hours, and no long term effect in terms of rates of subsequent attacks or deafness at one month. Rates of adverse effects are almost doubled in children receiving antibiotics compared with placebo. There is no clear evidence favouring a particular antibiotic.

Benefits

Versus placebo or no treatment: We found two systematic reviews. The first identified four RCTs of antibiotics versus placebo or no treatment in 535 children aged 4 months to 18 years with acute otitis media.[3] Co-intervention with analgesics and other means of relieving symptoms was allowed in most trials. Rate of treatment success (absence of all presenting symptoms and signs at around 7-14 days after treatment started) was significantly greater for active treatment (absolute risk 13.7% *v* 81%, absolute risk reduction 67.3%; no confidence interval given). This means that seven children would need to be treated with antibiotics for one additional child to achieve complete resolution of signs and symptoms, or that six of every seven children with acute otitis media either do not need or will not respond to antibiotic treatment (number needed to treat 7, no confidence interval given).

The second systematic review identified six RCTs comparing early use of antibiotics versus placebo in children aged 7 months to 15 years with acute otitis media.[4] Most trials did not state the time interval between onset of symptoms and starting treatment: the two that did gave intervals of 1-24 hours and about 30 hours. Data from the three trials that reported pain outcomes 24 hours after presentation (n = 633) suggested that antibiotic treatment had no effect (61% of children receiving antibiotics were pain free *v* 60% receiving placebo). Data from all six trials showed that, two to seven days after presentation (when only 14% of children receiving placebo still had pain), the proportion of children still in pain was significantly lower among those receiving antibiotics (relative risk reduction compared with placebo 41%, 95% confidence interval 15% to 60%, absolute risk reduction 5.6%), as was the rate of contralateral acute otitis media (relative risk reduction compared with placebo 43%; 9% to 64%). There was no significant difference in the rate of subsequent attacks of acute otitis media (absolute risk reduction 0.1%; −4% to 4%) or deafness at one month (absolute risk reduction 2.3%; −6% to 11%). This means that 20 children would need to be treated with antibiotics early to prevent one additional child from experiencing pain at 2-7 days after presentation (number needed to treat 20; 13% to 46%).[5]

Versus each other: We found one systematic review, which identified 33 RCTs of antibiotics in children aged 4 months to 18 years with acute otitis media (n = 5400).[3] Compared with placebo or no treatment, the rate of treatment success (absence of all presenting signs and symptoms of acute otitis media at around 7-14 days after treatment was started) was significantly higher with penicillin (increase in absolute risk 15.7%; 4.7% to 26.7%), ampicillin/amoxicillin (increase in absolute risk 12.9%; 6.8% to 19%), and for any antibiotic (increase in absolute risk 13.7%; 8.2% to 19.2%). No significant differences were found between antimicrobial agents in rate of treatment success at 7-14 days or of middle ear effusion at 30 days.

Harms

The first review gave no information on adverse events.[3] In the second review, antibiotics were associated with a near doubling of the risk of vomiting, diarrhoea, or rashes (odds ratio 1.97; 1.19 to 3.25).[4]

Comment

The first review[3] excluded two placebo controlled trials that were included in the second,[4] on the basis that they included myringotomy as part of treatment. This may have biased results in favour of antibiotic treatment and may explain the lower number needed to treat given in the first review.

Option: Short versus longer courses of antibiotics

A systematic review of RCTs found increased risk of relapse or reinfection around 10 days but no difference in long term outcome with short courses (≤5 days) rather than longer courses of antibiotics.[6]

Benefits

We found one systematic review, which identified 32 RCTs of antibiotic treatment in children aged 4 weeks to 18 years with acute otitis media.[6] Treatment failure,

relapse, or reinfection at an early evaluation (8-19 days) were significantly more likely with shorter courses of antibiotics (≤5 days) than with longer courses (8-10 days) (summary odds ratio compared with longer courses 1.52; 1.17 to 1.98). However, by 20–30 days there were no significant differences between treatment groups (1.22, 0.98 to 1.54; absolute risk reduction 2.3%, −0.2% to 4.9%).

Harms

An RCT of amoxicillin plus clavulanate potassium in 868 children aged between 2 months and 12 years reported protocol defined diarrhoea in 26.7% of children receiving three times daily treatment for 10 days, compared with 9.6% in children receiving twice daily treatment for 10 days ($P<0.0001$), and 8.7% in children receiving twice daily treatment for five days ($P<0.0001$).[7] No P value was quoted for the comparison between 10 day and 5 day twice daily treatments. The trial made no mention of other adverse effects such as rash.

Comment

The five day treatment group did not receive a placebo on days 6-10, which may have biased the results.

Question: What are the effects of preventive interventions?

Option: Long term antibiotic treatment

One systematic review of RCTs has found that long term antibiotic prophylaxis has a modest effect in preventing recurrences of acute otitis media.[8] The questions of which antibiotic to use, for how long, and how many episodes of acute otitis media justify treatment have not yet been adequately evaluated.

Benefits

Versus placebo: We found one systematic review, which identified 33 RCTs comparing antibiotics versus placebo to prevent recurrent otitis media and otitis media with effusion.[8] Nine of the trials (n=945) looked only at recurrent otitis media. It was not clear from the review which of the studies referred only to children; four either included the word "children" in the title or appeared in paediatric journals. Most studies defined recurrent otitis media as at least three episodes of acute otitis media in six months. The most commonly used antibiotics were amoxicillin, co-trimoxazole, and sulfamethoxazole, given for three months to two years. All nine studies showed a lower rate of recurrence with antibiotic treatment, although in seven the difference was not significant. Pooled results showed an absolute risk of 0.08 recurrences per patient per month for active treatment compared with 0.19 for placebo (absolute risk reduction 0.11 episodes per month; 0.03 to 0.19). This is a small effect favouring antibiotics, meaning that nine children with recurrent otitis media would need to be treated for a month to prevent one additional acute episode (number needed to treat 9, confidence interval not quoted).

Key messages

- We found limited evidence from one RCT that non-steroidal anti-inflammatory drugs are more effective than placebo in relieving pain in children with acute otitis media
- Evidence on the effectiveness of antibiotics is conflicting; we found no clear evidence favouring a particular antibiotic for acute otitis media
- One systematic review of RCTs has found greater immediate benefit but no difference in long term outcome with short (≤5 days) rather than longer courses of antibiotics
- One systematic review of RCTs has found that long term antibiotic prophylaxis has a modest effect in preventing recurrences of acute otitis media, but the questions of which antibiotic to use, for how long, and how many episodes of acute otitis media justify treatment have not yet been adequately evaluated

Choice and duration of antibiotic: The same systematic review found no significant difference in rate of recurrence between antibiotics.[8] Greater treatment effect was seen with treatment lasting more than six months, but the confidence intervals overlapped (absoulte risk of recurrence with courses <6 months 0.21, −0.07 to 0.49; with courses >6 months 0.04, −0.01 to 0.09).

Harms

No evidence was presented on the harmful effects of prophylactic treatment.

Comment

None.

Competing interests: None declared.

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