GIMBE®

Gruppo Italiano per la Medicina Basata sulle Evidenze

Evidence-Based Medicine Italian Group

Workshop

L'EBM nell'ambulatorio del pediatra di base

Sesto S. Giovanni (MI), 24 settembre 2005

arseducandi
Società Scientifica per l'Educazione Continua

Workshop Clinici Interattivi (1)

OTITE MEDIA ACUTA

Dalle evidenze scientifiche all'appropriatezza degli interventi sanitari

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Scenario Clinico (1)

- Andrea è un bambino di 30 mesi, nato a termine con peso adeguato, allattato esclusivamente al seno per 6 mesi, quindi con allattamento complementare fino alla data odierna.

- Dall'età di 6 mesi frequenta l'asilo nido comunale.

- Nulla di rilevante nella storia familiare

CLINICAL QUESTIONS

A. Ritieni che l'allattamento al seno sia un fattore protettivo nei riguardi dell'otite media acuta (OMA)?

1. No
2. Sì
3. Non so

clinical evidence

Acute otitis media

Search date March 2004

Paddy O'Neill and Tony Roberts

Otitis media with effusion

Search date March 2004

Ian Williamson

Linee guida OMA - 2003-2005

- Prodigy. January 2005
- Cincinnati Children's Hospital Medical Center. October 2004
- American Academy of Pediatrics, American Academy of Family Physicians,. May 2004
- Institute for Clinical Systems Improvement (ICSI). 2004 May
- SIGN. February 2003

Johnston BL, Conly BL

GUIDELINITIS
A new syndrome?

Can J Infect Dis 2000

Hibble A, Kanka D, Pencheon D, Pooles F

Guidelines in general practice: the new Tower of Babel?

BMJ 1998;317:862-863

Pile of 855 guidelines in general practices in the Cambridge and Huntingdon Health Authority

Hibble A, et al. BMJ,1998

www.agreecollaboration.org

AGREE
Appraisal of Guidelines for Research & Evaluation

- Strumento per la valutazione di qualità delle LG
- Elaborata da un gruppo internazionale
- Finanziamento della Comunità Europea
- Disponibile in versione italiana

- 23 item in 6 dimensioni
  - obiettivi della LG
  - coinvolgimento delle parti in causa
  - rigore metodologico
  - chiarezza espositiva
  - applicabilità
  - indipendenza editoriale

Guidelines for rating the overall assessment:

Strongly Recommend	the guideline rates high (3 or 4) on the majority of items and most domain scores are above 60%. This indicates that the guideline has a high overall quality and that it could be considered for use in practice without provisos or alterations
Recommend (with provisos or alterations)	the guideline rates high (3 or 4) or low (1 or 2) on a similar number of items and most domain scores are between 30 and 60%. This indicates that the guideline has a moderate overall quality. This could also be due to insufficient or lacking information in the guideline for some of the items. If provisos or alterations are made – and sufficient information is provided on the guideline development method - the guideline could still be considered for use in practice, in particular when no other guidelines on the same clinical topic are available.
Would not recommend	the guideline rated low (1 or 2) on the majority of items and most domain scores are below 30%. This indicates that the guideline has a low overall quality and serious shortcomings. Therefore it should not be recommended for use in practice.

Linee guida OMA 2003-2005

- Prodigy. January 2005
- Cincinnati Children's Hospital Medical Center. October 2004
- **American Academy of Pediatrics, American Academy of Family Physicians. May 2004** (score AGREE 73%)
- Institute for Clinical Systems Improvement (ICSI). 2004 May
- **SIGN. February 2003** (score AGREE 82%)

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Diagnosis and management of childhood otitis media in primary care

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ADVICE ON BREASTFEEDING

A large cohort study looked at the relationship between breastfeeding and OME.[22] This one study on breastfeeding shows a protective effect. This is consistent with other proven anti-infective benefits of breastfeeding. | 2++

C **Parents should be advised that breastfeeding may reduce the risk of their child developing otitis media with effusion.**

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Diagnosis and Management of Acute Otitis Media

RECOMMENDATION 5

Clinicians should encourage the prevention of AOM through reduction of risk factors. (This recommendation is based on strong observational studies and a preponderance of benefits over risks.)

- The implementation of **breastfeeding for at least the first 6 months** also seems to be helpful against the development of early episodes of AOM

Scenario Clinico (2)

• All'età di 9 mesi, Andrea presenta scolo sieroso nasale e tosse, trattati dai genitori - come d'abitudine - con lavaggi nasali di soluzione fisiologica.

• Dopo due giorni insorge febbre elevata (sino a 39.5 °C) ed il bambino diventa estremamente irrequieto.

• I genitori, molto preoccupati, lo accompagnano durante la notte al PS, dove, per la presenza di una membrana timpanica iperemica all'otoscopia, viene posta diagnosi di otite media acuta.

CLINICAL QUESTIONS

B. Quanto stimi l'accuratezza diagnostica dell'otoscopia nella diagnosi di OMA

1. Bassa
2. Intermedia
3. Elevata

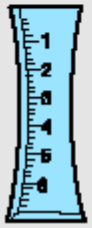
Rothman R, Owens, Simel DL

The Rational of Clinical Examination
Does this child have acute otitis media?

JAMA 2003;290:1633-40

Data sources: English language studies were identified by searching Medline (1966 to May 2002), scanning bibliographies of relevant studies, and searching general and specialty textbooks.

Study selection and assessment: studies were selected if they examined the accuracy of symptoms and signs in the diagnosis of AOM in children. Studies on the diagnosis of persistent otitis media with effusion were excluded. Studies were assessed for methodological quality including whether there was an independent blinded comparison of signs or symptoms against a criterion standard.



Outcomes: sensitivity, specificity, and likelihood ratios.

Rothman R, et al. JAMA 2003

- 6 studies met the selection criteria.

- 1 study (2911 children; age range 6 mo to 2.5 y) examined the accuracy of signs and reported the accuracy of signs on pneumatic otoscopy for diagnosing AOM in children.

Rothman R, et al. JAMA 2003

Accuracy of signs on pneumatic otoscopy for diagnosing acute otitis media in children*

Sign	Result	Adjusted +LR†
Colour	Cloudy colour	34
	Distinctly red colour	8.4
	Slightly red colour	1.4
	Normal colour	0.2
Position	Bulging position	51
	Retracted position	3.5
	Normal position	0.5
Mobility	Distinctly impaired mobility	31
	Slightly impaired mobility	4.0
	Normal mobility	0.2

Rothman R, et al. JAMA 2003

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CLINICAL ASSESSMENT

- ☑ In most situations, the GP will have to depend on history and otoscopy for diagnosing otitis media.
- ☑ Children who require hearing loss assessment should be referred to an audiologist.

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1. **History of acute onset of signs and symptoms**
2. **Presence of middle ear effusion** indicated by one of the following:
   - bulging tympanic membrane (ear drum)
   - decreased mobility of tympanic membrane
   - air-fluid level behind the tympanic membrane
   - discharge from the ear (otorrhea)
3. **Signs and symptoms of middle ear inflammation** indicated by either:
   - distinct erythema of the tympanic membrane *or*
   - distinct otalgia (discomfort clearly referable to the ear that results in interference with or precludes normal activity or sleep)

CLINICAL QUESTIONS

C. Cosa avresti prescritto ad Andrea?

1. Un analgesico (paracetamolo, ibuprofene)
2. Un antibiotico
3. Entrambi i farmaci
4. Nulla

Acute otitis media

Search date March 2004

Paddy O'Neill and Tony Roberts

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OPTION **ANALGESICS**

One RCT in children aged 1–6 years receiving antibiotic treatment found that ibuprofen or paracetamol reduced earache as assessed by parental observation after 2 days compared with placebo.

AOM. Analgesics

1. Utile
2. **Probabilmente utile**
3. Da valutare caso per caso
4. Di utilità non determinata
5. DI utilità discutibile
6. Inutile o dannoso

Clinical Evidence. September 2005

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ANALGESICS

One study of the efficacy of paracetamol for AOM has been identified.[56] The original study was flawed and relied on a parental pain observation scale. Recalculation from the original figures showed a statistically significant benefit for the use of paracetamol. Although non-steroidal anti-inflammatory drugs are frequently used by parents, caution should be exercised because of the side effect profile. 1+

D **Parents should give paracetamol for analgesia but should be advised of the potential danger of overuse.**

Rothman R, et al. JAMA 2003

Bertin L, Pons G, d'Athis P, et al.

A randomized double blind multicentre controlled trial of ibuprofen versus acetaminophen and placebo for symptoms of acute otitis media in children

Fundam Clin Pharmacol 1996;10:387-392

Acute otitis media

Search date March 2004

Paddy O'Neill and Tony Roberts

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OPTION **ANTIBIOTICS**

We found four systematic reviews comparing antibiotics versus placebo in acute otitis media. The reviews used different inclusion criteria and outcome measures. One review in children aged 4 months to 18 years found a reduction in symptoms with a range of antibiotics (cephalosporins, erythromycin, penicillins, trimethoprim–sulfamethoxazole [co-trimoxazole]) after 7–14 days of treatment compared with placebo. Another review in children younger than 2 years found no significant difference in clinical improvement after 7 days between antibiotics (penicillins, sulphonamides, amoxicillin/clavulanic acid [co-amoxiclav]) and placebo alone or placebo plus myringotomy. A third review in children aged 4 weeks to 18 years found that antibiotics (ampicillin, amoxicillin) reduced clinical failure rate within 2–7 days compared with placebo or observational treatment. The fourth review in children aged 6 months to 15 years found that, compared with placebo, the early use of antibiotics (erythromycin, penicillins) reduced the proportion of children still in pain 2–7 days after presentation, and reduced the risk of developing contralateral acute otitis media. This review also found that antibiotics increased the risk of vomiting, diarrhoea, or rashes.

Glasziou PP, Del Mar CB, Sanders SL, Hayem M.

Antibiotics for acute otitis media in children

The Cochrane Database of Systematic Reviews
2005, Issue 3

MAIN RESULTS

- Eight trials (2,287 children), with high methodological quality, showed no reduction in pain at 24 hours, but a 30% relative reduction at 2-7 days.
- Since approximately 80% of patients will have settled spontaneously in this time, this means that about 15 children must be treated with antibiotics to prevent one child having some pain after two days.
- There was no effect of antibiotics on hearing problems, nor did antibiotics influence other complications or recurrence.
- There were few serious complications: only one case of mastoiditis occurred in a penicillin treated group.

Glasziou P et al. Cochrane Library, 2005

AUTHORS' CONCLUSIONS

- Antibiotics provide a small benefit for acute otitis media in children.
- As most cases will resolve spontaneously, this benefit must be weighed against the possible adverse reactions.
- Antibiotic treatment may play an important role in reducing the risk of mastoiditis in populations where it is more common.

Glasziou P et al. Cochrane Library, 2005

AOM. Antibiotics

1. Utile
2. Probabilmente utile
3. **Da valutare caso per caso**
4. Di utilità non determinata
5. Di utilità discutibile
6. Inutile o dannoso

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Antibiotics in comparison to placebo and observational treatment may have a modest benefit on symptom resolution and failure rates, as variously defined, in children over the age of two years with AOM. The available evidence on natural history of AOM shows that in studies with close follow up, very few episodes of mastoiditis or other suppurative complications are reported in children with AOM not initially treated with antibiotics.

B **Children diagnosed with acute otitis media should not routinely be prescribed antibiotics as the initial treatment.**

Scenario Clinico (3)

- I colleghi del pronto soccorso prescrivono ceftriaxone i.m. 500 mg/die per 7 giorni.

CLINICAL QUESTIONS

D. Ritieni che nel trattamento dell'OMA, i diversi antibiotici siano equivalenti in termini di efficacia?

1. Sì
2. No

Acute otitis media

Search date March 2004

Paddy O'Neill and Tony Roberts

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OPTION CHOICE OF ANTIBIOTIC REGIMEN

One systematic review in children aged 4 months to 18 years found no significant difference between a range of antibiotics in rate of treatment success at 7–14 days or of middle ear effusion at 30 days. Another systematic review in children aged 4 weeks to 18 years found no significant difference between antibiotics in clinical failure rates within 3–14 days. The second review also found that adverse effects, primarily gastrointestinal, were more common with cefixime than with amoxicillin or ampicillin, and were more common with amoxicillin/clavulanate (original formulation) than with azithromycin. Systematic reviews of placebo controlled RCTs have found that antibiotics increase the risk of vomiting, diarrhoea, and rashes.

Marcy M, Takata G, Shekelle P, et al.

Management of acute otitis media

Agency for Healthcare Research and Quality, 2001
Evidence Report/Technology Assessment No.15

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CHOICE AND DURATION OF ANTIBIOTIC THERAPY

A large number of studies have established that, where organisms have been isolated from the middle ear, two organisms, *Streptococcus pneumoniae* and *Haemophilus influenzae*, are the principal aetiological agents in bacterial infection.[49] Occasionally *Moraxella catarrhalis* can be isolated.

With *S. pneumoniae* and *H. influenzae*, broad spectrum antibiotics such as amoxicillin, or amoxicillin with clavulanic acid, are the drugs of choice if an antibiotic is to be used. Cefaclor, cotrimoxazole, trimethoprim and erythromycin can be effective, but are less safe than amoxicillin.[50]

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RECOMMENDATION 3B

If a decision is made to treat with an antibacterial agent, the clinician should prescribe amoxicillin for most children. (This recommendation is based on randomized, clinical trials with limitations and a preponderance of benefit over risk.)

When amoxicillin is used, the dose should be 80 to 90 mg/kg per day. (This option is based on extrapolation from microbiologic studies and expert opinion, with a preponderance of benefit over risk.)

Scenario Clinico (4)

• A 28 mesi rivedo Andrea nel mio ambulatorio per la comparsa di febbre (38.7 °C), scolo nasale sieroso e otalgia.

• In base ad un reperto di membrana timpanica sinistra diffusamente iperemica ed estroflessa pongo diagnosi di OMA e:

- prescrivo paracetamolo al bisogno
- propongo una vigile attesa per 48-72 ore

CLINICAL QUESTIONS

E. In quale delle seguenti categorie collocheresti la vigile attesa vs. l'inizio immediato del trattamento antibiotico?

1. Utile
2. Probabilmente utile
3. Da valutare caso per caso
4. Di utilità non determinata
5. Di utilità discutibile
6. Inutile o dannoso

Acute otitis media

Search date March 2004

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OPTION IMMEDIATE COMPARED WITH DELAYED ANTIBIOTIC TREATMENT

One RCT in children aged 6 months to 10 years found that immediate antibiotic treatment reduced the number of days of earache, ear discharge, and amount of daily paracetamol used after the first 24 hours of illness compared with delayed antibiotic treatment, but found no significant difference between groups in daily pain scores. It also found that immediate antibiotic treatment increased diarrhoea compared with delayed antibiotic treatment. Systematic reviews of placebo controlled RCTs have found that antibiotics increase the risk of vomiting, diarrhoea, and rashes.

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DELAYED ANTIBIOTIC TREATMENT

In a delayed treatment trial, 315 children aged six months to 10 years were allocated to one of two treatment strategies: immediate antibiotic or delayed antibiotic (antibiotic to be collected at parents' discretion after 72 hours if the child has not improved).[48] The outcome measures were symptom resolution, absence from nursery or school and paracetamol consumption. The main conclusions from this trial were that:

- immediate antibiotics provided symptomatic benefit mainly after the first 24 hours, when symptoms were already resolving
- immediate antibiotics increased the incidence of diarrhoea by 10%
- only 24% of the parents in the delayed prescription group used antibiotics
- a "wait and see" approach in the management of AOM is feasible and acceptable to most parents and results in a 76% reduction in the use of antibiotic prescriptions.

1+

Little P, Gould C, Williamson I, et al.

Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media

BMJ 2001;322:336–342

AOM. Delayed antibiotic treatment

1. Utile
2. Probabilmente utile
3. **Da valutare caso per caso**
4. Di utilità non determinata
5. Di utilità discutibile
6. Inutile o dannoso

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B **Delayed antibiotic treatment** *(antibiotic to be collected at parents' discretion after 72 hours if the child has not improved)* **is an alternative approach which can be applied in general practice.**

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Diagnosis and Management of Acute Otitis Media

Criteria for initial antibacterial-agent treatment or observation in children with AOM

Age	Certain Diagnosis	Uncertain Diagnosis
<6 mo	Antibacterial therapy	Antibacterial therapy
6 mo to 2 y	Antibacterial therapy	Antibacterial therapy if severe illness; observation option* if nonsevere illness
≥2 y	Antibacterial therapy if severe illness; observation option* if nonsevere illness	Observation option*

- **Observation** is an appropriate option only when follow-up can be ensured and antibacterial agents started if symptoms persist or worsen.
- **Nonsevere illness** is mild otalgia and fever < 39°C in the past 24 hours.
- **Severe illness** is moderate to severe otalgia or fever ≥ 39°C.
- A **certain diagnosis** of AOM meets all 3 criteria: rapid onset, signs of MEE and signs-symptoms of middle-ear inflammation.

Marchetti F, Ronfani L, Conti Nibali S,
for the Italian Study Group on Acute Otitis Media

Delayed prescription may reduce the use of antibiotics for acute otitis media

A prospective observational study in primary care

Arch Pediatr Adolesc Med 2005;159:679-684

Le Saux N, Gaboury I, Baird M, et al.

A randomized, double-blind, placebo-controlled noninferiority trial of amoxicillin for clinically diagnosed acute otitis media in children 6 months to 5 years of age

CMAJ 2005;172:335-41

Damoiseaux RA

Antibiotic treatment for acute otitis media: time to think again

CMAJ 2005;172:657-8

• A randomized controlled trial that compared routine antibiotic treatment of acute otitis media with a wait-and-see approach.

• There was a difference between the 2 treatment arms that favoured the antibiotic group: an 8.6% (CIs 95% 3-15%) improvement in clinical resolution at 2 weeks compared with the wait-and-see group.

• These results show only a moderate effect of antibiotics: 11 children would need to receive antibiotics immediately to prevent 1 failure, defined as the receipt of an antimicrobial within 14 days.

Damoiseaux RAMJ. CMAJ 2005

Scenario Clinico (5)

- Dopo 48 ore la madre, telefonicamente, mi riferisce che, dopo un iniziale miglioramento, da circa 6 ore le condizioni generali sono nettamente peggiorate.
- La temperatura non scende sotto i 39 °C e l'otalgia non è sensibile al paracetamolo.
- Decido allora di iniziare trattamento con amoxicillina 80 mg/Kg/die in 3 somministrazioni
- A 24 ore dalla somministrazione, Andrea è completamente sfebbrato; è più vivace, ricomincia a mangiare e solo occasionalmente presenta segni di otalgia

Scenario Clinico (6)

- Trascorsi due mesi dall'episodio di OMA, la mamma riferisce che Andrea, quasi giornalmente lamenta episodi di dolore all'orecchio, della durata di qualche minuto con remissione spontanea.

- Nel timore di complicanze dai pregressi episodi di OMA, la mamma consulta un'otorinolaringoiatra che rileva all'otoscopia una membrana timpanica opaca e protrusa e prescrive un esame impedenzometrico.

Scenario Clinico (7)

- L'impedenzometria mostra una curva piatta
- Lo specialista conferma la diagnosi di otite media essudativa (OME) e prescrive, per un mese, terapia con:
  - sobrerolo (1 cucchiaio da tavola mattina e sera)
  - citirizina (1 gtt/Kg di peso una volta al giorno)

CLINICAL QUESTIONS

F. I mucolitici e gli anti-istaminici sono efficaci nella terapia dell'OME?

1. Nessuno dei due
2. Solo i mucolitici
3. Solo gli anti-istaminici
4. Entrambi

Otitis media with effusion

Search date March 2004

Ian Williamson

clinical evidence

OPTION ANTIHISTAMINES PLUS ORAL DECONGESTANTS

One systematic review found no significant difference between antihistamines plus oral decongestants compared with placebo in clearance of effusion in children with otitis media with effusion after 4 weeks.

OME. Antihistamines plus oral decongestants

1. Utile
2. Probabilmente utile
3. Da valutare caso per caso
4. Di utilità non determinata
5. Di utilità discutibile
6. **Inutile o dannoso**

Clinical Evidence. September 2005

Otitis media with effusion

Search date March 2004

Ian Williamson

clinical evidence

OPTION **MUCOLYTICS**

One systematic review found no significant difference between 1–3 month courses of carbocisteine or carbocisteine lysine and placebo or no treatment in resolution of effusion. Three small RCTs of bromhexine versus placebo found inconclusive results.

OME: Mucolytics

1. Utile
2. Probabilmente utile
3. Da valutare caso per caso
4. Di utilità non determinata
5. **Di utilità discutibile**
6. Inutile o dannoso

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There is no evidence to support the routine use of antihistamines, decongestants or mucolytics in the management of OME, especially considering the potential adverse side effects.

B **Decongestants, antihistamines or mucolytics should not be used in the management of otitis media with effusion.**

Antihistamines, decongestants and mucolytics are ineffective for OME