Great moments in acute otitis media

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Albuquerque NM

An evidenced based approach to reducing antibiotic use in children with acute otitis media: controlled before and after study

- Cates C.
- Manor View Practice, Bushey Health Centre, Bushey Hertfordshire, UK.

Deferred antibiotics in AOM-2

- Change of office protocol based on recent reviews questioning routine antibiotics.
- AOM + “ill” child: antibiotics.
- AOM + “not particularly ill”:
  - Handout on limited benefit of antibiotics in OM
  - Antibiotic prescription for parents to fill if child did not get better “over a day or two.”
  - Acetaminophen prn.

Deferred antibiotics in AOM-3

- Amoxicillin used as antibiotic of choice.
- Comparison made with monthly antibiotic prescriptions in practice for previous year.
- Local practice acted as control.
- Prescriptions for other antibiotic suspensions scrutinized for substitutions.
- Comparison made with change in national antibiotic prescribing data.
### Deferred antibiotics in AOM-4

**Results**
- Median monthly prescriptions for amoxicillin fell from 75 to 47.
- Corrected for national antibiotic use: decline = 32%, vs 12% in control practice.
- Prescriptions for all antibiotics fell by 19%.
- AOM/Total antibiotics: 50% to 33%.

### Deferred antibiotics in AOM-5

**Conclusions**
- Not all acute otitis media requires antibiotics.
- Parents' tolerance for “masterful inactivity” is more than is usually admitted.
- Educational efforts and risk sharing work well in an office based practice.
- Reduction in antibiotic use is feasible without denial of care.

### Deferred antibiotics: shared-decision model

- 466 parents surveyed.
- Clinical vignettes: shared-decision vs “paternalistic” models
- Parents given “paternalistic” approach were 5 times more likely to use antibiotics than parents approached with shared-decision
- Parents in shared-decision groups more satisfied than those given paternalistic approach (89% vs 76%)

### Primary care based randomized, double blind trial of amoxicillin vs placebo for acute otitis media in children aged under 2 years

- University Medical Center, Utrecht, Nederland
- Damoiseaux RAMJ, van Balen AM, Hoes AW, et al.
- *BMJ* 2000;320:350-4

### Otitis media-2

- Age 6-24 months
- Randomized: amoxicillin 40 mg/kg/d x 10 days or placebo
- Outcome measurement
  - Symptoms at day 4 or clinical deterioration
  - Treatment failure at day 11 by examination
  - Middle ear effusion at 6 weeks
  - Sample size to achieve power of 80%, assuming a minimal 20% outcome difference

### Otitis media-3

**N = 240**
- Symptoms on day 4
  - Amoxicillin 59% vs placebo 72% (Δ risk = 13%, 95% CI = 1% to 25%)
- Treatment failure on day 11
  - Amoxicillin 64% vs placebo 70% (Δ risk = 6.0%, 95% CI = -6% to 18%)
- Duration of fever, pain, analgesic use
  - No difference between groups
- MEE at six weeks
  - Amoxicillin 64%, placebo 67% (Δ risk = 3.0%, 95% CI = -10% to 16%)
Deferred antibiotics in AOM

*BMJ* 2001;322:336-342

- Randomized controlled trial of immediate and delayed antibiotics in 315 children
- 93 general practices, SW England
- Age 6 mos - 10 years
- TM: dull or cloudy with redness, bulging, or perforation

**Deferred antibiotics-results**

- 24% deferred group took antibiotics (usually by day 2)
- Effect of ABX group was ~ 1 days benefit
- No Δ days school missed
- 77% deferred parents satisfied

Antibiotics in AOM:
The final word

- 8 double blinded, randomized, placebo controlled trials; N = 2287 children.
- No reduction of pain at 24 hours.
- Absolute reduction of pain at 2-7 days = 7.0%.
- NNT = 15.
- No effect of antibiotics on hearing, complication rate, recurrences.
- Risk of mastoiditis = 1/2287.

Diagnosis and management of AOM

*Pediatrics* 2004;113:1451-1465

<table>
<thead>
<tr>
<th>Child Age</th>
<th>Certain Diagnosis</th>
<th>Uncertain Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger than 6 mo</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>6 mo to 2 y</td>
<td>Antibiotics if severe illness, observe*</td>
<td>Antibiotics if severe illness, observe*</td>
</tr>
<tr>
<td>2 y or older</td>
<td>Antibiotics if severe illness, observe*</td>
<td>Observe*</td>
</tr>
<tr>
<td></td>
<td>if nonsevere illness</td>
<td>if nonsevere illness</td>
</tr>
</tbody>
</table>

Nonsevere illness implies mild otalgia and fever <39°C orally (about 102°F) or 39.5°C rectally in the past 24 hours. Severe illness is moderate to severe otalgia or higher fever. Certain diagnosis is a clinical picture suggesting AOM with a high probability of middle-ear effusion. Uncertain diagnosis is a clinical picture suggesting AOM with anything less than a high probability of middle-ear effusion.

The politics of AOM-1

- Non-treatment of AOM
  - < 6 m/o: treat
  - 6-24 m/o: treat if “certain” Dx or “severe illness”
  - > 24 m/o: treat if “certain” Dx and “severe illness”
  - Consultant: S. Michael Marcy MD
  - Note: “Dr. Ellen Wald withdrew from the Subcommittee before publication of this guideline”

The politics of AOM-2

- Dr. Wald (Editorial, 2003):
  - In conclusion the “evidence” presented in the recent literature is not sufficient to conclude that the role of antibiotics is minimal in most cases of acute otitis media. The intent of those who encourage watchful waiting is to curb the overuse of antibiotics. However, overuse of antibiotics does not result from treatment of *bona fide* cases of acute otitis media. Rather it is the result of misdiagnosis of middle ear effusion and the indiscriminant treatment of viral upper respiratory infections (including pharyngitis) with antibiotics.
The politics of AOM-3

- Dr Marcy (letter to the editor, 2003)
  - “[In her recent editorial] Dr. Wald overlooked the evidence gained from the largest (536 children) randomized, placebo-controlled, blinded study on management of AOM (Kaleida PH. Pediatrics 1991;87:466-474). Thus, despite Wald’s assertion to the contrary, the evidence would suggest that the role of antibiotics is indeed minimal in most cases of AOM and that a policy permitting an option of watchful waiting for AOM would be appropriate for selected children with assurance of reliable follow-up.”
  - Pediatr Infect Dis J 2003;22:673

The politics of AOM-4

- Dr. Wald (response):
  - “While I am proud to be a coauthor of the study by Kaleida et al, referenced by Dr. Marcy, a careful reading of the article shows that a substantial portion of the children classified as non-severe actually had OME rather than AOM, which likely skewed the results in favor of ‘no’ or little difference. I believe that we are better informed today.”
  - Pediatr Infect Dis J 2003;22:674

Antibiotics for acute otitis media: a meta-analysis with individual patient data

- Wihelmina Children’s Hospital, Utrecht, Netherlands
- Lancet 2006;368:1429-1435

Antibiotics for AOM-2

- Systematic review of Cochrane Library, PubMed, Embase, proceedings of international symposia
- 19 trials available; 10 included; 6 had raw data provided = 1643 children
- Risk factors for pain and/or fever at 3-7 days in placebo group
  - Bilateral disease
  - Otorrhea
- Significant antibiotic modification of pain and/or fever at 3-7 days
  - Otorrhea (NNT = 3)
  - Bilateral disease in age < 2 years (NNT = 4)

Reaction to deferred antibiotics

- 654 parents surveyed
  - 72% women, 71% white, 60% higher education
  - 72% unaware of natural history AOM
- 84 physicians surveyed
  - 100% pediatricians; 43% other specialty

![Graph showing parental and physician comfort levels with deferred antibiotics]
Deferred antibiotics

Conclusions

- While 55% of pediatricians are “comfortable” with deferred therapy for AOM, only 28% of suburban parents share that comfort level.
- Education of parents (and some physicians) is in the best interests of children with acute ear infections.

Education: deferred antibiotics

- 466 parents surveyed. 3 clinical vignettes: shared-decision vs “paternalistic” models.
- Parents given “paternalistic” approach were 5 times more likely to use antibiotics than parents approached with shared-decision.
- Parents in shared-decision groups more satisfied than those given paternalistic approach (89% vs 76%).

Acute otitis media extras

5 vs 10 day therapy

- Meta-analysis of randomized controlled trials.
- Ages 4 weeks to 18 years.
- 17 trials of short-acting antibiotics: 5 vs 10 d.
- Symptoms, relapse, reinfection (5-day) – 8-19 days evaluation: OR = 1.52
  - 30 day evaluation: OR = 1.22
- NNT (number needed to treat)
  - 8-19 days = 13
  - 30 days, NNT = 44
- JAMA 1998;279:1736-1742

Diagnosis and management of AOM

Pediatrics 2004;113:1451-1465

<table>
<thead>
<tr>
<th></th>
<th>Penicillin nonallergic</th>
<th>Penicillin allergic, non-Type 1</th>
<th>Penicillin allergic, Type 1 (urticaria or anaphylaxis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe AOM</td>
<td>High-dose amoxicillin/clavulanate</td>
<td>Ceftriaxone, IM or IV, 1-3 daily doses</td>
<td>Recommendation unclear? clindamycin? 3134</td>
</tr>
<tr>
<td>Nonsevere AOM</td>
<td>High-dose amoxicillin</td>
<td>Cefdinir, ceftiraxime axetil, or cepodoxime proxetil</td>
<td>Azithromycin clarithromycin, or less effective options? **</td>
</tr>
</tbody>
</table>

Severe AOM is accompanied by fever >38°C or severe otalgia, defined as discomfort clearly referable to the ear(s) and interfering with sleep or normal activity.
AOM after 2004 guideline
*Pediatr Infect Dis J* 2006;25:385-389

- 276 physicians
  - 80% Pediatricians; 20% Family Physicians
- Surveys mailed before and after appearance of 2004 Guidelines
- 50% had read the guideline; 40% had read summaries of recommendations

Diagnosis and management of AOM
*Pediatrics* 2004;113:1451-1465

- Recommendation 3B
  - When amoxicillin is used, the dose should be 80-90 mg/kg per day
  - In "severe illness" use high-dose amoxicillin-clavulanate
  - "This is based on extrapolation from microbiologic studies and expert opinion, with a preponderance of benefit over risk"

“Blue smoke and mirrors”

- Author: Jimmy Breslin (1929-)
- Quotation
  - “All political power is primarily an illusion. Mirrors and blue smoke, beautiful blue smoke rolling over the surface of highly polished mirrors, first a thin veil of blue smoke, then a thick cloud that suddenly dissolves into wisps of blue smoke, the mirrors catching it all, bouncing it back and forth.”
  - *How the Good Guys Finally Won* (1975), p 33

Empiric first-line antibiotic treatment of acute otitis in the era of the heptavalent pneumococcal conjugate vaccine

- Garbutt J, Rosenbloom I, Wu, J, Storch GA
- Washington University, St. Louis
- *Pediatrics* 2006;117:1087-1094

Otitis media therapy-2
Methods-1

- Prospective microbiological study for prevalence of pneumococcus
- Continuation of prior study
  - *Pediatrics* 2004;114:342-347
- Children < 7 years with upper respiratory tract infections (all)
- Posterior NP swabs obtained
- 5 years; pediatric offices in St. Louis
- Immunization with PCV-7 assessed
Otitis media therapy-3
Definitions

- Susceptibility to penicillin
  - Pen-S: MIC < 0.12 µg/ml
  - Pen-I: 0.12 ≥ MIC < 2.0 µg/ml
  - Pen-R: MIC ≥ 2.0 µg/ml
- Susceptibility to amoxicillin
  - Amox-S: MIC ≤ 2.0 µg/ml
  - Amox-I: 2.0 > MIC < 8.0 µg/ml
  - Amox-R: MIC ≥ 8.0
- All Pen-I and some Pen-R are susceptible to amoxicillin

NP carriage of pneumococcus in 327 children

<table>
<thead>
<tr>
<th>Year</th>
<th>Pen-S</th>
<th>Pen-I</th>
<th>Pen-R</th>
<th>Amox-I</th>
<th>Amox-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2001</td>
<td>15</td>
<td>15</td>
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<td>2003</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>2004</td>
<td>25</td>
<td>15</td>
<td>5</td>
<td>15</td>
<td>5</td>
</tr>
</tbody>
</table>

Otitis media therapy-5
Results

- Carriage of Pen-I/Pen-R pneumococcus
  - Increased in child care (OR = 2.1)
  - Independent of age
  - The same if < 3 doses of PCV-7
  - Decreased ≥ 3 doses of PCV-7 (OR = 0.4)
- Carriage of Amox-R pneumococcus
  - Increased in child care (OR = 5.3)
  - None with ≥ 3 doses of PCV-7

Otitis media therapy-6
Conclusions

- Prevalence of Pen-R pneumo declined
  - ?PCV-7 vs ?reduction in antibiotic Rx
- Prevalence of Amox-R pneumo is low
  - ~1% children with acute respiratory infection
  - <5% of all children with acute respiratory infection colonized with pneumococcus
- Since <40% of AOM is caused by pneumococcus, risk of Amox-R pneumo AOM is meaningful only in child care attendees and prior ABX use

Diagnosis and management of AOM
*Pediatrics* 2004;113:1451-1465

**Recommendation 3B**

- Amoxicillin dose should be 80-90 mg/kg per day
- In “severe illness” use high-dose amoxicillin-clavulanate
- “This is based on extrapolation from microbiologic studies and expert opinion, with a preponderance of benefit over risk”
AOM: studies confirming guideline recommendations

- Observation vs antibiotics
  - See next slides
- Low dose amox vs high-dose amox
  - None
- Amox vs Amox/Clav: “severe” AOM
  - None
- Are such studies even possible?
  - Doubtful: high spontaneous cure rate
  - Pediatr Infect Dis J 2002;21:891, 894

Trends in otitis media treatment failure and relapse

- Sox CM, Finkelstein JA, Yin R, et al.
- Boston Children’s Hospital
- Pediatrics 2008;121:674-679

Tx failure in otitis media-2
Methods-1

- Retrospective observational study
- Harvard Vanguard Medical Associates
  (14 practice sites; 80 pediatric clinicians); 9 years of data; 111,335 visits for AOM
- Inclusion
  - Age 2 mo. - 12 years
  - “Uncomplicated acute otitis media”
  - Treatment with antibiotics < 14 days
  - No underlying chronic disease

Tx failure in otitis media-3
Methods-2

- “Treatment failure” = 2nd AOM visit associated with different antibiotic RX before initial antibiotic completed
- “Relapse” = 2nd AOM visit associated with different antibiotic Rx after initial antibiotic completed but < 30 days

Annual use of specific antibiotics

Treatment failure and relapse
Antibiotic choice vs event rates
Odds ratio of high vs usual-dose amoxicillin = 1.0

Tx failure and relapse in AOM-4
Conclusions
• Treatment failure and relapse event rates fell marginally from 1996-2004 (TF: 3.9%→2.6%, R: 9.2%→8.9%)
• The proportion of children with AOM who received high-dose amoxicillin increased from 1.7% in 1996 to 41.9% in 2004
• The odds of treatment failure or relapse did not differ between children treated with usual or high-dose amoxicillin

Clinically Defined Treatment Failure at 48–72 Hours After Initial Management With Antibacterial Agents

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Alternative for Penicillin Allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin component, with 6.4 mg/kg per day of clavulanate</td>
<td>Non-type I: ceftriaxone, 3 days; type I: clindamycin</td>
</tr>
<tr>
<td>Ceftriaxone, 3 days</td>
<td>Tympanocentesis, clindamycin</td>
</tr>
</tbody>
</table>

Cultures of non-resolving AOM
• 3 studies
• N= 244 (USA, France, S. Africa)
• Tympanocentesis
• Sterile fluid in 45%, 57% and 73%
• Up to 1/4 had organisms susceptible to current antibiotic

Acute otitis media
Office management
• Default approach: deferred antibiotics
• Indications for initial antibiotics therapy (enhanced symptom relief at 3 days)
  – Young infants with bilateral disease
  – AOM with ototrauma
• Standard dose amoxicillin
• Short-course therapy
  – See: JAMA 1998;279:1736-1742
• Collaborative decision-making with “educated” parent

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“First they ignore you. Then they laugh at you. Then they fight you. Then you win.”

Mahatma Gandhi