Microbiologic Characteristics of Persistent Otitis Media

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Objective: To identify the pathogens isolated from children with acute otitis media who did not respond to antimicrobial drug therapy.

Methods: Retrospective analysis of cultures obtained by tympanocentesis from 46 children.

Results: Organisms were recovered from 34 children (74%), and 43 isolates were recovered from these individuals. The organisms were Streptococcus pneumoniae (16 isolates), Haemophilus influenzae non–type b (12 isolates), Moraxella catarrhalis (5 isolates), Streptococcus pyogenes (5 isolates), Staphylococcus aureus (3 isolates), and Peptostreptococcus species (2 isolates). Resistance to the antimicrobial agent used was found in 27 (63%) of 43 isolates found in 22 patients (48%). Of patients who did not respond to amoxicillin therapy, H influenzae predominated. Streptococcus pneumoniae was recovered from 5 (56%) of 9 of those who did not respond to trimethoprim and sulfamethoxazole therapy, 4 (44%) of 9 patients after azithromycin therapy, 3 (25%) of 12 patients after amoxicillin therapy, and 2 (40%) of 5 patients after cefixime therapy. Streptococcus pyogenes was recovered from 2 (40%) of 5 patients after trimethoprim and sulfamethoxazole therapy and from 2 (40%) of 5 patients after cefixime therapy.

Conclusions: The data illustrate the relation between resistance to antimicrobial drug therapy and failure of patients with otitis media to improve. They also highlight the importance of diagnostic tympanocentesis in establishing the presence of resistant microorganisms.


Growing resistance to the use of antimicrobial agents of all respiratory tract bacterial pathogens has made the management of acute otitis media (AOM) more difficult. Failure of antimicrobial drug therapy to clear the infection can be due to persistence of the pathogen(s) that is often resistant to the antimicrobial drug used.1-7

This study reports our recent experience in evaluating the organisms isolated from the middle ear of infants and children with persistent or unresponsive AOM.

RESULTS

Organisms were recovered from 34 children (74%), and 43 isolates were recovered from these individuals. A single isolate was recovered from 29 children (63%), and 2 organisms were found in 7 patients (15%). The organisms isolated were Streptococcus pneumoniae (16 isolates), Haemophilus influenzae non–type b (12 isolates), Moraxella catarrhalis (5 isolates), Streptococcus pyogenes (5 isolates), Staphylococcus aureus (3 isolates), and Peptostreptococcus species (2 isolates) (Table).

Resistance to the antimicrobial agents used occurred in 27 (63%) of 43 isolates found in 22 patients (48%). These included 10 (62%) of 16 S pneumoniae, 6 (50%) of 12 H influenzae (the 6 were β-lactamase producers), 4 (80%) of 5 M catarrhalis (all were β-lactamase producers), 4 (80%) of 5 S pyogenes, and all 3 S aureus (all were β-lactamase producers).

In 12 patients who did not respond to amoxicillin therapy, H influenzae predominated. Streptococcus pneumoniae was recovered from 5 (56%) of 9 patients who did not respond to trimethoprim and sulfamethoxazole therapy, 4 (44%) of 9 patients after azithromycin therapy, 3 (25%) of 12 patients after amoxicillin therapy, and 2 (40%) of 5 patients after cefixime therapy. Streptococcus pyogenes was recovered from 2 (40%) of 5 patients after trimethoprim and sulfamethoxazole therapy and from 2 (40%) of 5 patients after cefixime therapy.
PATIENTS AND METHODS

Middle ear exudates were aspirated through tympanocentesis from children seen consecutively as referrals between June 1996 and December 1997 with bilateral AOM who did not respond to a single course of at least 7 days of oral antimicrobial drug therapy. The referring physician chose the antimicrobial drug that the child was taking at the time. A total of 57 patients were examined; however, only 46 patients were included in the final analyses. Seven patients were excluded because their external ear canal culture was not sterile, and 4 patients were excluded because insufficient amounts of middle ear fluid were obtained.

All patients had clinical signs of active infection (ie, fever and irritability), including opacified red-gray or yellow bulging tympanic membranes, despite antimicrobial drug therapy. Patient ages ranged from 10 months to 4 years 8 months, and 27 patients were boys.

Tympanocentesis was performed to relieve the pain and irritability, to attempt to recover the organism(s) causing the infection, and to assist in the correct choice of antimicrobial drug therapy. Acute otitis media was defined as the presence of irritability, ear tugging, or middle ear effusion determined by pneumatic otoscopy. The antimicrobial drugs given to the children before tympanocentesis (Table) were selected according to the patients’ needs, taking into consideration past medical history, previous antimicrobial drug use, tolerance, adverse effects, cost, and compliance. The dosages of the antimicrobial drug were those recommended by the manufacturer. Excluded were children who had serous ear effusion, otorrhea, tympanostomy tubes, craniofacial anomalies, and severe and long-term medical problems. Also excluded were those receiving antimicrobial drugs in the past 3 months.

Compliance with administration of antimicrobial drugs was evaluated in all instances by examining the unused amount of medication and was deemed to be good.

COLLECTION OF SPECIMENS

Specimens were collected only from the ear that was still infected. Bilateral tympanocentesis was performed in 7 children; however, the microbiologic data were reported per patient. The external ear canal was cleaned of cerumen with a blunt curette when indicated, swabbed with povidone-iodine (Betadine) and a 70% alcohol solution, and allowed to dry for 2 to 3 minutes. A swab of the external auditory canal was obtained for culture for aerobic and anaerobic bacteria to document the sterility of the external auditory canal. The only cultures considered for study were those obtained from patients whose external ear canal cultures showed no growth. Exudate was collected with an 18-gauge needle covered by a plastic cannula attached to a 2-mL syringe (Medicut, Sherwood Medical Instruments, St Louis, Mo). The needle was bent to a 45° angle, and the cannula was slipped forward to cover the tip. When the tympanic membrane was approached via an otoscope, the cannula was retracted, the eardrum was penetrated in the posterior inferior quadrant, and the exudate was collected. Thus, the needle tip did not make contact with the speculum or the auditory canal.

MICROBIOLOGIC STUDIES

Each middle ear aspirate was diluted 1:10 in preduced thioglycolate broth (Difco Laboratories, Detroit, Mich). The suspension was shaken vigorously and used immediately for quantitative colony count by inoculation onto aerobic and anaerobic media. Sheep blood agar, chocolate agar, and MacConkey agar plates were inoculated for aerobes. The plates were incubated at 37°C aerobically (MacConkey) or under 5% carbon dioxide and were examined at 24 and 48 hours. For anaerobes, the material was plated on preduced phytanadione-enriched Brucella blood agar and anaerobic blood agar plates containing kanamycin sulfate and vancomycin hydrochloride and then placed into enriched thioglycolate broth (containing hemin, sodium bicarbonate, and phytanadione). The plates were incubated in anaerobic jars and examined at 48 and 96 hours. The thioglycolate broth was incubated for 14 days. Aerobes and anaerobes were identified by techniques described previously. Standard quality control strains were included in each run. Minimum inhibitory concentrations were determined by the agar dilution method with Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md) supplemented with 5% sheep blood. For minimum inhibitory concentration determinations, suspensions with a turbidity equivalent to that of a 0.5 McFarland standard were prepared by suspending growth from blood agar plates in 2 mL of Mueller-Hinton broth (BBL Microbiology Systems). Suspensions were further diluted 1:10 to obtain a final inoculum of 10⁶ colony-forming units per spot. Plates were inoculated with a Steers replicator and incubated overnight in ambient air at 37°C. Standard quality control strains were included in each run. In addition, minimum inhibitory concentration determinations of azithromycin were read after an additional 24 hours of incubation.

If the same organism was isolated from both aspirates in a case of bilateral disease, it was considered a single isolate for that patient.

These data illustrate the relation between resistance to antimicrobial drug therapy and failure of patients with otitis media to improve. Some antimicrobial drugs used seemed to be less effective in eradication of the infection than others (eg, amoxicillin, trimethoprim and sulfamethoxazole, cefixime, and azithromycin), whereas others were not associated in this study with antimicrobial drug therapy resistance–related failures (eg, amoxicillin and clavulenate potassium, cilprozil, and cefuroxime axetil). These findings confirm previous reports in which such a relationship was found. Harrison et al illustrated a higher isolation of H influenzae and S aureus in patients with recently treated or persistent otitis media compared with untreated AOM. In contrast, Pichichero and Pichichero showed a smaller rate of recovery of organisms from persistent otitis media. The lack of recovery of any organism in approximately a quarter
of the patients may be due to infection caused by viruses or atypical organisms.\textsuperscript{13}

The recovery in 12 of our patients (26\%) of organisms that were susceptible to the antimicrobial agent used is similar to that found by Pichichero and Pichichero\textsuperscript{14} (42 [31\%] of 137 patients). These findings suggest that factors other than antimicrobial susceptibility can contribute to persistent infection. These include the presence of a concomitant viral infection, bioavailability of the antimicrobial drugs, penetration into the middle ear fluid, and activity in the pus.

\textit{Haemophilus influenzae} susceptible to azithromycin use was isolated in 2 ear aspirates in this study in patients treated with this agent. Dagan et al.\textsuperscript{13} who also observed this phenomenon, explained the persistence of the organism as a result of concentration of azithromycin only within the middle ear white blood cells and not in the middle ear fluid.

Although the number of patients reported in this study is relatively small, our results highlight the important role of antibiotic-resistant pathogens in the failure to eradicate otitis media. Further studies using 2 ear taps\textsuperscript{8} could shed more light on this problem because they can compare bacterial resistance before and after antimicrobial drug therapy. The growing resistance of organisms in the community and by consideration of improved by knowledge of the resistant pattern of the species that were susceptible to the antimicrobial agent used within the middle ear white blood cells and not in the middle ear fluid.

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