Management of chronic suppurative otitis media: superiority of therapy effective against anaerobic bacteria

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The aerobic and anaerobic microbiology and management of 69 children who had chronic suppurative otitis media were studied retrospectively. A total of 188 isolates (103 anaerobic and 85 aerobic) were recovered. Anaerobic organisms alone were isolated from 11 (16%) aerobic bacteria only in 21 (30%) and mixed aerobic and anaerobic flora was present in 37 (54%). Forty-five beta-lactamase-producing bacteria were recovered from 60 (58%) patients. The most rapid time for resolution was

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abnormalities were present; (6) none had ear tubes in place at the time they were treated. (However, 16 of the children had had prior placement of ear tubes.)

Four had had previous surgery for chronic mastoiditis. That procedure was done at least 8 months before the study. The children's ages ranged from 4 years to 17 years and 6 months (average, 14 years and 3 months) and they presented to the ear, nose and throat clinic with unilateral or bilateral CSOM. The exacerbation included an increase in the purulent secretion from the middle ear, local pain and fever. They all had a past medical history of repeated ear infections for 9 months to 8 years (average, 21 months) and had received previous courses of local therapies and systemic antimicrobial therapy for their infection. The agents that were given were ampicillin (32 patients), a cephalosporin (24), dicloxacillin (18), erythromycin (12), cefaclor (9) and penicillin (8).

Collection of specimen. Cultures were performed in all cases before therapy and in those who failed to respond to therapy within 7 to 15 days of therapy. The external ear canal was cleaned of cerumen and pus with a blunt curet when indicated. It then was swabbed with povidone-iodine (Betadine®) and a 70% alcohol solution and allowed to dry for 3 minutes. A culture of the external auditory canal was obtained using a swab soaked in sterile saline. The swab was spread immediately onto media supportive for the growth of aerobic and anaerobic bacteria in order to document the sterility of the external canal. The only cultures considered in the study were obtained from patients whose external ear canal culture showed no growth after the above procedure. In this manner 7 additional patients were excluded from the study. Five more patients in whom sufficient amounts of middle ear fluid were obtained also were excluded from the study.

Collection of the exudate was done through a perforation in the tympanic membrane with an 18-gauge Medicut® (Sherwood Medical Instruments, St. Louis, MO), which consisted of an 18-gauge needle covered by a plastic cannula and attached to a 2-ml syringe. The needle was bent to a 45-degree 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 entered through the perforation and the exudate was collected. Thus no contact by the needle tip was made with the speculum or the auditory canal, and pus was collected only from the middle ear.

Microbiology. Each middle ear aspirate was inoculated onto aerobic and anaerobic media. The number of organisms was determined semiquantitatively.

Sheep blood agar, chocolate agar and MacConkey's agar plates were inoculated for aerobes. The plates were incubated at 37°C aerobically (MacConkey's) or under 5% CO₂ and examined at 24 and 48 hours. For anaerobes the material was plated on prerduced vi-
Antimicrobials were administered for 10 to 35 days. Patient evaluation. Evaluation of patients' responses was made on a daily basis by the treating physicians from the departments of pediatrics or otorhinolaryngology. It was done immediately after collection of the specimen and therefore was not influenced by the microbiology of the infected ear. The oral antimicrobials prescribed to the patients were clindamycin hydrochloride (150 to 300 mg every 6 hours) in 20 patients, ampicillin trihydrate (250 mg every 8 hours) in 24, erythromycin ethyl succinate (500 mg every 8 hours) in 13, cefaclor monohydrate (250 to 500 mg every 8 hours) in 12. Intramuscular gentamicin sulfate (5 mg/kg) was given in addition to the above agents to 20 patients whose ear aspirates culture showed the presence of moderate to large numbers of (3+ to 4+) Gram-negative aerobic bacilli (9 with clindamycin, 8 with ampicillin, 2 with cefaclor and 1 with erythromycin). No local antibiotic therapy was given. However, the patients had daily ear cleansing and suction of secretions. Gentamicin therapy was started 24 to 48 hours after the therapy with the initial antimicrobial was started.

Patient evaluation. Evaluation of patients' responses was made on a daily basis by the treating physician as the patients were in a chronic care facility, and the patients were followed with the use of an otoscope for at least 6 months. Patients' responses to therapy were judged as either cure or failure. Clinical cure was defined as elimination of all the signs and symptoms of CSOM and the disappearance of otorrhea. Whenever both ears were affected the patient was considered cured when both ears were cured. Antimicrobials were administered for 10 to 35 days (mean, 22). No difference was noted in the age, sex, primary illness that required admission to the chronic care facility, duration of chronic otitis media, frequency of prior placement of ear tubes or occurrence of mastoiditis among the four groups of patients who received the different antimicrobials. The antimicrobials were well-tolerated and the only side effect noted was diarrhea in 2 patients who received ampicillin. Patients who failed to respond to antimicrobial therapy had their therapy changed, and some were referred to acute care facilities for further medical and surgical therapy. Statistical analysis was done using the chi square and Wilcoxon tests.

RESULTS

In 25 patients aspirates were obtained from both ears, but only those from the right ears were included in the final analysis (Table 1). A total of 188 organisms, 85 aerobic (1.2/specimen) and 103 anaerobic isolates (1.5/specimen), were recovered from middle ears of the patients. Aerobic bacteria only were isolated in 21 patients (30%) and anaerobic organisms only in 11 patients (16%). Mixed aerobic and anaerobic isolates were recovered from 37 patients (54%). Thus anaerobes were recovered from 70% and aerobes from 84% of the patients studied. Some of the microbiologic data were presented in detail in a previous publication. The organisms recovered from the 4 therapeutic groups are presented in Table 1. No differences were noted in the number of isolates per patient and types of bacteria recovered in each of the groups.

The most common bacteria isolated from the middle ear aspirates, in descending order of frequency, were anaerobic Gram-positive cocci, Prevotella sp., Bacteroides sp., Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae and Fusobacterium sp. (Table 1).

In 11 patients (16%; with 8 aerobic and 3 anaerobic bacteria present) only 1 isolate was recovered. In the rest of the cases in which mixed anaerobic and aerobic bacteria were present, 2 to 7 isolates/specimen (average, 3.1 isolates/specimen) were recovered. The combinations of the different isolates varied, and there was no consistent pattern. There were 45 beta-lactamase-producing bacteria (BLPB) (30 aerobes and 15 anaerobes) recovered from 40 (58%) patients. They were equally distributed among the 4 therapy groups. These organisms included all 14 isolates of S. aureus and 4 Bacteroides fragilis group, 7 of the 15 Prevotella sp., 4 of the 7 Porphyromonas asaccharolytica, 5 of 12 of P. aeruginosa, 7 of 10 of K. pneumoniae, 3 of 6 of Haemophilus influenzae and 2 of the 4 of Staphylococcus epidermidis.

The patients' response to therapy (Table 2) was the...
fastest and the best with clindamycin ($P < 0.05$ compared to all other therapies). Eighty percent of the patients responded to clindamycin as compared to 50% of those treated with ampicillin, 46% with erythromycin and 33% with cefaclor.

Thirty-six organisms resistant to the antimicrobials given were recovered in 26 of the 31 patients who failed to respond to therapy. These included 21 anaerobic and 15 aerobic organisms (Table 1). The most common ones were Prevotella sp. (8 isolates), S. aureus (4), Bacteroides sp. (6) and P. aeruginosa (4).

**DISCUSSION**

The organisms recovered in this study are similar to those found in previous studies of CSOM where $S.\\ aureus$, $P.\\ aeruginosa$, Proteus sp., Peptostreptococcus sp., Bacteroides sp., Prevotella sp. and Porphyromonas sp. were the major pathogens. Many of the anaerobic bacteria that were recovered from the patients with CSOM are resistant to beta-lactam antibiotics through the production of beta-lactamase. More than 40% of the isolates of Prevotella and Porphyromonas sp. (previously Bacteroides melaninogenicus group) resist beta-lactam antibiotics through the production of beta-lactamase, and are also not inhibited by erythromycin. The recovery of BLPB is not surprising because most of our patients had received in the past multiple courses of antimicrobial agents including penicillins, which might have selected for BLPB.

$P.\\ aeruginosa$ was recovered from only 12 (17%) of our patients. This relatively lower recovery rate of this organism in this report than in others may be attributable to the methods used to collect the pus specimens from the middle ear, avoiding any possible contamination of the specimen from the bacteria present in the ear canal.

Our previous report described that cultures collected from the external auditory canal before sterilization can be misleading. This is particularly important in the case of $P.\\ aeruginosa$ which was more frequently
recovered in the external auditory canal than in the middle ear. Although this organism is a common inhabitant of the external auditory canal, it can also be recovered from the middle ear, where it may participate in the inflammatory process. Direct middle ear aspirations through the perforation in the eardrum are therefore more reliable in establishing the bacteriology of chronic otitis media and can assist in the selection of proper antimicrobial therapy.

The appearance of penicillin resistance among Gram-negative anaerobic bacteria has important implications for chemotherapy. Many penicillin-resistant bacteria can produce enzymes that degrade penicillins or cephalosporins. Such organisms, when present in a localized infection, can release the enzyme into the environment. By so doing they might degrade penicillin in the area of infection, and protect not only themselves but also penicillin-susceptible pathogens. Therefore penicillin therapy directed against a susceptible pathogen might be rendered ineffective by the presence of a BLPB.

We were recently able to detect the actual enzyme activity in the ear aspirate of over 70% of patients with CSOM who were infected with BLPB. This finding raises the possibility that this enzyme not only is able to protect the BLPB but also can degrade penicillin in the ear fluid, thus protecting penicillin-susceptible organisms.

The results of this retrospective study illustrate the efficacy of clindamycin therapy over other therapies that do not provide adequate coverage against resistant aerobic and anaerobic bacteria. This study illustrates that failure to respond to beta-lactam antibiotics or macrolides is often associated with the presence of resistant organisms. Recent studies illustrated the increased recovery rate of BLPB in numerous upper respiratory infections in children. The number of these BLPB was shown to increase after administration of beta-lactam antimicrobial therapy.

Clindamycin, an analog of lincomycin, is distributed rapidly in body fluid and was found to have good bone penetration and to be very effective in the treatment of anaerobic infections. However, clindamycin has poor penetration into the central nervous system. It is also a very effective drug in the treatment of many aerobic organisms, especially S. aureus which is one of the pathogens frequently isolated from cases of CSOM. Usually the drug is very well-tolerated; however, diarrhea and colitis have rarely been reported. Diarrhea or colitis, however, have been rarely observed in pediatric patients.

Although judicious selection of antimicrobial agent is essential for the treatment of CSOM and its complications, surgical intervention for correction of pathology and the evacuation of pus is frequently required, especially in patients who fail to improve with antimicrobial therapy. In patients who do not respond to appropriate initial antimicrobial therapy within 14 days, surgical drainage is usually required. Surgical drainage is therefore an integral part of the management of these cases.

The recovery of these aerobic and anaerobic BLPB requires the administration of appropriate antimicrobial agents such as clindamycin, lincomycin, metronidazole plus a macrolide or one of the newer agents that were not available at the time of this study, such as the combination of a penicillin and a beta-lactamase inhibitor or imipenem. Therapy directed against P. aeruginosa and Enterobacteriaceae should be added to those agents who do not possess antibacterial activity against these bacteria whenever they are also isolated from the middle ear. These antimicrobials include aminoglycosides, quinolones (in adults) and cefazidime.

Antimicrobial therapies should be adjusted to the specific organisms isolated in each patient and sometimes are administered for prolonged periods of time that may range from 21 to 42 days.

The early initiation of appropriate antimicrobial therapy in CSOM, with consideration of the probable presence of resistant aerobic and anaerobic organisms, is of utmost importance. Appropriate early medical and surgical therapy of CSOM could reduce the likelihood of the irreversible destructive sequelae in the middle ear and other complications.

Although this retrospective study demonstrates the superiority of clindamycin over agents less effective against aerobic and anaerobic BLPB, prospective studies are warranted further to investigate the management of CSOM and conclusively establish the optimum therapeutic approach toward this infection.

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REFERENCES

Comparison of a three-component acellular pertussis vaccine with whole cell pertussis vaccine in two-month-old children

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An acellular pertussis vaccine (DTaP) containing pertussis toxoid, filamentous hemagglutinin and the 69-kDa outer membrane protein (pertactin) was compared with United States-licensed whole cell pertussis vaccine (DTwP) as a three dose sequence at 2, 4 and 6 months of age. Eighty infants were enrolled; 62 received DTaP and 18 received DTwP. Sixty-two infants had preimmunization and 1 month postimmunization sera available for pertussis antibodies. No infant experienced a serious adverse reaction. Significantly fewer infants in the DTaP group experienced irritability (P < 0.001) and moderate to severe injection site pain and redness (P < 0.001, and P = 0.03, respectively). The DTaP group also had significantly greater increases in geometric mean titers of antibodies against filamentous hemagglutinin (P < 0.001) and pertactin (P = 0.006). This three-component DTaP vaccine induced an antibody response to pertussis toxin, filamentous hemagglutinin and pertactin but caused fewer adverse reactions than DTwP when administered as a three-dose schedule.

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