Effects of Amoxicillin and Cefdinir on Nasopharyngeal Bacterial Flora

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Objective: To compare the effects of cefdinir (14 mg/kg per day) and amoxicillin (90 mg/kg per day) antimicrobial therapy on the nasopharyngeal flora of children with acute otitis media.

Design: Nasopharyngeal cultures for aerobic and facultative bacteria were obtained before therapy and 2 to 4 days after completion of therapy.

Setting: Outpatient clinic.

Patients: Fifty children, aged 7 months to 5 years 4 months.

Main Outcome Measures: After completion of therapy, 22 (88%) of the 25 patients treated with cefdinir and 16 (64%) of the 25 patients treated with amoxicillin were considered clinically cured (P < .05). A significant reduction in the number of all isolates occurred following therapy in those treated with cefdinir (36 vs 71, P < .01) or with amoxicillin (56 vs 73, P < .05). However, the total number of isolates recovered after therapy was significantly lower in those treated with cefdinir (36) compared with those treated with amoxicillin (56) (P < .01).

Results: The recovery of potential pathogenic organisms (eg, Streptococcus pneumoniae, Staphylococcus aureus, β-hemolytic streptococci, Haemophilus species, and Moraxella catarrhalis), as well as penicillin-resistant bacteria, was lower following completion of therapy in the cefdinir group (6 pathogens, including 5 that were penicillin resistant), compared with the amoxicillin group (27 pathogens, including 16 that were penicillin resistant) (P < .01).

Conclusion: This study illustrates the greater ability of cefdinir compared with amoxicillin to reduce the number of potential nasopharyngeal pathogens as well as penicillin-resistant bacteria in children with acute otitis media.


Carriage of potential respiratory pathogens such as Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis is significantly higher in children prone to otitis media and in the general population of young children with respiratory illness. Administration of antimicrobial agents can affect the composition of the nasopharyngeal bacterial flora. Elimination of potential pathogens may reduce the risk of subsequent respiratory tract infection.

This study compared the effects of cefdinir with those of amoxicillin on the nasopharyngeal flora of children with acute otitis media (AOM). Cefdinir is a broad spectrum second-generation cephalosporin that is effective against aerobic β-lactamase–producing bacteria (BLPB), while amoxicillin is a relatively narrower spectrum antibiotic.

Methods

Children diagnosed as having AOM and treated with either cefdinir or amoxicillin were included in the retrospective analysis. Acute otitis media was defined as the presence of new onset of irritability, ear tugging, and the presence of middle ear effusion determined by pneumatic otoscopy. Sixty-one subjects were entered in the study, but only 50 subjects were evaluated because 11 (5 in the amoxicillin group and 6 in the cefdinir group) were found not to have met the entry criteria (those children who had received antimicrobial therapy in the previous 3 months, had attended any type of daycare facility, or who had underlying illnesses or facial anomalies). The evaluated children were 25 consecutive patients who received cefdinir and 25 who received amoxicillin, had completed their course of therapy, and were monitored for cultures as outlined in the “Methods” section. The patients were treated during the winter season (November to March). The choice of antimicrobial agent...
was made by the examining physician at his or her discretion. The age range of each group was similar: 8 months to 5 years 4 months (mean age, 2 years 7 months) in the cefdinir group, and 7 months to 5 years 1 month (mean age, 2 years 4 months) in the amoxicillin group. Sex distribution was also similar in the 2 groups; there were 16 male and 11 female patients in the cefdinir group and 14 male and 12 female patients in the amoxicillin group.

Six patients in the cefdinir group and 3 in the amoxicillin group had a history of recurrent AOM.

Nasopharyngeal cultures were obtained through the nasal route before the patients began antimicrobial therapy and on follow-up visits 2 to 4 days after completion of 10 days of therapy. These cultures were obtained with calcium alginate swabs that were immediately plated into media supportive of the growth of aerobic bacteria. Specimens were processed semiquantitatively, and organisms were identified and β-lactamase production was determined as previously described.1 All isolates of S pneumoniae were screened for penicillin susceptibility with a 1-µg oxacillin sodium disk using the Kirby-Bauer disk diffusion method. Resistance was confirmed by microdilution cation-adjusted method. Resistance was determined as previously described.3 All isolates of S pneumoniae, S aureus, and M catarrhalis were divided into serotype groups according to the National Committee for Clinical Laboratory Standards.4 Intermediate resistance to penicillin was defined as a minimum inhibitory concentration of 0.1 to 1.0 µg/mL, and high resistance to penicillin was defined as a minimum inhibitory concentration of 2.0 µg/mL or greater.

Patients received either 14 mg/kg per day of cefdinir in 1 dose or 90 mg/kg per day of amoxicillin divided into 2 doses. Both drugs were administered for 10 days. Compliance with therapy was assessed by inspecting unused medicine after completion of treatment. Patients who failed to take more than 2 doses or whose caregivers failed to return their medicine bottles and dosage cards were excluded. Patients were evaluated clinically 2 to 4 days after completion of antimicrobial therapy. Patients were considered clinically cured if their initial clinical symptoms of AOM were no longer present and if the signs of tympanic membrane inflammation subsided. The protocol was approved by the institutional review board. Statistical analysis was done using the Fisher exact test (P value represents a 2-sided test).

RESULTS

After completion of therapy, 17 (68%) of the patients treated with amoxicillin and 22 (88%) of those treated with cefdinir were considered clinically cured (P<.05). Persistence of middle ear fluid was present in 11 (44%) of those treated with amoxicillin and in 7 (28%) treated with cefdinir.

The most commonly recovered aerobic species in both therapy groups were α-hemolytic and nonhemolytic streptococci, S pneumoniae, β-hemolytic streptococci, H influenzae, Staphylococcus aureus, and M catarrhalis (Table).

A significant reduction in the total number of the different isolates occurred following antimicrobial therapy in those treated with amoxicillin (56 vs 73; P<.05) or cefdinir (36 vs 71; P<.01). However, the number of isolates recovered after therapy was significantly lower in those treated with cefdinir (36) compared with amoxicillin (56) (P<.01) (Table).

The recovery of potential pathogenic organisms (eg, S pneumoniae, S aureus, β-hemolytic streptococci, Hae
mophilus species, and M catarrhalis) as well as penicillin-resistant bacteria was lower following completion of antimicrobial therapy in the cefdinir group (6 pathogens, including 5 that were penicillin resistant) compared with the amoxicillin group (27 pathogens, including 16 that were penicillin resistant) (P<.01).

Thirty-three potential pathogens (1.32 isolates per specimen) were recovered from 19 (76%) of the amoxicillin-treated patients prior to antimicrobial therapy, compared with 27 (1.08 isolates per specimen) recovered from 15 patients (60%) after therapy (P>.50). Thirty-two potential pathogens (1.28 isolates per speci-

<table>
<thead>
<tr>
<th>Organism</th>
<th>Amoxicillin Therapy (n = 25)*</th>
<th>Cefdinir Therapy (n = 25)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before Therapy</td>
<td>After Therapy</td>
</tr>
<tr>
<td>Gram-positive cocci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Streptococcus pneumonia†</td>
<td>10 (4)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>*α-Hemolytic streptococcus</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>*β-Hemolytic streptococcus</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Group A†</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>*Staphylococcus aureus†</td>
<td>3 (3)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>*Staphylococcus epidermidis</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Gram-negative cocci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Moraxella catarrhalis†</td>
<td>6 (6)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Gram-positive bacilli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactobacillus species</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Diphtheroid species</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Haemophilus influenzae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type b†</td>
<td>2 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Non-type b†</td>
<td>9 (4)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>73 (18)</td>
<td>58 (16)</td>
</tr>
</tbody>
</table>

*The number of penicillin-resistant isolates is given in parentheses.
†Potential pathogens.
Eighteen penicillin-resistant bacteria were isolated from 15 (60%) of the amoxicillin-treated patients before therapy (Table). This included 4 penicillin-resistant \textit{S. pneumoniae} and 14 BLPB. Following therapy, 16 penicillin-resistant organisms were recovered from 12 patients (48%), including 2 \textit{S. pneumoniae} and 14 BLPB (P > .05). Nineteen penicillin-resistant bacteria were recovered for 16 (64%) of the cefdinir-treated patients before therapy. These included 5 penicillin-resistant \textit{S. pneumoniae} and 14 BLPB. After therapy, 5 penicillin-resistant organisms were recovered from 4 patients (16%), including 2 \textit{S. pneumoniae} and 3 BLPB (P < .005).

No differences were noted in the microbiological findings between those patients who were clinically cured and those who were not cured.

Adverse effects were noted in 6 patients; diarrhea (more than 3 watery stools in 24 hours) was noted in 2 patients in the amoxicillin group and in 2 in the cefdinir group, and vomiting in 1 patient in the amoxicillin group.

**COMMENT**

This study compared the effects on the nasopharyngeal bacterial flora of 2 antibiotics: cefdinir and amoxicillin. A greater reduction in the number of colonizing species was achieved with cefdinir. The greater eradication ability of cefdinir may be the result of its ability to eradicate BLPB. These organisms (ie, \textit{H. influenzae} and \textit{M. catarrhalis}) may not only cause infection but may also “shield” penicillin-susceptible \textit{S. pneumoniae} from antimicrobial activity. \textsuperscript{3}Eradication of nasopharyngeal pathogens may have a beneficial effect because it may prevent recurrent infection. \textsuperscript{2}

Even though increasing the dose of amoxicillin is recommended for the treatment of AOM caused by penicillin-resistant \textit{S. pneumoniae}, \textsuperscript{6} this may not be sufficient to reduce the colonization of the oropharynx and the adenoids \textsuperscript{7} by this organism, where it may be protected by the presence of BLPB. In fact, in our study, amoxicillin reduced the number of \textit{S. pneumoniae} isolates from 8 to 7, whereas cefdinir reduced it from 9 to 2. The persistence of colonization by \textit{S. pneumoniae} may allow for later reinfection of the middle ear and reoccurrence of AOM.

The phenomena of “shielding” was demonstrated in vitro as well as in vivo and is one of the explanations for the failure of penicillin in the treatment of group A streptococcal tonsillitis. \textsuperscript{9} \textit{β}-Lactamase activity was detected in various upper respiratory tract infection sites. These include middle ear, sinus cavity, and tonsillar tissue. \textsuperscript{9} Actual enzyme activity in the ear fluid was detected in aspirates of more than 70% of patients with otitis media who were infected with BLPB. These included all those who were infected with \textit{β}-lactamase–producing \textit{H. influenzae} and 75% of those infected with \textit{M. catarrhalis}. \textsuperscript{7}

Further evidence of the “shielding” effect of \textit{β}-lactamase comes from a study that investigated \textit{β}-lactamase activity in middle ear aspirates obtained from 12 children with AOM who failed to respond to oral amoxicillin therapy. \textsuperscript{9} \textit{β}-Lactamase–producing bacteria were recovered in all 19 culture-positive aspirates, and \textit{β}-lactamase activity was detected in 17 (89%) of the 19 culture-positive aspirates, which suggests that the enzyme might not only protect the BLPB but also shield amoxicillin-susceptible organisms. Amoxicillin was not detected or was present in lower concentrations in the middle ear aspirates with BLPB, and non-BLPB were able to survive alongside BLPB in the face of amoxicillin therapy in 8 instances.

These data demonstrate the superiority of cefdinir compared with amoxicillin in reducing the number of potential AOM pathogens as well as the number of penicillin-resistant bacteria in children with AOM. Further long-term studies are warranted to explore whether such therapy can reduce the failure as well as recurrent rate of AOM and how quickly recolonization of the nasopharynx occurs following therapy.

**Submitted for Publication:** October 4, 2004; accepted April 15, 2005.

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**Financial Disclosure:** None.

**REFERENCES**