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Efficacy of Penicillin versus Cefdinir in Eradication of Group A Streptococci and Tonsillar Flora

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Core tonsillar cultures were obtained from 40 children with recurrent tonsillitis treated with either penicillin or cefdinir. Group A beta-hemolytic streptococci were isolated from 11 penicillin- and 3 cefdinir-treated ($P < 0.001$) patients. β-Lactamase producers were recovered from 17 penicillin- and 3 cefdinir-treated ($P < 0.01$) patients. Inhibiting alpha-hemolytic streptococci were isolated less often from penicillin-treated patients than from cefdinir-treated patients.

Penicillin failure to eradicate group A beta-hemolytic streptococci (GABHS) from inflamed tonsils is of great concern (8). One explanation of this phenomenon is that β-lactamase-producing bacteria (BLPB) protect GABHS by inactivating penicillin (1). Another explanation is that the preservation of alpha-hemolytic streptococci (AHS) that possess interfering capabilities against GABHS contribute to the eradication of this organism (13).

Several classes of antimicrobials that are active against GABHS and BLPB are more effective than penicillin in eradicating GABHS from recurrently inflamed tonsils (1, 5, 7). A possible explanation for the improved efficacy of cephalosporins over penicillin is the activity of cephalosporins against BLPB and their relative inactivity against AHS.

This study investigated the effects of penicillin and cefdinir therapies on the core tonsillar aerobic bacterial flora of children with recurrent tonsillitis.

Patients consecutively scheduled for elective tonsillectomies because of recurrent GABHS tonsillitis were included. Criteria for inclusion were a history of recurrent GABHS pharyngotonsillitis (at least six episodes within the preceding 2 years, with at least four by GABHS) and an age of >4 years. Excluded were subjects who received antimicrobials or had any infection during the previous month. The study was performed between June 1998 and June 2002 and was approved by the Institutional Review Board. Each subject had general physical and otolaryngological examinations, a complete blood cell count, and urinalysis.

Following a tonsillectomy, one tonsil was cauterized with a heated scalpel, and an incision was made through the area. The tonsillar core was swabbed with a sterile, cotton-tipped applicator that was placed onto an anaerobic transport medium (Port-A-Cul; BBL, Cockeysville, Md.) and inoculated within 24 h onto sheep's blood (5%), chocolate, and MacConkey agar plates (all media from BBL, Becton Dickinson Co., Cockeysville, Md.). The plates were incubated aerobically at 37°C (MacConkey) and under 5% CO_2 and were examined at 24 and 48 h (11). β-Lactamase activity was determined on five colonies of each morphological feature of all isolates by using a Cefinaz disk (BBL, Cockeysville, Md.).

Inhibitory activities of five separate colonies of AHS from each patient were tested against one strain of a recent clinical isolate of GABHS. Minidrops of log-phase broth cultures of the isolates were transferred with a Steers steel pin replicator to vitamin K1-enriched *Brucella* blood agar plates and allowed to dry for 15 min. A log-phase broth culture of the target strain was applied adjacent to each of the isolated strains, and the plates were incubated in 5% CO_2 at 37°C for 48 h. Bacterial interference was defined as any reproducible inhibition of growth.

Penicillin V (17 mg/kg of body weight, or 250 mg every 8 h) was routinely prescribed prior to surgery. Cefdinir (14 mg/kg, or 600 mg once a day) was administered to those with a history of a non-type I penicillin allergy. Included were the first 20 patients who received penicillin and the first 20 who got cefdinir that met the inclusion criteria. Patients were instructed to take the medication prior to surgery for 10 days. Compliance was checked by inspection of the unused medication. Statistical significance was calculated by Fisher's exact test (two-sided), unadjusted.

Forty patients (24 males) participated in this study. Their mean age was 7 years, 4 months (range, 4 to 12 years). The distributions of the patients' ages, genders, urinalyses, white blood counts, and previous antimicrobial therapies were similar for the two groups.

GABHS were isolated from 11 (55%) of the penicillin-treated group and 3 (15%) of the cefdinir-treated group ($P = 0.019$). (Table 1) Thirty-three BLPB (*Staphylococcus aureus*, *Haemophilus influenzae*, and *Moraxella catarrhalis)* were recovered from 17 (85%) of those treated with penicillin, and four BLPB were found in 3 (15%) of those treated with cefdinir.

Patients treated with penicillin had a significantly lower number of AHS (including those with inhibiting capability) and gamma-hemolytic streptococci compared to those treated with cefdinir (6 versus 15, total number of AHS [$P = 0.01$], and 2 versus 10, AHS with inhibiting capability [$P = 0.014$], respectively) (Table 1).

This study compared two modes of therapy for recurrent tonsillitis due to GABHS, one using penicillin and the other an

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TABLE 1. Aerobic organisms isolated from the cores of excised tonsils from 40 children

Organism	No. of isolates (no. of BLPB)		Exact *P* value (*P* value for BLPB)
	Penicillin group (n = 20)	Cefdinir group (n = 20)	
Gram-positive cocci			
Streptococcus pneumoniae	2	0	0.490
alpha-Hemolytic *Streptococcus*[a]	6	15[b]	0.01 (0.014)
gamma-Hemolytic *Streptococcus*	8	14	0.111
beta-Hemolytic *Streptococcus*			
Group A	11	3[b]	0.019
Group C	1	1	1.0
Group F	1	0	1.0
Staphylococcus aureus	13 (13)[c]	1 (1)[b]	0.0001 (0.0001)
Staphylococcus epidermidis	3 (1)	2 (0)	1.0
Gram-negative cocci			
Moraxella catarrhalis	8 (7)	2 (2)	0.648 (0.127)
Gram-positive bacilli			
Diphtheroid species	1	2	1.0
Gram-negative bacilli			
Haemophilus influenzae			
Type b	4 (2)	0 (0)	0.106 (0.487)
Non-type b	11 (7)	2 (1)[b]	0.006 (0.044)
Haemophilus parainfluenzae	2 (2)	0 (0)	0.487
Eikenella corrodens	2	1	1.0
Pseudomonas aeruginosa	1 (1)	0 (0)	1.0 (1.0)
Total	74 (33)	45 (4)	

[a] Numbers of strains inhibiting GABHS were 2 and 10 for the penicillin and cefdinir groups, respectively.
[b] Statistically significant *P* value.
[c] Number of BLPB in parentheses.

expanded-spectrum cephalosporin (cefdinir). Cefdinir was more effective in eradicating GABHS, reducing the number of BLPB, and preserving AHS that are capable of inhibiting GABHS. The superiority of cefdinir may be due to its activity against the aerobic BLPB (*Staphylococcus aureus*, *Haemophilus influenzae*, and *Moraxella catarrhalis*) recovered from the patients and its relative lack of activity against AHS (including interfering ones) (10).

One explanation for the failure of penicillin to eradicate GABHS tonsillitis is that repeated administration of penicillin may select BLPB that can protect GABHS from penicillin (1). The recovery of aerobic and anaerobic BLPB in over three-quarters of patients with recurrent GABHS tonsillitis (1, 7, 13), the ability to measure β-lactamase activity in the tonsillar core (2), and the response of patients with recurrent GABHS tonsillitis to antimicrobials effective against BLPB (1, 5, 7, 13) support this explanation.

An additional untoward effect of penicillin therapy is the potential eradication, in the absence of BLPB, of AHS that possess inhibiting activity of GABHS (6, 9, 13). In contract, AHS are usually more resistant to cephalosporins (6, 10). This difference in susceptibility and the resistance of cephalosporins to β-lactamase may explain the improved activity of cephalosporins compared with that of penicillin in the treatment of acute GABHS tonsillitis (5). These phenomena were demonstrated with a subcutaneous-abscess mouse model (3).

The presence of AHS that inhibit growth of GABHS through bacteriocin production was described by Crowe et al. (6), who postulated that these substances might inhibit colonization and aid in eradication of GABHS. Roos et al. (13) and Brook and Gober (4) showed that the presence of BLPB and the lack of tonsillar colonization by inhibiting AHS were associated with the failure of penicillin to cure GABHS tonsillitis. A series of three studies from Göteborg, Sweden (14–16), demonstrated the utility of inoculation of the nasopharynx with interfering AHS in the prevention of recurrent GABHS pharyngotonsillitis.

This study offers an explanation for the observed superiority of cefdinir as well as other cephalosporins over penicillin in the eradication of GABHS tonsillitis (5, 12). Further studies are warranted to evaluate the efficacy of these agents on BLPB and AHS in the treatment of acute and recurrent tonsillitis.

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