



Barbara Rinehart

POSTER

INFECTIOUS DISEASE: ANTIBIOTICS: CEPHALOSPORIN

My responsibilities were:

Worked with agency editorial staff

Wrote copy for all 16 posters

Designed tables & figures

Verified author's references

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53 Comparative In Vitro Activity of Cefdinir (CI-983, FK-482) against Respiratory Pathogens

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ABSTRACT

The activity of cefdinir (CI-983, FK-482) was compared with cefuroxime, erythromycin and ampicillin against 116 recent isolates obtained from sputum. MICs were determined using an agar dilution method. Ampicillin was highly active against *S. pneumoniae* and most of the non-β-lactamase producing strains of *M. catarrhalis* and *H. influenzae*. Erythromycin was highly active against *M. catarrhalis* and *S. pneumoniae* but not against *H. influenzae*. Cefuroxime was highly active against *S. pneumoniae*; however, its activity against both β-lactamase and non-β-lactamase producing strains of *M. catarrhalis* and *H. influenzae* was comparable with the activity of cefdinir. All *S. pneumoniae* and nearly all *M. catarrhalis* strains were inhibited by 0.5 μg/ml of cefdinir.

INTRODUCTION

Cefdinir is a new oral cephalosporin antibacterial agent. The MIC values of cefdinir were determined for 116 isolates of three species of respiratory pathogens and compared to the antimicrobial activity of ampicillin, erythromycin, and cefuroxime.

MATERIALS AND METHODS

Iso-sensitest agar (Oxoid CM 471) supplemented with lysed horse blood (50 ml/l) and NAD (11.5 mg/l) was used.

Stock antibiotic solutions were made in accordance with the manufacturer's recommendations. Doubling dilutions of each antibiotic were incorporated into agar plates, the range of concentrations being 0.03 mg/l to 16 mg/l.

Fresh clinical isolates of *S. pneumoniae*, β-lactamase positive and β-lactamase negative strains of *M. catarrhalis*, and *H. influenzae* were used in this study. Isolates taken from patients prior to antibiotic therapy, during therapy and after failed therapy were subcultured from non-selective culture media. Each organism was incubated overnight in either XV broth (for *H. influenzae*) or Todd-Hewitt broth (for all others). Dilutions of the overnight cultures, varying from 1:2 for *S. pneumoniae* to 1:20 for *H. influenzae*, were made in fresh broth and loaded into the inoculum peps of an automatic multipoint inoculator (Denley Ltd., England). Spots of 1 μl were delivered to the culture plates resulting in approximately 10⁸ CFU per spot. Agar dilutions and antibiotic-free control plates were then inoculated. The end point, or inhibition of growth, was determined based on two or fewer colonies seen at the site of the inoculum.

RESULTS

Results were recorded and analyzed. Table 1 shows individual drug dilutions and the numbers of various organisms inhibited at each dilution. The calculated MIC₅₀, MIC₉₀ and range of MICs were determined for each group of organisms.

DISCUSSION

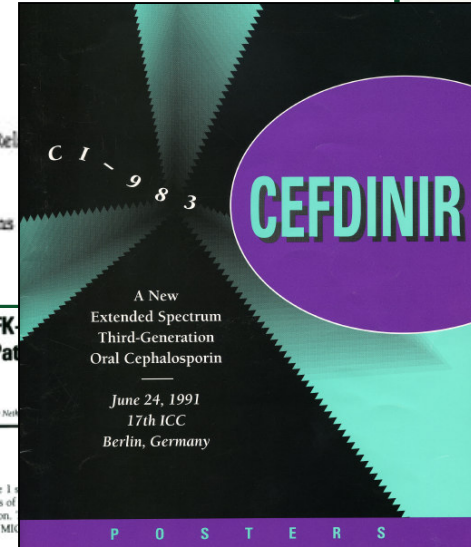
As expected, ampicillin was highly active against *S. pneumoniae* and most of the non-β-lactamase producing strains of *M. catarrhalis*. The MICs for *H. influenzae* were 0.5 mg/l to 1 mg/l, except for the single β-lactamase producing strain. However, β-lactamase production by many *M. catarrhalis* strains (roughly 70% in The Netherlands) limits the usefulness of ampicillin for blind empirical therapy.

Erythromycin, although highly active against *M. catarrhalis* and *S. pneumoniae* (with resistance in only 1/42 [$n=20$] *M. catarrhalis*, β-lactamase positive + 22 *M. catarrhalis*, β-lactamase negative), was not very active against *H. influenzae* (MIC₅₀ = 8 mg/l).

Cefuroxime was extremely active against *S. pneumoniae* and moderately active against the non-β-lactamase producing strains of *M. catarrhalis*. However, the MICs for the β-lactamase producing strains of this organism and those for *H. influenzae* were 1 mg/l to 2 mg/l. These concentrations can be attained in the sputum after parenteral drug administration but not after oral administration. This is also true for most second generation cephalosporins.

Cefdinir yielded MIC results which did not show high activity but the strains were not really resistant. All *S. pneumoniae* and nearly all of the *M. catarrhalis* strains were inhibited by 0.5 mg/l. The *H. influenzae* strains were much less susceptible, requiring 1 mg/l or 2 mg/l for inhibition of growth.

There was no difference in MICs between β-lactamase producing strains and non-producing strains.



Ampicillin, Cefuroxime, Erythromycin and Cefdinir (CI-983, FK-482)																	
Strains with these MICs in (mg/l):					Numbers of Strains with these MICs in (mg/l):												
0.5	1	2	4	8	16	>16	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	>16
Erythromycin																	
15	1	1	1	1	1	1	7	5	7	1	1	1	1	1	1	1	1
21	1	1	1	1	1	1	2	19	1	1	1	1	1	1	1	1	1
1	8*	13	1	1	1	1	1	1	1	1	2*	13	6	1	1	1	1
7	1	1	1	1	1	1	24	8	19	1	1	1	1	1	1	1	1
Cefuroxime																	
1	1	1	1	1	1	1	1	1	9	4	5	1	1	1	1	1	1
2	1	8	2	1	1	1	1	1	1	5	14	3	1	1	1	1	1
17	4	1	1	1	1	1*	1	1	1	2	7	13*	1	1	1	1	1
1	1	1	1	1	1	1	52	1	1	1	1	1	1	1	1	1	1

Erythromycin and Cefdinir												
MIC ₅₀			Range			Mean			MIC Values For:			
MIC ₅₀	Range	Mean	MIC ₅₀	MIC ₉₀	Range	Mean	MIC ₅₀	MIC ₉₀	Range	Mean		
Erythromycin												
M. catarrhalis (β-lact. neg.)	0.06	0.5	0.25 to 0.5	0.48	0.06	0.125	0.03 to 0.16	0.08				
M. catarrhalis (β-lact. pos.)	0.5	0.5	0.25 to 0.5	0.48	0.125	0.125	0.06 to 0.25	0.12				
H. influenzae	8	2	0.5 to 2	1.46	8	16	4 to >16	0.66				
S. pneumoniae	0.06	0.5	0.06 to 0.5	0.24	0.06	0.125	0.03 to 0.8	0.06				
Cefuroxime												
M. catarrhalis (β-lact. neg.)	0.25	1	0.03 to 2	0.06	0.25	1	0.125 to 16	0.48				
M. catarrhalis (β-lact. pos.)	1	4	0.03 to 8	0.75	1	2	0.5 to 2	0.94				
H. influenzae	0.5	1	0.5 to >16	0.69	2	2	0.5 to 2	1.41				
S. pneumoniae	0.03	0.06	0.03 to 0.06	0.04	0.03	0.03	0.03 only	0.03				