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Contemporary Cefdinir Activity Against North American Isolates from Community-Acquired Urinary Tract Infections

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ABSTRACT

Background: Cefdinir is an oral cephalosporin approved by the US Food and Drug Administration in 1997 for the treatment of community-acquired (CA) respiratory tract and uncomplicated skin and soft tissue infections. The objective of the present study was to evaluate the *in vitro* activity of cefdinir against recent clinical isolates collected from CA-urinary tract infections (UTIs), a possible expanded indication.

Methods: 456 isolates from CA-UTI were collected from medical centers in North America (NA; United States and Canada) in 2003, including: *E. coli*, *Klebsiella* spp. (KSP), *P. mirabilis* (PM), *Staphylococcus saprophyticus* (SSAP), and *Citrobacter koseri* (CK). All susceptibility (S) tests were performed using NCCLS reference broth microdilution methods comparing >35 antimicrobial agents. The applied S/resistant (R) breakpoints for cefdinir were ≤1/≥4 mg/L. All QC results were within acceptable NCCLS ranges.

Results: The *in vitro* activities of cefdinir and selected comparators are summarized in the table.

	MIC_{90} (mg/L)/% Susceptible				
Organisms (n)	Cefdinir	Cefuroxime	Cefprozil	Cefpodoxime	Trimethoprim/ sulfamethoxazole (T/S)
E. coli (205)	0.5/98.5	8/75.1	8/93.6	0.5/98.5	>4/82.0
Klebsiella spp. (38)	0.25/97.4	8/86.4	2/97.4	0.25/97.4	>4/89.5
S. saprophyticus (32)	1/100.0	4/100.0	2/100.0	>4/18.8	≤0.5/96.2
P. mirabilis (20)	0.12/100.0	2/100.0	2/100.0	0.06/100.0	>4/85.0
C. koseri (11)	0.25/100.0	8/45.5	2/100.0	0.5/100.0	≤0.5/90.9

Cefdinir was 8- to 16-fold more potent than cefuroxime axetil and cefprozil against *E. coli*, KSP and SSAP. The activity of cefdinir was most similar to that of cefpodoxime against *E. coli* and KSP, but cefpodoxime showed inferior activity against SSAP. Cefdinir spectrum was significantly superior (+3.8 to 16.5%) to that of T/S against all pathogens evaluated. R to cefdinir was rare and found only among *E. coli* (1.5%) and KSP (2.6%).

Conclusion: Cefdinir spectrum and potency was comparable or superior to other orally administered β-lactams tested against recent (2003) clinical isolates from CA-UTI. Clinical studies should be performed to evaluate the role of cefdinir in the treatment of urinary infections as an alternative to compromised first-line agents such as T/S.

BACKGROUND

Cefdinir is an advanced-generation, orally administered cephalosporin antimicrobial agent that has been approved for the treatment of community-acquired pneumonia, acute bacterial exacerbations of chronic bronchitis, acute maxillary sinusitis, pharyngitis/tonsillitis, acute bacterial otitis media, and uncomplicated skin and skin-structure infections in adult and pediatric patients.

Community-acquired urinary tract infections (CA-UTI) are very common in both adults and children. This infection is usually caused by *Escherichia coli*, but other frequently isolated pathogens include *Klebsiella* spp., *Proteus mirabilis*, *Citrobacter* spp. and *Staphylococcus saprophyticus*.

Cefdinir is primarily eliminated by renal clearance of unchanged drug and may prove useful for the treatment of CA-UTI. The objective of the present study was to evaluate the *in vitro* activity of cefdinir against recent clinical isolates collected from CA-UTI, as a possible expanded indication.

MATERIALS AND METHODS

Bacterial Strains

A total of 456 strains from CA-UTI were collected from 23 medical centers located in the United States and five centers located in Canada. The vast majority of isolates were collected in 2003. All isolates were identified at the participant institution by routine methodologies in use at each laboratory. Upon receipt by the monitoring center (JMI Laboratories, North Liberty, IA), isolates were subcultured on blood agar to ensure viability and purity. Confirmation of species identification was performed with the Vitek System (bioMerieux, Hazelwood, MO) or conventional methods, as required.

Susceptibility Testing

Antimicrobial susceptibility testing was performed using broth microdilution methods as described by the National Committee for Clinical Laboratory Standards [NCCLS, 2003]. Antimicrobial agents were obtained from their respective manufacturers as reagent grade powder. Quality control measures were utilized by testing *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853. Breakpoint interpretive criteria used were those established by the NCCLS [2004]. Isolates of *Klebsiella pneumoniae* and *E. coli* with an increased minimum inhibitory concentration (MIC; ≥2 mg/L) for ceftazidime or ceftriaxone or cefotaxime or aztreonam were considered as possible extended-spectrum β-lactamase (ESBL)-producing phenotypes [NCCLS, 2004]. The ESBL phenotype strains were confirmed by using Etest ESBL strips (AB BIODISK, Solna, Sweden) that contain 4 mg/L of clavulanate.

COMMENTS

- Cefdinir and cefpodoxime (MIC_{50}, 0.25 mg/L) were 16-fold more potent than cefuroxime (MIC_{50}, 4 mg/L) and eight-fold more potent than cefprozil (MIC_{50}, 2 mg/L) against *E. coli*. Resistance was very rare (1.7%) for cefdinir and cefpodoxime.
- Cefdinir and cefpodoxime (MIC_{50}, 0.12 mg/L) were also the most active oral cephalosporins against *Klebsiella* spp. These compounds were 32-fold more potent than cefuroxime (MIC_{50}, 4 mg/L) and 16-fold more potent than cefprozil (MIC_{50}, 2 mg/L). Cefdinir resistance (2.4%) was detected only in two ESBL-producing isolates.
- *Proteus mirabilis* was highly susceptible to all oral cephalosporins tested and to amoxicillin/clavulanate. However, 16.1% of isolates tested showed resistance to trimethoprim/sulfamethoxazole.
- *Citrobacter koseri (C. diversus)* was highly susceptible to all antimicrobial agents tested except cefuroxime (45.5% susceptibility).
- *Staphylococcus saprophyticus* represents an important cause of CA-UTI. Although this pathogen is usually considered resistant to oxacillin (MIC, ≥0.5 mg/L), it generally shows low MICs for cephalosporins and aminopenicillins. In the present study, all *S. saprophyticus* isolates evaluated showed very low cefdinir MICs (MIC_{90}, 0.5 mg/L; range, 0.12–0.5 mg/L). MICs were also low (within the susceptible range) for amoxicillin/clavulanate, cefprozil and cefuroxime. On the other hand, only 9.7% of isolates were inhibited at 2 mg/L of cefpodoxime (NCCLS breakpoint for *Staphylococcus* spp.).
- When the entire collection of CA-UTI isolates were analyzed, the highest spectrum of coverage was provided by cefdinir (98.5%), followed by cefprozil (94.7%) and cefpodoxime (92.3%).

Table 1. Antimicrobial Activity of Cefdinir and Selected Orally Administered Antimicrobial Agents Against Strains from Community-Acquired Urinary Tract Infections

	MIC (mg/L)				
Organism/Antimicrobial Agent (No. tested)	50%	90%	Range	% Susceptible[a]	% Resistant[a]
E. coli (300)					
Cefdinir	0.25	0.5	0.06->4	98.3	1.7
Cefprozil	2	8	0.5->16	93.6	3.0
Cefuroxime	4	8	0.25->8	76.0	24.0[b]
Cefpodoxime	0.25	0.5	0.06->4	98.3	1.7
Amoxicillin/Clavulanate	4	>8	0.25->8	88.3	11.7[b]
Trimethoprim/Sulfamethoxazole	≤0.5	>2	≤0.5->2	80.3	19.7
Klebsiella spp. (83)					
Cefdinir	0.12	0.25	≤0.03->4	97.6	2.4
Cefprozil	1	4	0.5->16	94.0	4.8
Cefuroxime	2	8	0.12->8	85.5	14.5[b]
Cefpodoxime	0.12	0.25	≤0.03->4	97.6	2.4
Amoxicillin/Clavulanate	2	8	1->8	95.2	4.8[b]
Trimethoprim/Sulfamethoxazole	≤0.5	>2	≤0.5->2	87.6	13.2
Proteus mirabilis (31)					
Cefdinir	0.12	0.12	≤0.03-0.25	100.0	0.0
Cefprozil	2	2	0.5-2	100.0	0.0
Cefuroxime	1	2	0.5-4	100.0	0.0
Cefpodoxime	0.06	0.06	≤0.03-0.12	100.0	0.0
Amoxicillin/Clavulanate	1	2	0.5-2	100.0	0.0
Trimethoprim/Sulfamethoxazole	≤0.5	>4	≤0.5->4	83.9	16.1
Citrobacter koseri (11)					
Cefdinir	0.25	0.25	0.12-0.25	100.0	0.0
Cefprozil	1	2	0.5-2	100.0	0.0
Cefuroxime	8	8	4->8	45.5	54.5[b]
Cefpodoxime	0.25	0.5	0.12-1	100.0	0.0
Amoxicillin/Clavulanate	2	4	2-4	100.0	0.0
Trimethoprim/Sulfamethoxazole	≤0.5	≤0.5	≤0.5-2	100.0	0.0
Staphylococcus saprophyticus (31)[b]					
Cefdinir	0.5	0.5	0.12-0.5	(100.0)[c]	(0.0)[c]
Cefprozil	1	2	0.5-2	(100.0)[c]	(0.0)[c]
Cefuroxime	4	4	1-4	(100.0)[c]	(0.0)[c]
Cefpodoxime	4	>4	0.25->4	(9.7)[c]	(22.6)[c]
Amoxicillin/Clavulanate	0.5	1	0.25-2	(100.0)[c]	(0.0)[c]
Trimethoprim/Sulfamethoxazole	≤0.5	≤0.5	≤0.5-4	96.8	3.2
Oxacillin	1	2	0.5->8	0.0	100.0
All isolates (456)					
Cefdinir	0.25	0.5	≤0.03->4	98.5	1.5
Cefprozil	2	8	0.5->16	94.7	2.9
Cefuroxime	4	8	0.12->8	80.3	19.7[b]
Cefpodoxime	0.25	1	≤0.03->4	92.3	3.1
Amoxicillin/Clavulanate	4	8	0.25->8	91.4	8.6
Trimethoprim/Sulfamethoxazole	≤0.5	>4	≤0.5->4	83.3	16.7

[a] The remaining percentage below 100% represents the proportion of strains in the intermediate category.
[b] Includes resistant and intermediate strains.
[c] Based on the breakpoint for oxacillin-susceptible staphylococci since oxacillin-resistant strains should be considered resistant to all β-lactams [NCCLS, 2004].

CONCLUSIONS

- Cefdinir showed the broadest spectrum against recent (2003) clinical isolates from CA-UTI among the orally administered β-lactam antimicrobial agents evaluated.
- Cefdinir potency was comparable or superior to other orally administered β-lactams tested against recent (2003) clinical isolates from CA-UTI.
- Clinical studies should be performed to evaluate the wide potential role of cefdinir in the treatment of urinary infections.

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