Oral Cefdinir, a Low Bioavailable Antibiotic Compared to Alternative Oral Antibiotics for Gram Negative Bacteremia

SOUTHERN ILLINOIS UNIVERSITY EDWARDSVILLE

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SCHOOL OF PHARMACY

BACKGROUND

- Oral β-lactam antibiotics can be considered as a suitable alternative treatment for gram-negative bacteremia from a urine source, following initial treatment with intravenous antibiotics.[1]
- There has been controversy of cefdinir's use in gram-negative bacteremia due to its low bioavailability.
- Estimated bioavailability of cefdinir capsules is 21% following administration of a 300 mg capsule dose.[2]

PURPOSE

To explore whether cefdinir is an appropriate alternative antibiotic agent in gram-negative bloodstream infections who meet criteria for oral antibiotic step-down therapy as compared to other oral antibiotics.

METHODS

Study Design:
- Single-center, retrospective chart review
- IRB approval obtained
- Data collection performed through electronic medical records, and protected health information was separate from data collection sheet

Inclusion Criteria:
- Ages ≥ 18 with first episode of gram-negative bloodstream infection
- 1 or more gram-negative blood cultures between January 2018 to October 2023
- Uncomplicated gram-negative bacteremia
- Received oral antibiotic therapy

Exclusion Criteria:
- Intravenous (IV) therapy for more than 7 days
- Blood cultures containing *Pseudomonas spp.*, *Sphingomonas spp.*, atypical organisms, anaerobes, or polymicrobial blood cultures with gram-positive organisms

Outcomes:
- **Primary Endpoints:**
  - 30-day all-cause mortality
  - 30-day recurrence of bacteremia
- **Secondary Endpoints:**
  - Length of stay
  - Length of antibiotic therapy (oral and intravenous therapy)
  - 90-day development of *Clostridioides difficile* infection

Data Analysis:
- Descriptive statistics, Fisher's exact test, and t-test

RESULTS

Figure 1. Group Allocation (n=366)

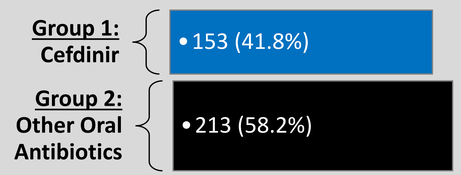

Figure 2. Top 5 Most Used IV & Oral Antibiotics

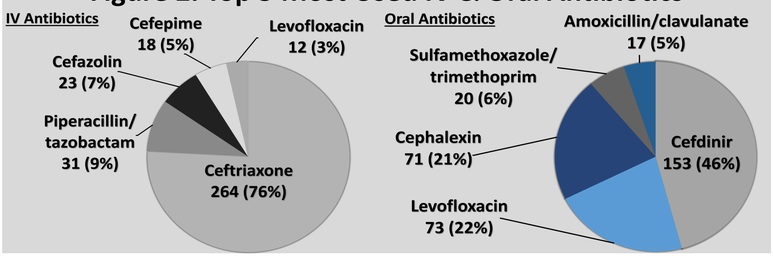

Figure 3. Group Characteristics (n=366)

Characteristics		Group 1 (n=153)	Group 2 (n=213)
Age in Years (18-90) Mean		63.1	62.0
Sex, Female Count (%)		101 (66.0%)	136 (63.8%)
Race Count (%)	**White/Caucasian**	111 (72.6%)	151 (70.9%)
	African American	35 (22.9%)	51 (23.9%)
	Hispanic/Latino	2 (1.3%)	4 (1.9%)
	Asian	1 (0.7%)	2 (0.8%)
Body Mass Index (kg/m²) Mean ± SD		32.8 ± 8.4	30.6 ± 8.4
Creatinine Clearance (mL/min) Mean ± SD	**Day 1 of Admission**	54.14 ± 26.66	58.76 ± 32.30
	Day of Switch to Oral Antibiotic	81.32 ± 40.97	81.76 ± 38.49
Immunocompromised Count (%)		8 (2.2%)	11 (3.0%)
Charlson Comorbidity Index (CCI) Median		3	3
Most Common Causative Pathogens Count (%) **n=373***	***Escherichia coli***	116 (74.4%)	137 (63.1%)
	Klebsiella pneumoniae	20 (12.8%)	36 (16.6%)
	Proteus mirabilis	8 (5.1%)	19 (8.8%)
	Other	12 (7.7%)	25 (11.5%)
Most Common Sources of Bacteremia Count (%)	**Urinary Tract**	103 (67.3%)	146 (68.5%)
	Kidney Stone(s)	20 (1.3%)	23 (10.8%)
	Biliary Tract	8 (5.2%)	16 (7.5%)
	Other	22 (14.4%)	28 (13.1%)
IV Antibiotic Duration (Days) Median		4	5

*: Polymicrobial gram negative bacteria cultures resulting in a total pathogen count of 373

Figure 4. Primary Outcomes

	Group 1 (n=153)	Group 2 (n=213)
30-Day All-Cause Mortality Count (%)	0 (0.0%)	1 (0.5%)
30-Day Recurrence of Bacteremia Count (%)	2 (1.3%)	1 (0.5%)

Figure 5. Secondary Outcomes

	Group 1 (n=153)	Group 2 (n=213)
Length of Stay (Days) Median	4	4
Length of Antibiotic Treatment (Days) Median	13	12
90-Day Development of *Clostridioides difficile* Count (%)	1 (0.7%)	1 (0.5%)

Statistical Significance
- $p > 0.05$ for patient demographics, duration of IV antibiotics, and total duration of antibiotics
- $p > 0.05$ for all outcomes

LIMITATIONS

- Single-centered, retrospective design
- Unable to guarantee antibiotic adherence
- 90-day development of *Clostridioides difficile* infection could be a result of IV antibiotic therapy.
- Inappropriate dosing for IV antibiotics and oral antibiotics could skew results.
- Patients were given IV therapy up to 7 days which can be argued that this alone is enough to treat gram negative bacteremia.[3]

DISCUSSION

Cefdinir, despite its low bioavailability, has demonstrated comparable effectiveness to other oral antibiotics in the treatment of gram-negative bacteremia. While cefdinir has a relatively low bioavailability, this study shows that it can still effectively treat gram-negative bacteremia. This is likely due to factors such as the drug's mechanism of action, ability to penetrate infected tissues, and its overall pharmacokinetic profile.

It is important to note that the choice of antibiotic should be determined based on individual patient factors, such as the severity of the infection, the causative pathogen, and the source of the infection.

REFERENCES

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3. Yahav D, Franceschini E, Koppel F, et, al. Bacteremia Duration Study Group. Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia. Clin Infect Dis. 2019 Sep 13.