

BACKGROUND

- Several studies have concluded that oral step down therapy is appropriate for treatment of Gram negative bacteremia (GNB) after IV therapy^{1,2,3}
- One study compared high (>95%), moderate (75-94%) and low bioavailability (BA) (<75%) oral antibiotics for GNB. Antibiotics with a high BA were associated with a 2% treatment failure, compared to 12% in moderate and 14% in the low bioavailability group (p=0.02)³
- Oral FQs have been used frequently for GNB given their high BA; however, their unfavorable safety profile has called their use into question
- Cefprozil is a potential option for GNB as its BA is 95%
- The goal of this study is to compare outcomes of patients who were treated for Gram-negative bacteremia with a fluoroquinolone (either levofloxacin or ciprofloxacin) to cefprozil.

METHODS

- Study Design:** Retrospective, non-inferiority cohort study
- Inclusion Criteria: Age >18, bacteremia with *Proteus*, *Klebsiella*, or *E. coli* susceptible to cefprozil, ciprofloxacin, and levofloxacin, receipt of the aforementioned antibiotics
- Exclusion Criteria: Pregnancy, endocarditis, osteomyelitis, meningitis, <7 day or >16 days of antibiotics, polymicrobial bacteremia, receipt of both cefprozil and FQ, immunocompromised
- Primary Outcome:** Rate of treatment failure (all-cause mortality or recurrent infection with same organism within 30 days of the initial episode of bacteremia)
- Secondary Outcomes:** mortality within 30 days, bacteremia-related mortality, recurrent infection, ADRs, *CDI*
- Assuming an 85% success rate, to achieve 80% power with a non-inferiority margin of 15%, 71 patients were required in each arm.

RESULTS

- 174 patients received a FQ or cefprozil for GNB from January 1, 2016 through February 28, 2020 (283 patients were excluded)

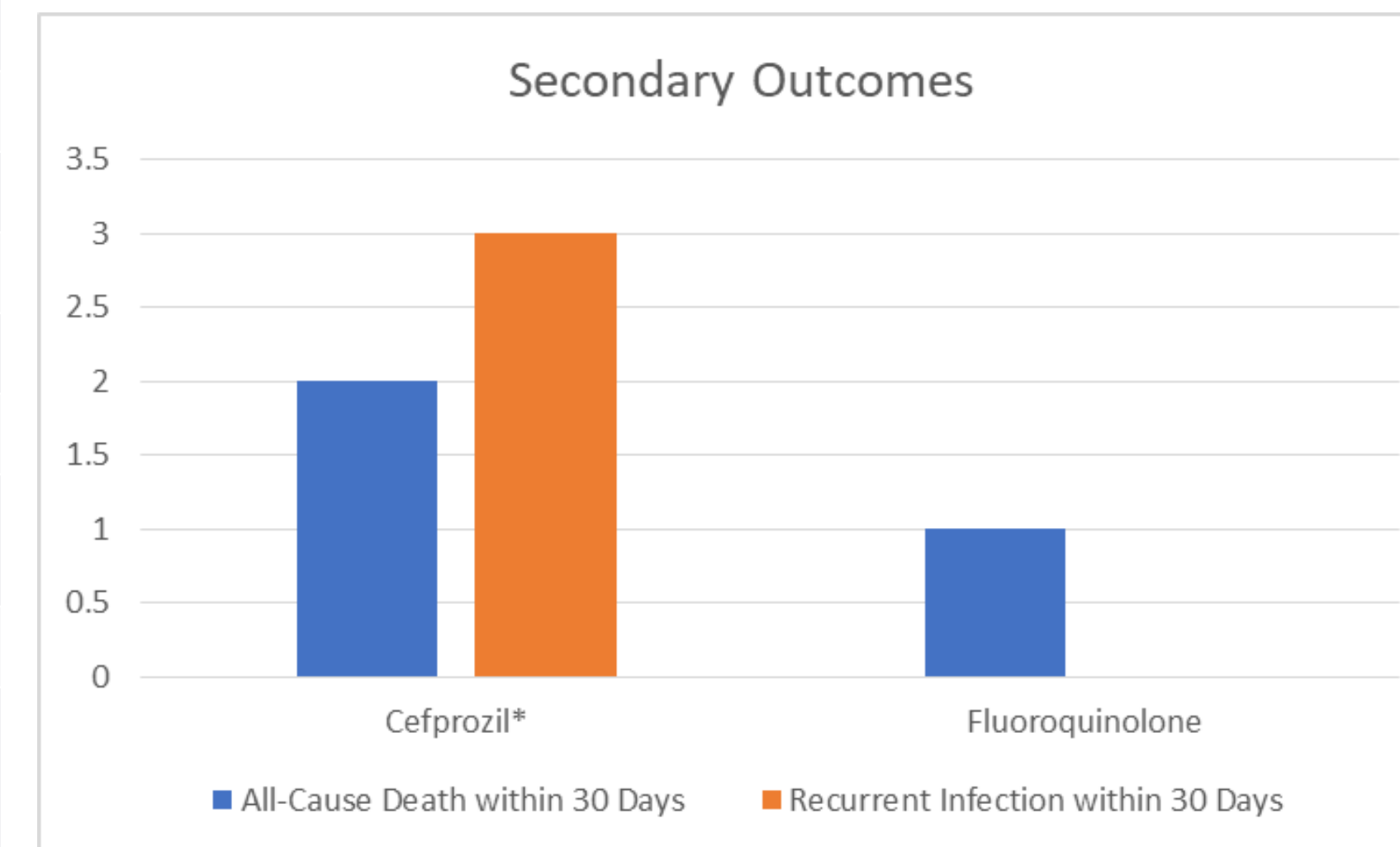
Table 1. Baseline Characteristics

Characteristic	Cef (n=103)	FQ (n=71)	P value
Mean Age, years \pm SD	71.3 \pm 17.2	63.8 \pm 18	0.006
Female, n (%)	66 (64)	47 (66)	0.773
ICU, n (%)	22 (21)	5 (7)	0.010
Penicillin allergy, n (%)	21 (20)	15 (21)	0.906
Pitt Bacteremia Score, score \pm SD	1.6 \pm 1.5	0.7 \pm 1	<0.001
Duration of IV abx, days \pm SD	5.2 \pm 2.2	4.1 \pm 1.6	<0.001
Duration of PO abx prior to discharge, days \pm SD	8.1 \pm 3.1	9.5 \pm 2.9	0.005
Duration of abx total, days \pm SD	13.1 \pm 2.7	13.2 \pm 2.7	0.75
Initial IV antibiotic, n (%)			
Cefepime	53 (51)	18 (25)	0.001
Ceftriaxone	90 (87)	45 (62)	<0.001
Meropenem	14 (14)	1 (1)	0.005
Urologic complications, n (%)	21 (20)	11 (15)	0.413
Immunocompromised, n (%)	13 (13)	3 (4)	0.067
Diabetes, n (%)	40 (39)	25 (35)	0.627

Table 2. Infection Characteristics

	Cef (n=103)	FQ (n=71)	P value
Organism, n (%)			
<i>E. coli</i>	79 (77)	48 (68)	0.184
<i>Proteus spp</i>	18 (14)	21 (30)	0.060
<i>Klebsiella spp</i>	6 (6)	2 (3)	0.475
Source of bacteremia			
Urinary	81 (79)	50 (70)	0.217
GI	17 (17)	13 (18)	0.757

Primary outcome occurred in 3.88% of cefprozil vs 1.41% FQ (mean difference: -2.47%; 95% CI -7.52% to 2.58%) which met the criteria for non-inferiority



*1 pt experienced infection recurrence and all-cause death within 30 days

Table 4. Secondary Outcomes

Variable	Cef (n=103)	FQ (n=71)	P-value
Development of C difficile during admission, n (%)	0	1 (1)	0.408
ADRs, n (%)	3 (3)	9 (13)	0.016

Most Frequent Doses Used for Each Antimicrobial:

- Cefprozil 500 mg PO every 12 hours
- Ciprofloxacin 500 mg PO every 12 hours
- Levofloxacin 750 mg PO daily

LIMITATIONS

- Retrospective nature may result in underreporting of outcomes and differences in baseline characteristics
- Unable to assess patient compliance to antibiotics after discharge
- Unable to determine an optimal timeframe for switching from IV to PO antibiotics
- Admission to other hospitals may not be captured
- Death post discharge may not be captured
- Adverse drug reactions may not be captured post discharge
- Dosing of oral antibiotics were not standardized due to the retrospective nature of the study
- Differences in initial IV antibiotic therapies

CONCLUSIONS

- Cefprozil was non-inferior to FQ regarding treatment failure
- Cefprozil is an efficacious alternative to FQ for oral step-down treatment of GNB and was associated with significantly fewer adverse effects overall
- Prospective studies would aid in determining the preferred oral antibiotic for Gram negative bacteremia

REFERENCES

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