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Oral beta-lactam step down in bacteremic *E. coli* urinary tract infections

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Introduction

- Pyelonephritis is a common indication for antibiotic use and *E. coli* is the most common causative organism.
- Treatment guidelines for pyelonephritis have historically favoured use of fluoroquinolones for oral therapy.
- Fluoroquinolones have multiple serious side effects and resistance is increasing.
- We sought to compare the clinical outcomes of adult patients with urinary tract infection and *E. coli* bacteremia who received oral beta-lactam step down compared to oral fluoroquinolone following initial empiric intravenous beta-lactam therapy.

Methods

- We conducted a multicentre retrospective cohort study including patients with first positive concurrent blood and urine cultures for E. coli from January 1, 2016 to December 31, 2016 within Fraser Health Region (Population 1.8 million).
- Patients were only included if they received empiric intravenous beta-lactam therapy and followed by step down to oral beta-lactam or oral fluoroquinolone for treatment completion.
- Primary outcome was clinical cure defined by meeting all of the following criteria: resolution or improvement of symptoms during treatment, no recurrence of symptoms or signs of urinary tract infection within 30 days, and no discontinuation or change of treatment because of worsened or persistent symptoms or occurrence of adverse events.
- Secondary outcomes included length of hospitalization, all-cause mortality within 30 days, and *C. difficile* positive stool sample within 30 days.

Results

Table 1: Baseline characteristics of patients

	Oral Fluoroquinolone Step-Down (n=130)	Oral Beta-lactam Step-Down (n=77)	p-value
Age, median, years (IQR)	70.5 (56.25-80.75)	71 (54-80)	0.72
Female	92 (71)	54 (70)	
Male	38 (29)	23 (30)	
Charlson comorbidity index, median (IQR)	1 (0-2)	1 (0-3)	0.96
Catheter associated UTI	6 (5)	4 (5)	0.85
Hospital admission	101 (78)	62 (81)	0.63
ICU admission	9 (7)	5 (6)	0.91
Sepsis	31 (25)	25 (33)	0.2
Septic shock	8 (6)	5 (6)	0.92
Pitt bacteremia score, median (IQR)	0.5 (0-1)	1 (0-1)	0.53
Site of acquisition			0.02
Community-acquired	110 (85)	53 (69)	
Community-acquired health-care associated	15 (12)	20 (26)	
Hospital-acquired	5 (4)	4 (5)	
Beta-lactam allergy	15 (12)	7 (9)	0.58
Inadequate empiric treatment	1 (1)	1 (1)	1.0
Stable at oral switch	125 (96)	74 (96)	0.99
Duration of intravenous treatment, median, days (IQR)	5 (3-7)	5 (3-7)	0.20
Duration of oral treatment, median, days (IQR)	7 (7-10)	7 (5.75-10)	0.38
Total treatment duration, median, days (IQR)	14 (12-14)	14 (11-14)	0.91

Table 2: Thirty-day outcomes for patients

	Oral fluoroquinolone step down (n=130)	Oral beta-lactam step down (n=77)	p-value
Primary Outcome			
Clinical cure	127 (98)	72 (94)	0.13
Secondary Outcomes			
30-day mortality	1 (1)	0 (0)	0.43
Clostridioides difficile infection	1 (1)	1 (1)	1
Length of hospitalization, median, days (IQR)	6 (3.25-9)	6 (4-10)	0.43

- The primary outcome of clinical cure was achieved in 127 patients (98%) in the oral fluoroquinolone group and in 72 patients (94%) in the oral beta-lactam group (absolute difference -4.2%, 95% CI, -10.3% to 1.9%, p=0.13).

No significant difference between oral beta-lactam and oral fluoroquinolone groups for clinical cure:

- Unadjusted analysis (OR 0.34; 95% CI, 0.08 – 1.47, p=0.15).
- Multivariate adjustment (adjusted OR, 0.31; 95% CI, 0.05 – 1.90, p=0.2).
- Propensity scoring adjustment (OR, 0.31; 95% CI, 0.07 – 1.38, p=0.12).

Conclusions

- Our results suggest that oral beta-lactams are a safe and effective step down for patients with *E. coli* bacteremic urinary tract infections.
- Future research is needed to further establish the safety, efficacy, and optimal duration of oral step down therapy for bacteremic urinary tract infections, in particular with oral beta-lactams.

Limitations:

- Retrospective study design.
- Choice of oral agent may have been influence by unaccounted factors.
- Length of treatment may have reduced the chance to find a difference between the groups.

References

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