Efficacy of Non-Carbapenem Antibiotics for the Treatment of Ceftriaxone-Resistant Enterobacterales

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BACKGROUND[1-3]

- Extended spectrum beta-lactamase (ESBL) producing Enterobacterales are responsible for significant morbidity and mortality
- Carbapenem antibiotics have become standard of care for most ESBLs
- Surrogate markers of ESBL production, such as ceftriaxone resistance, may overestimate true ESBL presence
- Excess carbapenem use may lead to increased cost and resistance

METHODS

- IRB approved single center retrospective analysis
- Data collected: January 2018 to October 2021
- Patients screened from report of all ceftriaxone-resistant isolates
- Intervention/Comparator: carbapenem vs. Non-carbapenem therapy

Table 1: Patient Selection

Inclusion	Exclusion
Adult (> 18 years old)	Poly-microbial Infection
Positive culture for ceftriaxone-resistant E.coli, Klebsiella spp., P. mirabalis	> 1 documented infection during encounter
	Infection confined to urinary tract only
	Expired within 48 hr of positive culture
	Decision to withdraw treatment

Objectives

- Primary Outcome: Composite of Treatment Failure
  1. 30-Day All Cause Mortality
  2. 30-Day Readmission
  3. Microbiological recurrence
  4. Clinical worsening requiring antibiotic change
- Secondary Outcomes:
  1. Differentiation of composite outcomes
  2. *Clostridioides difficile* infection (CDI)

References:
1. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019
2. Harris P, Tambyah P, Lye D, et al. Effect of piperacillin-tazobactam vs. meropenem on 30-day mortality for patients with e coli or Klebsiella pneumoniae bloodstream infection and ceftriaxone resistance: a randomized trial. JAMA; 2018:320:984-994.
3. Wilson A Peter. Sparing carbapenem usage. J Antimicrob Chemother. 2017;72:2410-2417.

Disclosures:
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RESULTS

Table 2:Baseline Characteristics (n=130)

	Carbapenem (n=101)	Non-Carbapenem (N=29)
Age in years - mean (SD)	65.8 (13.9)	54.7 (17.8)
Female sex - n (%)	50 (49.5)	16 (55.2)
White race - n (%)	61 (60.4)	15 (51.7)
Source - n (%)		
Blood (1°)	50 (49.5)	10 (34.5)
Blood (2°)	26 (25.7)	2 (6.9)
Abdomen	9 (8.9)	10 (34.5)
Respiratory	10 (9.9)	5 (17.2)
Other	6 (5.9)	2 (6.9)
Enterobacterales - n (%)		
E.coli	84 (83.2)	22 (75.9)
K. pneumoniae	15 (14.9)	4 (13.8)
K. oxytoca	2 (1.9)	3 (10.3)
H/o ceftriaxone-R w/I 1 yr - n (%)	28 (27.7)	3 (10.3)
Empiric therapy - n (%)		
Cefepime	31 (30.7)	13 (44.8)
Carbapenem	34 (33.7)	-
Piperacillin/Tazobactam	17 (16.8)	10 (34.5)
Other	19 (18.8)	6 (20.7)
Inpatient antibiotic days - median [IQR]	7 [4-10]	4 [2-7]
Discharged on antibiotics - n (%)	51 (50.5)	23 (79.3)
Hospital LOS - median [IQR]	9 [7-17]	7 [4-15]

Figure 1: Definitive Non-Carbapenem Therapy

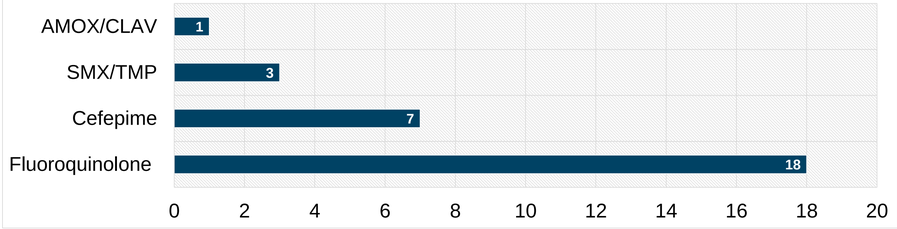

Figure 2: Primary Outcome: Treatment Failure

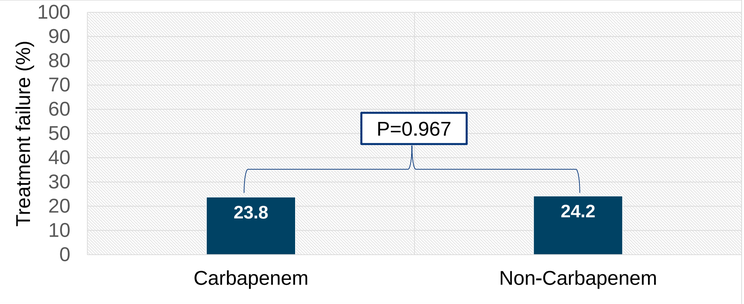

Table 3: Secondary Outcomes

	Carbapenem (n=101)	Non-Carbapenem (n=30)
30 day readmission - n (%)	19 (18.8)	3 (10.3)
30 day mortality - n (%)	4 (3.9)	4 (13.8)
Microbial recurrence - n (%)	4 (3.9)	--
Failure requiring antibiotic switch - n (%)	--	--
CDI - n (%)	2 (1.9)	1 (3.5)

CONCLUSIONS

- No statistically significant difference was found among patients receiving carbapenem vs. non-carbapenem for infections caused by ceftriaxone resistant-Enterobacterales
- A higher mortality rate was observed in those on non-carbapenem therapy; this was not statistically significant
- Non-carbapenem therapy led to shorter lengths of stay and more frequent discharge on antibiotics
- Our findings, albeit non-randomized, continue to call into question the need for carbapenem therapy for **all** patients infected with ceftriaxone-resistant Enterobacterales and support the ongoing investigation of alternatives.