Treatment Failure Rates Among 7 Antibiotics For the Treatment of *Enterobacter Spp* Bloodstream Infections

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Background

- The Centers for Disease Control and Prevention have listed *Enterobacterale* infections as a significant threat for emerging drug resistance
- Inducible Amp-C resistance, commonly seen with *Enterobacter spp*, is a concerning mechanism as it limits narrow spectrum antibiotic treatment options
- Data surrounding which antibiotics carry a higher likelihood of treatment failure for *Enterobacter spp* bloodstream infections has been limited and variable
- MERINO-2 Trial (Stewart et al. 2021)
  - Meropenem versus piperacillin-tazobactam for Amp-C ß-lactamase-producing *Enterobacter spp* bloodstream infections
  - Statistically significant difference for less microbiological failures with meropenem (P=0.03)
  - No statistical difference in mortality, length of stay, clinical failure
- The aim of this study is to describe differences in treatment failure rates among meropenem, ertapenem, imipenem, levofloxacin, ciprofloxacin, cefepime, and piperacillin-tazobactam when treating *Enterobacter* bloodstream infections
- This study will also help to identify areas for practice improvement within Regions Hospital when treating *Enterobacter* bloodstream infections

Outcomes

Primary Outcome

- A composite of: All-cause mortality at 30 days after initiation of definitive treatment, clinical failure, and/or microbiological failure
  - Clinical failure: Ongoing fever (>38◦C) or leukocytosis (white blood cell count >12 x 10^9/L) on day 5 after initiation of definitive treatment
  - Microbiological failure: Growth of the index organism from a blood culture or another sterile site on day 3-5 after initiation of definitive treatment
  - Definitive treatment: Antibiotic chosen to treat the *Enterobacter* bloodstream infection after cultures and sensitivities resulted

Secondary Outcomes

- Subsequent infections
  - Readmission with any type of infection due to the same organism within 30 days after discharge
- Length of hospital stay
- Length of ICU stay
- *Clostridium difficile* infection within 30 days of definitive treatment initiation
- Need for antibiotic escalation at least 72 hours after initiation of definitive treatment

Exploratory Outcome

- Number of patients positive for COVID-19 at the time of hospital admission

Methods

- A single-center, retrospective chart review from September 1st 2019 to August 31st 2021

Inclusion Criteria

- 18 years and older
- At least one positive blood culture for *Enterobacter cloacae* or *Klebsiella aerogenes*
- Started antibiotics within 72 hours after obtaining first positive blood culture
- "Definitive" treatment, started within 5 days of blood culture collection

Exclusion Criteria

- Poly-microbial cultures (unless likely contaminant)
- Treatment without curative intent
- Patients who have opted out of research participation

Of note, 6 patients were either excluded from the study due to the use of ceftriaxone as definitive treatment, or were a started on ceftriaxone at some point during the definitive treatment period

Results

Baseline Characteristic	N=28
Sex	Males 21 (75%) Females 7 (25%)
Enterobacter cloacae complex	19 (67.8%)
Klebsiella (Enterobacter) aerogenes	9 (32.2%)
Invasive procedure 14 days prior to start of treatment	12 (42.8%)
Surgery 14 days prior to start of treatment	7 (25%)

Baseline Characteristic	N=28
Central line placement at least 48 hours prior to culture collection	10 (35.7%)
Indwelling catheter placement at least 48 hours prior to culture collection	13 (46.4%)
IV antibiotic use in past 90 days	11 (39.3%)
COVID-19 diagnosis at time of hospital admission	2 (7.1%)
Days in hospital before initiation of definitive treatment	5.9 (±8.4)

Primary Outcome	Meropenem (N=2)	Ertapenem (N= 9)	Imipenem (N=0)	Levofloxacin (N= 12)	Ciprofloxacin (N=1)	Cefepime (N= 3)	Piperacillin-tazobactam (N=1)
Composite outcome	1	5	0	3	1	0	0
Individual outcomes							
30 day mortality (N=3)	0	2	0	1	0	0	0
Microbiological failure (N=4)	0	3	0	1	0	0	0
Clinical failure (N=7)	1	4	0	1	1	0	0

Secondary Outcomes	Meropenem (N=2)	Ertapenem (N=9)	Imipenem (N=0)	Levofloxacin (N=12)	Ciprofloxacin (N=1)	Cefepime (N=3)	Piperacillin-tazobactam (N=1)
Subsequent infection within 30 days	0	0	0	1	0	0	0
Length of hospital stay (days)	13 (±10)	48.1 (±43.9)	0	10.8 (±15.2)	13	10 (±13)	4
Length of ICU stay (days)	4 (±6)	15.8 (±20.1)	0	4.5 (±12.5)	9	0.33 (± 1)	1
Clostridiodies infection with 30 days	0	0	0	0	0	1	0
Need for antibiotic escalation after 72 hours	0	0	0	0	0	0	0

Limitations

- Small sample size
- Retrospective chart review
- Patients with multiple transitions between "definitive" antibiotics
- Meeting the clinical failure outcome could be due to newly developing or concomitant infection not caused by *Enterobacter spp*

Conclusions and Future Direction

- Due to small sample size, no specific conclusions can be drawn at this time regarding treatment failure rates
- No differences noted for secondary outcomes
- Patients with *Enterobacter* bloodstream infections commonly had an underlying risk factor for infection (IV antibiotic use, central line placement, indwelling catheter, etc.)
- Ceftriaxone was found to be used in multiple different scenarios for the treatment of *Enterobacter* bloodstream infections, which increases risk for inducible Amp-C resistance. This will be addressed with further education
- A Noon Lecture will be provided to medical residents on the 2021 IDSA Guidance on the Treatment of Antimicrobial-Resistance Gram-Negative Infections

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