Treatment Outcomes with Carbapenems vs. Non-Carbapenem Beta-Lactams in Infections with Carbapenem-Discordant *Enterobacter cloacae* Complex

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BACKGROUND

- Optimal therapy is not well defined for carbapenem-discordant *Enterobacter cloacae* complex (ECC) infections which is defined as ertapenem non-susceptible and meropenem susceptible isolates
- ECC can express multiple resistance mechanisms simultaneously which makes the optimal therapy hard to ascertain
- The IDSA AMR guidance recommends meropenem-extended infusion for carbapenem-discordant ECC infections; however comparative data amongst different treatment regimens are not available

PURPOSE

The purpose of this study is to compare treatment outcomes with meropenem (MEM) vs non-carbapenem beta-lactams (NCBL) in infections caused by carbapenem-discordant *Enterobacter cloacae* complex infections

METHODS

- Retrospective, observational cohort study conducted at The University of Kansas Hospital from January 1, 2016 – June 30, 2021
- Reviewed 154 isolates and included 29

Inclusion Criteria

- Non-urinary culture positive for carbapenem-discordant ECC
- Treatment with MEM or NCBL

Exclusion Criteria

- Less than 18 years of age
- Polymicrobial infection
- Death or transition to hospice/comfort-only interventions within 72 hours of hospital admission

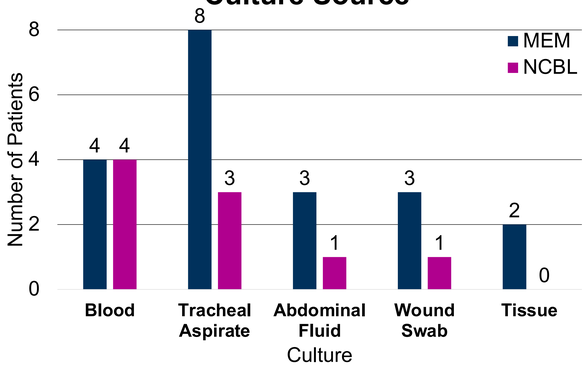
Endpoints

- Clinical failure, defined as a composite of the following:
- In-hospital 30-day mortality
- Change of initial antimicrobial agent
- Addition of a supportive agent (such as vasopressor agents) due to clinical decompensation
- Relapsed bloodstream infection within the same hospitalization
- Acquisition of a secondary infection with any organism that is resistant to the initial drug being used

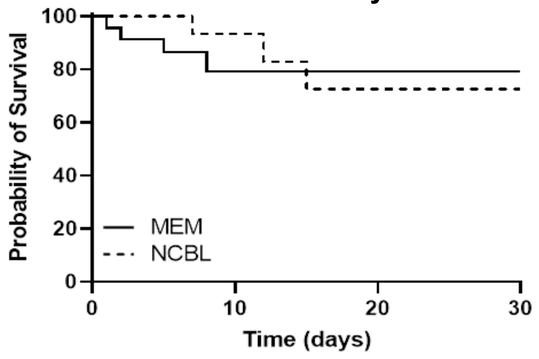
RESULTS

Baseline Characteristics (N=29)	MEM (n=20)	NCBL (n=9)
Male, n (%)	13 (65)	9 (100)
Age, mean (range)	51.5 (21 - 80)	69.5 (58 - 89+)
Race, White n (%)	14 (70)	8 (89)
Charleson Comorbidity Score, mean (SD)	4.25 (3)	5.5 (2)
Hospital length of stay, mean (range)	26.4 (7 - 172)	28.3 (4 - 103)
Initial monotherapy used, n (%)	16 (80)	5 (56)

Culture Source



Survival Analysis



Endpoints (N=29)	MEM (n=20)	NCBL (n=9)	*P*-value
Clinical failure, n (%)	6 (30)	6 (67)	0.11
In-hospital 30-day mortality, n (%)	4 (20)	4 (44)	0.21
Change of initial antimicrobial agent, n (%)	1 (5)	4 (44)	0.02
Addition of a supportive agent due to clinical decompensation, n (%)	2 (10)	2 (22)	0.57
Relapsed bloodstream infection within the same hospitalization, n (%)	1 (5)	0	1
Emergence of resistance, n (%)	1 (5)	0	1

Logistic Regression for NCBL OR, (95% CI)	
In-hospital 30-day mortality	3.2 (0.52-17.72)
Change of agent	15.2 (1.37-168)
Addition of a supportive agent	2.57 (0.3-22)

DISCUSSION

- In 29 cases, 12 patients met our primary outcome; 6 in the MEM group and 6 in the NCBL group with no difference found
- Univariate logistic regression suggested that treatment with NCBL trends toward higher mortality odds
- Univariate logistic regression found that initial NCBL agents were more likely to be modified
- No significant difference found between the other components of the composite end point

LIMITATIONS

- Small sample size
- Routine use of extended-infusion MEM not started until 2019
- Genotypic resistance mechanisms were not assessed
- NCBL limited to piperacillin-tazobactam and ceftazidime-avibactam

CONCLUSION

- There was no significant difference in the rate of clinical failure in patients treated with MEM vs NCBL
- Treatment with NCBLs were more likely to have therapy modified as compared with patients treated with MEM
- Further studies are needed to explore treatment options

REFERENCES & DISCLOSURES

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3. Adelman, M. et al. *Open Forum Infect Dis* Vol. 9, No 1. 2022

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