Evaluating Clinical Outcomes of Bacteremic Patients Treated with AmpC-Inducing Versus -Stable Agents

Barbara Barsoum, PharmD, AAHIVP; Gabriel Karkenny, MD; Henry Donaghy, MD; Thien-Ly Doan, PharmD, BCIDP
Long Island Jewish Medical Center, New Hyde Park, New York

Barbara Barsoum
bbarsoum@northwell.edu
Tel 718-470-5835

INTRODUCTION

- AmpC enzymes belong to the Class C Ambler structural classification of β-lactamases and can rapidly hydrolyze penicillins, cephalosporins, and monobactams.
- The genes encoding these β-lactamases are typically found in the chromosomes of *Enterobacter* species and *Citrobacter* species.
- Antimicrobial agents are classified as weak inducers, able to withstand AmpC hydrolysis with moderate concentrations, versus strong inducers, which may cause rapid induction of AmpC production and confer resistance.
- Due to this induction potential, agents that appear susceptible may quickly become resistant, complicating the treatment choices for these infections.

OBJECTIVES

Primary Objective: To evaluate treatment outcome in patients treated with strong AmpC inducers compared to weak inducers and agents with limited clinical experience.

Secondary Objectives: To evaluate the impact of the antimicrobial agent(s) on various outcome measures, including time to decompensation, 30-day readmission related to infection, microbiologic relapse, in-hospital mortality, and hospital length of stay.

METHODS

Study design: multi-center retrospective observational chart review that was approved by Northwell Health® IRB

Study period: July 2017 – January 2022

Population:

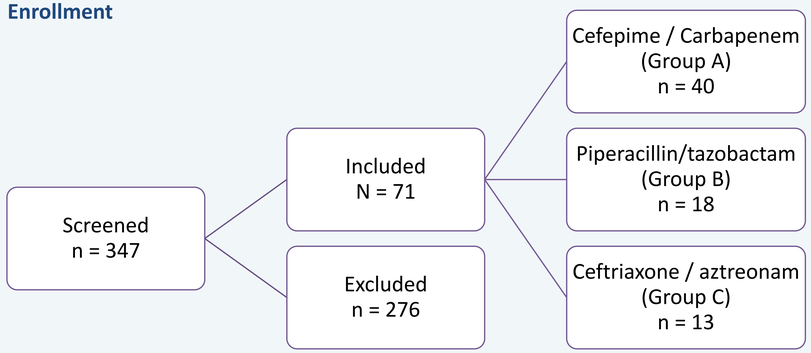
Inclusion Criteria	• Age ≥ 18 • Admitted to Northwell Health® System • Positive blood culture demonstrating *E. cloacae*, *E. aerogenes*, or *C. freundii* and cefoxitin resistance • Treatment with a β-lactam antibiotic for a minimum of 72 hours and at least 75% of the treatment course
Exclusion Criteria	• Blood cultures with polymicrobial growth • Organisms with ESBL or KPC • Patients that expired within 5 days of a positive blood culture • Facility that does not utilize Sunrise® system

Data collection: Utilized the electronic medical record to screen subjects, collect demographics, duration of therapy, microbiologic data, empiric and definitive antibiotics.

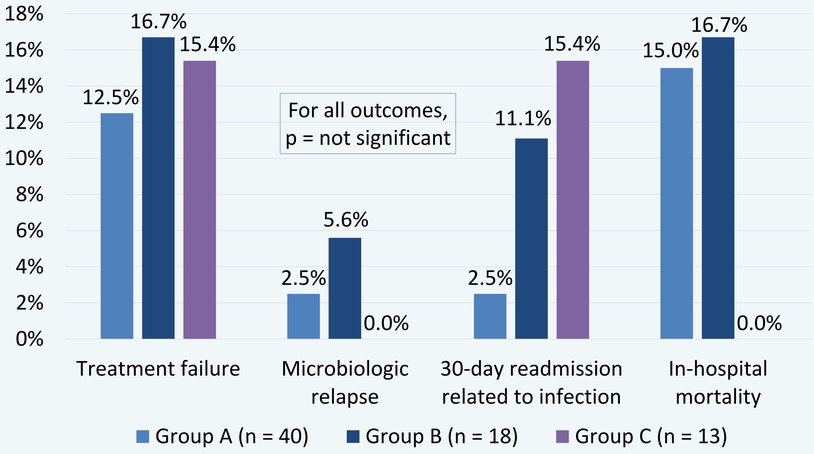
Statistical analysis: Descriptive statistics were calculated. A fisher's exact test was used to determine significant differences in incidence rates. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Enrollment



Clinical Outcomes (N = 71)



	Group A (n = 40)	Group B (n = 18)	Group C (n = 13)	p-value
Age – Years (mean ± SD)	64.4 ± 17.8	68.4 ± 17.6	69.9 ± 21.7	NS
Sex, Male – no. (%)	21 (52.5)	15 (83.3)	9 (69.2)	NS
Quick Pitt Bacteremia Score – median (IQR)	0.5 (0,2)	1 (0,2)	1 (0,1)	NS
qSOFA Score – median (IQR)	1 (0,2)	1 (0,2)	1 (1,2)	NS
Antibiotic use within previous 90 days – no. (%)	16 (40)	7 (38.9)	3 (23.1)	NS
Organism – no. (%)				
Enterobacter cloacae	38 (95)	11 (61.1)	6 (46.2)	<0.0001
Enterobacter aerogenes	1 (2.5)	3 (16.7)	6 (46.2)	
Citrobacter freundii	1 (2.5)	4 (22.2)	1 (7.7)	
Duration of empiric therapy – days (mean ± SD)	1.5 ± 1.3	0.3 ± 0.6	1.3 ± 1.4	0.0016
Duration of IV definitive therapy – days (mean ± SD)	11.3 ± 10.5	7.6 ± 3.5	10.2 ± 12.7	NS
Total course of therapy – days (mean ± SD)	16.0 ± 9.2	13.1 ± 3.9	17.2 ± 10.0	NS
	Group A (n = 20)	**Group B (n = 11)**	**Group C (n = 11)**	**p-value**
Day switched to oral therapy – days (mean ± SD)	7.6 ± 3.4	7.1 ± 2.8	7.3 ± 2.3	NS

NS: not significant

STUDY LIMITATIONS

- Retrospective design
- Small sample size due to standard of care
- Repeat blood cultures not necessary for gram negative infections
- Not capturing patients readmitted to any other health systems
- Many patients were transitioned to oral therapy with a non-β-lactam
- Selection bias

CONCLUSION

- Patients who received piperacillin/tazobactam had numerically more treatment failure, microbiologic relapse, and in-hospital mortality.
- Based on this study, piperacillin/tazobactam cannot confidently be placed in the same treatment category as carbapenems or cefepime.
- Further studies with larger sample sizes are needed to confirm these results.