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Outcomes Associated with Empiric Aztreonam Use Compared to Anti-Pseudomonal β-lactams in Patients with Sepsis: An Opportunity for Allergy Stewardship

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Background

- Penicillin allergies are reported in approximately 8% of patients, resulting in therapy changes 30% of the time[1,2]
- Inferior outcomes have been reported for patients with alternative therapy including[3]:

Increased length of stay	Higher ICU admission rates	Increased antibiotic exposure	Higher rates of drug resistant organisms

- Surviving Sepsis Campaign guidelines recommend anti-pseudomonal β-lactams (APBLs) as empiric therapy for patients with sepsis[3]
- Septic patients are especially vulnerable to these inferior outcomes given high mortality rates, even when adhering to guidelines[4]
- Aztreonam is often administered to patients with β-lactam allergies, however it has shortcomings in comparison to APBLs:
  - Lack of Gram-positive coverage
  - Increased resistance of Gram-negative aerobes to aztreonam[5]
- No studies have examined the effects of receiving aztreonam on clinical outcomes in septic patients

Objective

To determine whether septic patients treated with aztreonam experience inferior outcomes compared to those treated with APBLs

Methods

Design and Patient Selection

- Retrospective, multicenter cohort study of patients at metro Charlotte Atrium Health facilities from January 2014 to October 2017
- Patients identified through system-wide sepsis database
- Data collected from electronic medical records and managed in REDCap®

Inclusion Criteria

- Adult patients (≥ 18 years old)
- Diagnosed with sepsis or septic shock in the emergency department
- Discharged with an infection-related ICD-9 or ICD-10 code

Exclusion Criteria

- Transferred from facility outside of the system
- Sepsis diagnosed outside of the Emergency Department
- Received fewer than 2 doses of aztreonam or APBL
- Received both aztreonam and APBL within the first 8 hours of presentation
- Received two different APBLs in the first 24 hours
- Previous inclusion

Outcomes

- Primary Endpoint: in-hospital mortality
- Secondary Endpoints:
  - Use of other antimicrobial agents
  - Length of intensive care unit (ICU) stay in surviving patients
  - Hospital length of stay in surviving patients

Statistical Analysis

- Performed in SAS®
- Primary endpoint: χ^2 test
  - Multivariable logistic regression to account for confounding
- Secondary endpoints:
  - Normally distributed continuous data: Student's t-test
  - Ordinal and non-normally distributed continuous data: Wilcoxon rank sum
  - Nominal data: χ^2 or Fisher's exact

Results

Figure 1. Inclusion/Exclusion

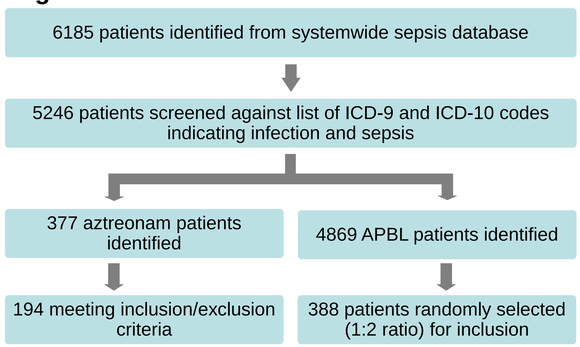


Table 1. Baseline Characteristics

	Aztreonam (n = 194)	APBL (n = 388)	p-value
Age, mean (SD)	65.6 (16.3)	64.5 (16.3)	0.4252
Sex (% female)	69.6	51.3	<0.0001
Race (%)			0.0004
Black or African American	14.4	27.6	
White	79.4	65.7	
Allergy to Beta-Lactam, n (%)	189 (97.4)	55 (14.2)	
Penicillin	172 (88.7)	51 (13.1)	<0.0001
Cephalosporin	50 (25.8)	8 (2.0)	<0.0001
Carbapenem	5 (2.5)	0 (0)	0.0141
APACHE II score, mean (SD)	22.6 (8.3)	21.1 (7.0)	0.0299
Bacteremia, n (%)	30 (15.5)	98 (25.3)	0.0072
Admission lactate, mean (SD)	4.24 (2.66)	4.38 (2.39)	0.5232
Requiring vasopressors, n (%)	102 (52.6)	187 (48.2)	0.3190

Figure 2. APBLs Administered

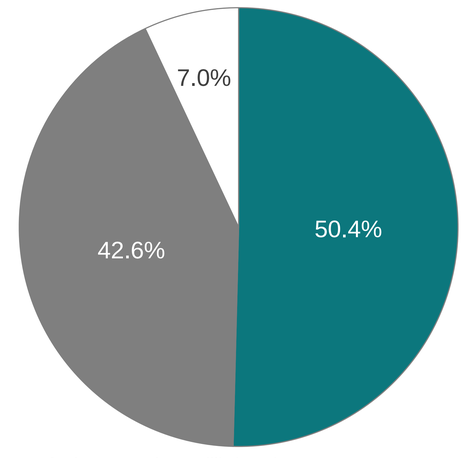
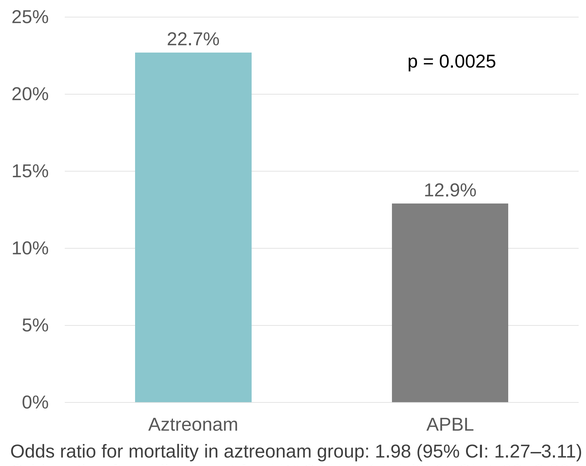


Figure 3. In-Hospital Mortality



Odds ratio for mortality in aztreonam group: 1.98 (95% CI: 1.27–3.11)
Odds ratio after adjustment for APACHE II: 1.74 (95% CI: 1.08–2.80)

Figure 4. Concomitant Antibiotic Usage

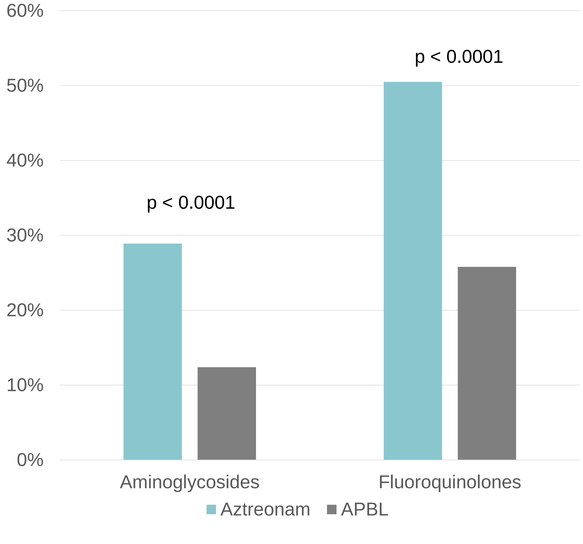
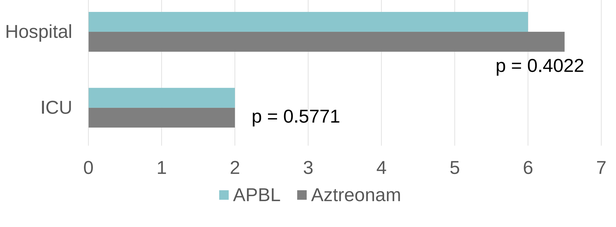


Table 2. Sepsis Treatment Factors

	Aztreonam (n = 194)	APBL (n = 388)	p-value
Time to first dose of any antibiotic from ED arrival, mean in hours (SD)	1.5 (1.4)	1.5 (1.5)	0.3735
Time to first dose of anti-pseudomonal antibiotic from ED arrival, mean in hours (SD)	2.6 (3.2)	1.9 (2.7)	0.0004
Fluid resuscitation within 3 hrs, mean in mL/kg (SD)	38.7 (27.5)	39.2 (22.3)	0.4865
Fluid resuscitation within 6 hrs, mean in mL/kg (SD)	43.6 (25)	45.0 (26.4)	0.2761

Figure 5. Length of Stay in Surviving Patients



Discussion

- First study looking at clinical outcomes in patients with septic shock receiving aztreonam vs. APBLs
- Previous studies have shown increased mortality, length of stay, health care costs, and antibiotic exposure in patients reporting β-lactam allergies
- Higher rates of allergies in aztreonam group (97.4% vs. 14.2%)
- Absolute increase in mortality of 10% in patients receiving aztreonam
  - After analysis of potential confounders, only APACHE II score and antibiotic selection affected mortality
  - After adjustment for APACHE II score, signal of increased mortality in patients receiving aztreonam remained
- Increased time to first dose of antibiotic in aztreonam group, likely due to additional decision-making time
- No difference in hospital length of stay or ICU length of stay in surviving patients
- Increased use of aminoglycosides and fluoroquinolones in patients receiving aztreonam
- 36% of patients receiving aztreonam eventually received a β-lactam

Limitations

- Differences in baseline characteristics
  - Higher APACHE II scores in the aztreonam group
  - Lower rates of bacteremia in aztreonam group
- Absence of source data
- Lack of culture and susceptibility data prevent conclusions about how often empiric therapy was appropriate
- Retrospective study, unable to show causality

Conclusions

- Empiric aztreonam is associated with increased mortality in patients with sepsis and septic shock
- Findings highlight importance of stewardship interventions such as obtaining accurate and comprehensive allergy histories
- Administration of APBLs should be prioritized over allergy avoidance whenever feasible in patients with sepsis

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Disclosures

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or this presentation.

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