Evaluation of clinical outcomes in bacteremia due to AmpC β-lactamase producing organisms stratified by treatment

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Poster #2431

BACKGROUND

- *Enterobacter* spp., *Citrobacter* spp., *Serratia marcescens*, and *Pseudomonas aeruginosa* are some of the most common bloodstream pathogens isolated from hospitalized patients.
- These microorganisms harbor genes that encode for AmpC β-lactamase production.
- The incidence of AmpC β-lactamase hyperproduction among Enterobacteriaceae (24-91%) and *P. aeruginosa* (16-86%) isolates varies widely among the literature.
- Cefepime or a carbapenem is considered the treatment of choice for infections caused by microorganisms that produce AmpC β-lactamases.

OBJECTIVE

To compare the clinical outcomes for patients receiving a carbapenem or cefepime (CC) and alternative therapy (AT) for bacteremia caused by microorganisms known to have the ability to produce AmpC β-lactamases

METHODS

Study design / Inclusion

- Retrospective cohort study conducted at CHI St. Luke's Health - Baylor St. Luke's Medical Center, which is an 850–bed quaternary care hospital in Houston, Texas
- Included all adult patients with a monomicrobial bacteremia due to a microorganism that is known to have the ability to produce AmpC β-lactamases between June 1st, 2016 and December 31st, 2017
- Primary outcome: all-cause inpatient mortality
- Secondary outcomes: treatment failure and hospital and intensive care unit (ICU) length of stay (LOS) following the date of index blood culture

Definitions

- Empiric therapy: the most broad-spectrum systemic antibiotic active against Gram-negative aerobic microorganisms administered after the time a culture was obtained but before susceptibilities were known
- Definitive therapy: the most narrow-spectrum systemic antibiotic active against Gram-negative aerobic microorganisms administered after susceptibilities were known but before day 14
- Persistent disease: ≥1 blood culture growing the same species greater than 24 hours but less than 14 days after the index culture was obtained
- Treatment failure: death on or before day 14 or a combination of the following
  1. Lack of normalization of temperature and white blood cells by day 14
  2. Persisting or recurrent infection requiring additional intervention (e.g. positive blood cultures with the same species on or after day 14 but before hospital discharge, additional intervention including surgery/source control measures on or after day 14 but before hospital discharge, or retained hardware thought to be the source of infection)
  3. Antimicrobial escalation for ongoing symptoms of infection on or before day 14

Statistical analysis

- Categorical variables were compared using χ^2 or Fisher's exact test.
- Continuous variables were compared using Student's t-test or Man-Whitney U test.
- To identify the independent risk factors for all-cause inpatient mortality, variables with a *P*-value <0.2 in the crude analysis were included in a multiple regression model.

RESULTS

Figure 1. Diagram of the study isolates identified

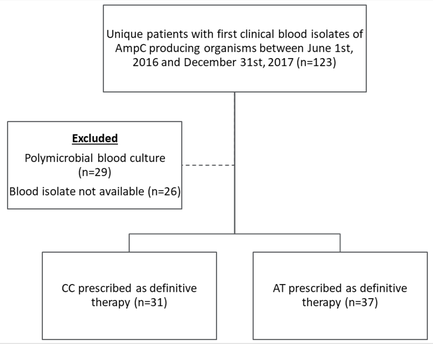


Table 1. Treatment choices

Empiric Treatment	Definitive Treatment
Carbapenems (54%)	PO fluoroquinolones (34%)
Cefepime (37%)	Carbapenems (28%)
Piperacillin-tazobactam (4%)	Cefepime (18%)
Aztreonam (3%)	Third generation cephalosporins (7%)
IV fluoroquinolones (1%)	IV fluoroquinolones (6%)
	Piperacillin-tazobactam (4%)
	Aztreonam (1%)
	Tobramycin (1%)

Table 2. Baseline characteristics

Covariate	Definitive CC (n = 31)	Definitive AT (n = 37)	*P*-value
Age, years, mean ± SD	60.5 ± 21.8	61.3 ± 14.8	.86
Female, n (%)	13 (41.9)	15 (40.5)	.91
Caucasian, n (%)	9 (29.0)	16 (43.2)	.23
Underlying illness/conditions, n (%)			
DM	18 (58.0)	18 (48.6)	.44
Cirrhosis	2 (6.5)	5 (13.5)	.44
SOT	7 (22.6)	5 (13.5)	.33
Immunocompromised	5 (16.1)	5 (13.5)	.76
Causative organism, n (%)			
Pseudomonas aeruginosa	17 (54.8)	17 (45.9)	.47
Enterobacteriaceae	14 (45.2)	18 (48.6)	.77
Non-*P. aeruginosa*/ Enterobacteriaceae	0 (0.0)	2 (5.4)	.50
Source, n (%)			
Pneumonia	9 (29.0)	6 (16.2)	.20
Catheter-associated infection	7 (22.6)	6 (16.2)	.51
UTI	3 (9.7)	7 (18.9)	.33
Extra-biliary IAI	3 (9.7)	4 (10.8)	1.0
Biliary infection	2 (6.5)	2 (5.4)	1.0
SSTI	2 (6.5)	1 (2.7)	.59
Other	1 (3.2)	7 (18.9)	---
Unknown	4 (12.9)	4 (10.8)	1.0
APACHE II, mean ± SD	20.1 ± 9.6	16.9 ± 8.0	.15
ICU on day 1, n (%)	22 (71.0)	21 (56.8)	.15
Source control, n (%)	13 (41.9)	20 (54.0)	.32

Figure 2. All-cause inpatient mortality

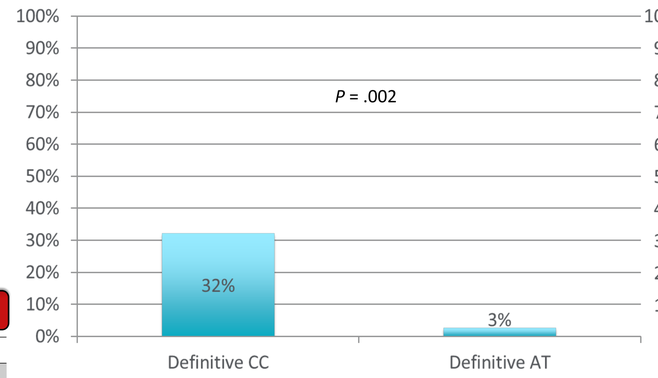


Figure 3. Treatment failure

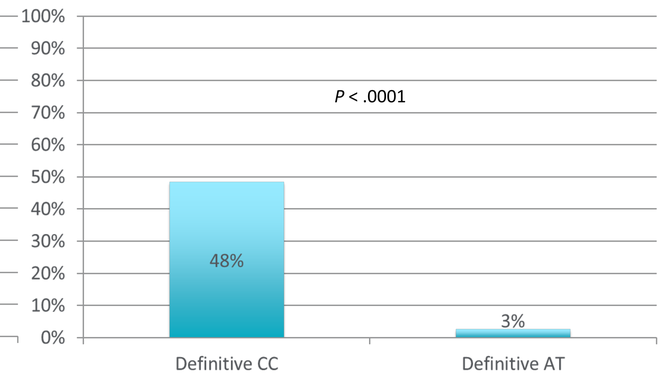
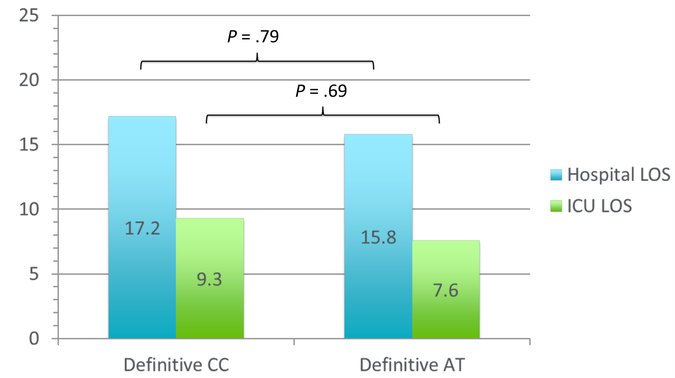


Table 3. Statistical analysis of risk factors for mortality

	Univariate Analysis		Multiple Regression Analysis	
Covariate	**Odds Ratio (95% CI)**	***P*-value**	**Odds Ratio (95% CI)**	***P*-value**
Definitive CC	17.14 (2.05-143.52)	.002	15.17 (1.69-135.76)	.02
Empiric CC	---	.58		
Empiric & definitive AT	---	.58		
Pseudomonas aeruginosa	0.80 (0.22-2.94)	.74		
Enterobacteriaceae	1.43 (0.39-5.23)	.59		
Non-*P. aeruginosa*/ Enterobacteriaceae	---	1.0		
Age >70	1.67 (0.45-6.17)	.44		
Immunocompromised	0.53 (0.06-4.70)	1.0		
SOT	0.42 (0.05-3.62)	.67		
RRT on day 1	1.57 (0.37-6.90)	.68		
ICU on day 1	7.27 (0.87-60.70)	.05	4.25 (0.39-46.04)	.23
APACHE II score ≥20	2.60 (0.70-9.65)	.14	1.26 (0.24-6.68)	.79
Persistent bacteremia	2.31 (0.39-13.79)	.32		
Appropriate antibiotics within 24 hours	1.88 (0.21-16.51)	1.0		
Appropriate dosing 100% of the time	0.65 (0.18-2.39)	.51		
ID consult	0.64 (0.15-2.80)	.68		
Source control achieved	0.19 (0.04-0.94)	.05	0.26 (0.04-1.61)	.15

Figure 4. Hospital and ICU LOS (days)



CONCLUSIONS

- Definitive therapy with CC was an independent predictor of mortality.
- Alternative therapy, specifically oral fluoroquinolones, may be a convenient de-escalation treatment strategy for clinicians to consider.
- Delay of appropriate empiric therapy did not predict mortality.
- Emergence of resistance was not observed.