Antimicrobial prescribing patterns in bloodstream infections caused by cefepime-susceptible extended-spectrum β-lactamase Enterobacterales

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Background

- The Clinical and Laboratory Standards Institute guidance suggests minimum inhibitory concentration (MIC) breakpoints alone are adequate to guide antimicrobial therapy for infections caused by extended-spectrum β-lactamase Enterobacterales (ESBL-E) [1,2]
- The Infectious Diseases Society of America recommends against the use of cefepime and piperacillin-tazobactam for the treatment of blood stream infections (BSIs) caused by ESBL-E, even when in-vitro susceptibility is demonstrated [3,4]
- The Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center microbiology laboratory does not provide labeled designations specifying the presence of an ESBL and susceptibility results are subject to provider interpretation alone
- The microbiology laboratory suppresses piperacillin-tazobactam susceptibilities on ESBL-E identified on blood culture
- Cefepime susceptibilities are reported on ESBL-E identified on blood culture, using a susceptibility breakpoint of ≤1 µg/mL

Objectives

Primary Objective

- Evaluate proportion of patients who received appropriate antimicrobials to treat BSIs caused by cefepime-susceptible ESBL-E within 24 hours of susceptibility results

Secondary Objective

- Determine average time to appropriate ESBL-E coverage
- Characterize empiric and susceptibility-directed antimicrobial selection
- Describe impact of infectious diseases specialist intervention

Methods

Study Design: Multicenter retrospective observational study

Study Period: August 1, 2018 through August 1, 2021

Study Population: Adult patients with blood cultures positive for ESBL-E (defined as: *Escherichia coli, Klebsiella* spp., *Proteus mirabilis* intermediate or resistant to ceftriaxone, ceftazidime, or cefepime) were screened for the following criteria:

Inclusion Criteria	Exclusion Criteria
• Blood isolate susceptible to cefepime	• Concomitant Gram-negative infection • True beta lactam allergy

Data Analysis:

- **Appropriate ESBL coverage:** carbapenem, fluoroquinolone, novel beta lactam/beta lactamase inhibitor, or sulfamethoxazole-trimethoprim within ≤24 hours following the availability of susceptibility results
- **Time to appropriate ESBL coverage:** time from the availability of susceptibilities to time of antimicrobial order

Results

Figure 1: Study Inclusion

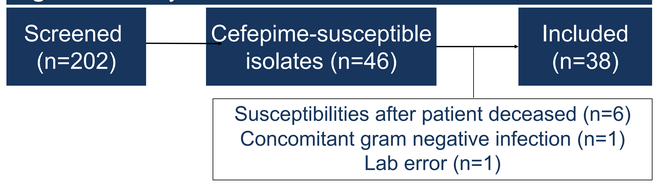

Table 1: Baseline Characteristics*

	Appropriate Coverage (n=20)	Inappropriate Coverage (n=18)
Age, median (IQR)	62 (13)	61.2 (17.6)
Sex, % male	8 (40)	7 (39)
MDRO History	6 (30)	7 (39)
Infectious Diseases Specialist Intervention		
ID Consult	14 (70)	12 (67)
ASP Intervention	5 (25)	-
Infectious Source		
Intra-abdominal	6 (30)	5 (28)
Urinary	4 (20)	5 (28)
Unknown	4 (20)	3 (16)
Osteomyelitis	2 (10)	1 (6)
Pneumonia	2 (10)	-
Line-related	1 (5)	3 (16)
Other	1 (5)	1 (6)
Pathogens		
E. coli	12 (60)	13 (72)
K. oxytoca	5 (25)	-
K. pneumoniae	3 (15)	4 (22)
P. mirabilis	-	1 (6)

Table 2: Empiric antimicrobial selected* (n = 38)

Cefepime	19 (50)
Piperacillin-tazobactam	9 (24)
Meropenem	5 (13)
Ceftriaxone	4 (10)
Ceftazidime- avibactam	1 (3)

Figure 2: Antimicrobial selected within ≤24 hours of susceptibility results (n=38)

Table 3: Antimicrobial continued or selected within ≤24 hours of susceptibility results*

	Appropriate Coverage (n=20)	Inappropriate Coverage (n=18)
Cefepime	-	13 (72)
Ceftriaxone	-	4 (22)
Piperacillin-tazobactam	-	1 (6)
Meropenem	10 (20)	-
Levofloxacin	5 (25)	-
Ertapenem	3 (15)	-
Sulfamethoxazole- trimethoprim	2 (10)	-

Table 4: Time to appropriate therapy*

	Appropriate Coverage (n=20)	Inappropriate Coverage (n=18)
Selected prior to susceptibilities	7 (35)	-
Selected post-susceptibilities	13 (65)	-
Delayed appropriate coverage (≥24 hours)	-	9 (50)
	Time to Appropriate Therapy (n=13)	(n=9)
Time to appropriate coverage (hours), median (IQR)	3.5 (4.6)	29.2 (24.9)

MDRO – Multidrug resistant organism **ID** – Infectious Diseases **ASP** – Antimicrobial Stewardship Program

*** All figures are n (%) unless otherwise noted**

Discussion

- Inappropriate antimicrobial coverage was continued or initiated in 47% (18/38) patients with cefepime (13/18) being the most commonly selected agent followed by ceftriaxone (4/18), and piperacillin-tazobactam (1/18)
- Among patients with initially inappropriate coverage, 50% (9/18) were eventually switched to an appropriate therapy, primarily due to ID consult intervention (7/9)
- In patients who never received appropriate therapy, ID consult was involved in 56% (5/9) of cases; (2/5) were urinary sources, (1/5) documented to consider carbapenem if clinically worsened, and (1/5) occurred early in the study period in August 2018 preceding the publication of the MERINO trial [5]
- Time to appropriate coverage was 3.5 hours (IQR 4.6) in patients initiated on appropriate therapy (<24 hours) (n=13) compared to 29.2 hours (IQR 24.9) in patients with delayed appropriate coverage (≥24 hours) (n=9)
- Cefepime susceptibility results were occasionally delayed due to confirmatory testing (n=4), which may have impacted treatment decisions

Conclusion

Reporting cefepime susceptibility on ESBL-E blood isolates may contribute to inappropriate prescribing of cefepime for the treatment of ESBL-E BSIs. As a result of our findings, our microbiology lab will now suppress cefepime susceptibility interpretation results on ESBL-E with cefepime minimum inhibitory concentrations ≤ 1 µg/L.

References

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