Outcomes of empiric and definitive carbapenem use in Gram-negative infections

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MAD-ID
MAKING A DIFFERENCE IN INFECTIOUS DISEASES PHARMACOTHERAPY

Introduction

Carbapenems are often reserved for use against resistant Gram-negative pathogens. The rationale for using as a carbapenem as empiric or definitive therapy can be vastly different between institutions and clinicians. We sought to describe contemporary use of and outcomes for carbapenem therapy across 18 North American acute-care hospitals.

Methods

Study Design

This was an IRB-approved multi-center cross-sectional study conducted across 18 hospitals located in North America.

Study Population

The study population included patients admitted to a hospital and treated with ≥ 24 hours of an intravenous carbapenem from January 2011 to December 2013.

Inclusion Criteria	Exclusion Criteria
• Age ≥ 18 years • Inpatient treatment with any of the following for ≥ 24 hours: • Meropenem, ertapenem, doripenem, imipenem/cilastatin	• No documentation of carbapenem administration

Data Collection

Data was collected from electronic medical records using a standardized case report form and included the following: patient demographics, select comorbid conditions, carbapenem usage and duration of therapy, infection and microbiological characteristics, discharge disposition and outcomes. Susceptibility classification was performed by the local site according to their standard of practice. Prescribing patterns were compared between empiric and definitive carbapenem groups.

Key Definitions

Empiric Therapy	Definitive Therapy
• Suspected infection or diagnosis of infection without supportive culture results to guide antibiotic selection	• Diagnosis of an infection with supporting culture data available to guide antibiotic selection

Statistical Analysis

Descriptive and bivariate analyses were used to evaluate differences in carbapenem utilization. Categorical data were assessed with the Pearson's Chi-square or Fisher's exact test; continuous data were assessed with Mann-Whitney U test. Statistical tests were two-sided; a P-value of ≤ 0.05 was considered significant. All analyses were performed using SPSS version 23.0.

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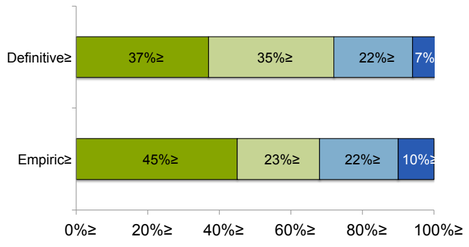
Results

Patient Characteristics and Drug Selection

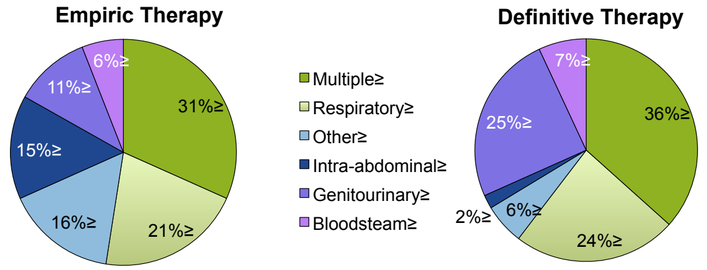
Characteristics (*n*, % or median, IQR)	*n* = 594
Age, < 90 years	62 (49–74)
≥ 90 years	10 (2)
Infection Risk factors	
Prior hospitalization, ≤ 3 months	300 (51)
Prior ICU stay, ≤ 3 months	98 (17)
Nursing home resident	79 (13)
Immunocompromised*	169 (29)
Hx Gram-negative infection, ≤ 12 months	129 (22)
Carbapenem indication at initiation	
Empiric	470 (79)
Definitive	124 (21)



*Ertapenem patients were less likely to be immunocompromised (*P*=0.001)

*Patients were defined as immunocompromised if they had any of the following: Absolute neutrophil count < 500 cells/mm; current diagnosis of leukemia, lymphoma, or solid tumor; history of 30-day chemotherapy, recipient of solid organ or stem cell transplant, or ≥ 10 mg of prednisone within prior 30 days of admission

Infection Sites

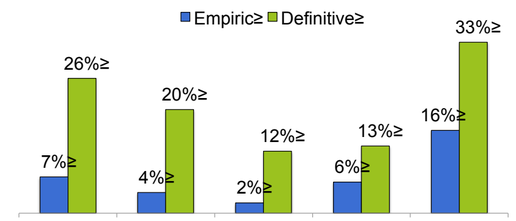


Carbapenem Treatment Duration

	Empiric Therapy Median days, (IQR) *n* = 470	Definitive Therapy Median days, (IQR) *n* = 124	*P*-value
Overall	6 (4-9)	7.5 (4-12)	0.007
Site of infection			
Multiple	6.5 (4-10)	7 (4-13.3)	0.46
Respiratory	7 (4-9)	8 (4.8-14)	0.07
Other	6 (3-10)	10 (3-14)	0.30
Intra-abdominal	5 (3-9)	6.5 (6-6.5)	0.64
Genitourinary	5 (3-8)	7 (5-9)	0.14
Bloodstream	5 (3-7)	7.5 (4.5-13.8)	0.06

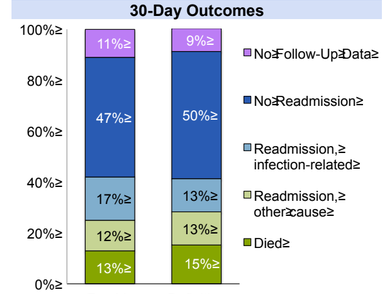
Microbiology and Outcomes

Cultured Organisms*



*Organisms were isolated from 192 (41%) of patients receiving empiric carbapenem use

30-Day Outcomes



De-escalation Opportunities

Definitive Therapy	Culture Susceptibility by Antibiotic (*n* of total isolates tested)						
	A/S	CTR	CEP	CAZ	FQL	TOBRA	PTZ
Acinetobacter sp.	60%, *n* = 5	N/A	33%, *n* = 6	33%, *n* = 6	33%, *n* = 9	56%, *n* = 9	60%, *n* = 5
Citrobacter sp.	N/A	N/A	67%, *n* = 3	0%, *n* = 2	50%, *n* = 2	67%, *n* = 3	N/A
Enterobacter sp.	N/A	N/A	70%, *n* = 10	50%, *n* = 8	73%, *n* = 11	91%, *n* = 11	N/A
E. coli	30%, *n* = 10	40%, *n* = 50	60%, *n* = 42	53%, *n* = 17	23%, *n* = 44	71%, *n* = 49	81%, *n* = 27
Klebsiella sp.	7%, *n* = 15	25%, *n* = 36	36%, *n* = 22	46%, *n* = 13	24%, *n* = 10	31%, *n* = 36	31%, *n* = 32
Proteus sp.	83%, *n* = 6	83%, *n* = 6	83%, *n* = 6	100%, *n* = 3	33%, *n* = 6	100%, *n* = 7	100%, *n* = 6
P. aeruginosa	N/A	N/A	58%, *n* = 26	55%, *n* = 22	38%, *n* = 32	77%, *n* = 31	61%, *n* = 33
Serratia sp.	N/A	N/A	70%, *n* = 10	67%, *n* = 6	82%, *n* = 11	73%, *n* = 11	N/A

Abbreviations:
A/S = ampicillin/sulbactam; CTR = ceftriaxone; CEP = cefepime; CAZ = ceftazidime; FQL = fluoroquinolone; TOBRA = tobramycin; PTZ = piperacillin/tazobactam

Summary

- Among 18 North American hospitals, the majority (79%) of carbapenem use was empiric. In this population, positive cultures were obtained in less than half of patients.
  - The most commonly used carbapenem among all indications was meropenem.
  - Each carbapenem was typically used for multiple infection types. For single infection types, ertapenem was more commonly used for intra-abdominal infections compared to other carbapenems
  - For patients receiving definitive carbapenem therapy, a large percentage of cultured organisms were susceptible to narrower-spectrum antibiotics.
- Carbapenem-targeted antimicrobial stewardship interventions would be valuable to optimize antibiotic therapy in scenarios where alternatives antibiotics can be used.