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

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Background: Carbapenems are often reserved for use against resistant Gram-negative pathogens. The rationale for using 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.

Materials/Methods: Retrospective cohort included patients admitted to a hospital and treated with ≥ 24 hours of an intravenous carbapenem from 1/2011-12/2013. Inclusion criteria were: i) age ≥ 18 years and ii) treatment with intravenous meropenem (MERO), doripenem (DORI), imipenem/cilistatin (IMI) or ertapenem (ETP). Carbapenem use was categorized as empiric or definitive on day one of therapy. Infection characteristics, antimicrobial therapy and outcomes were described for empiric and definitive therapy.

Results: 594 patients were included: 470 (79%) empiric therapy; 124 (21%) definitive therapy. Carbapenem selection: empiric- MERO 210 (45%), ETP 110 (23%), IMI 102 (22%), DORI 48 (10%); definitive- MERO 46 (37%), IMI 43 (35%), ETP 27 (22%), DORI 8 (7%). Median duration of therapy (DOT) (6 days, IQR: 4-10 v. 7.5 days, IQR: 4-12, p=0.007) and hospital length of stay (13 days, IQR: 7-25 v. 19.5 days, IQR: 11-35, p=<0.0001) was different between empiric and definitive therapy, respectively. Dosing strategies varied between groups, but extended infusion was utilized in 2% and <1% of those receiving empiric and definitive therapy. Most frequent carbapenem indications and organisms are listed in Table 1. At least 40% of all definitive therapy isolates were susceptible to a non-carbapenem antibiotic. Thirty-day all-cause mortality (1% v. 3%, p=0.44) and infection-related readmissions (19% v. 14%, p=0.28) were not different between empiric and definitive therapy.

Conclusions: Thirty-day outcomes were not different between patients who received empiric or definitive carbapenem therapy. The majority of patients who received empiric therapy were culture negative.

Table 1: Carbapenem infection and microbiological characteristics

	Empiric therapy *n* = 470		Definitive therapy *n* = 124	
	n (%)	Median DOT, IQR (days)	*n* (%)	Median DOT, IQR (days)
Site of infection				
Multiple	150 (32%)	6.5 (4-10)	46 (37%)	7 (4-13.3)
Respiratory	97 (21%)	7 (4-9)	30 (24%)	8 (4.8-14)
Other	76 (16%)	6 (3-10)	7 (6%)	10 (3-14)
Intra-abdominal	70 (15%)	5 (3-9)	2 (2%)	6.5 (6-6.5)
Genitourinary	49 (11%)	5 (3-8)	31 (25%)	7 (5-9)
Bloodstream	27 (6%)	5 (3-7)	8 (7%)	7.5 (4.5-13.8)
Organism				
Polymicrobial	73 (16%)	7 (4-10)	41 (33%)	8 (4-14)
E. coli	32 (7%)	6 (3.5-9)	32 (26%)	6.5 (4.3-9)
Klebsiella spp.	18 (4%)	4.5 (3-6)	20 (16%)	8 (7-13)
Pseudomonas spp.	10 (2%)	6 (4-11.3)	15 (12%)	8 (5-11)
Other	27 (6%)	7 (4-13)	16 (13%)	5 (3-12.5)
None	312 (66%)	6 (3-9)	0	N/A