Criteria Restricting Inappropriate Meropenem Empiricism (CRIME):

A Quasi-Experimental Carbapenem Restriction Pilot at a Large Academic Medical Center

Drew A. Wells[1], Asia Johnson[1], Jack Lukas[2]; Darius Mason[1]; Kerry O. Cleveland[3,4]; Aaron Bissell[1], Athena L.V. Hobbs[5]

[1]Department of Pharmacy, Methodist Le Bonheur Healthcare (MLH) - Memphis, TN; [2]Department of Pharmacy, Cleveland Clinic - Cleveland, OH; [3]Infectious Diseases, MLH - Memphis, TN 38104, USA; [4]Division of Infectious Diseases, University of Tennessee Health Science Center - Memphis, TN; [5]Cardinal Health Innovative Delivery Solutions - Stafford, TX

Background

- Carbapenems possess a broad spectrum of activity and are an appealing choice for empiric use; however, their use is associated with the development of resistance and *Clostridioides difficile* infections (CDI)[1]
- Limiting carbapenem use for difficult-to-treat infections, including extended-spectrum beta-lactamase producing organisms (ESBLs), ensures these broad spectrum agents remain effective against resistant organisms[2,3]
- Following the results of a medication use evaluation, the hospital system's Antimicrobial Stewardship Program (ASP) Committee initiated a pilot study implementing meropenem restriction criteria:

Active ESBL infection

History of ESBL infection within 90 days

Clinically worsening after receiving 48 hours of either piperacillin/tazobactam or cefepime

Septic shock (i.e. sepsis & lactate > 2 mmol/L & vasopressor use) and high suspicion of ESBL infection, *approved for 48 hours pending culture results*

Intra-abdominal infection with severe anaphylactic penicillin allergy

Purpose

- The objective of this study was to compare overall meropenem utilization after the implementation of restriction criteria.

Methods

- Quasi-experimental study at Methodist University Hospital
- Included patients 18+ years who received ≥ 24 hours of meropenem

Primary Outcome
Inappropriate utilization defined as non-adherence to the criteria

Secondary Outcomes
- Days of therapy/ 1,000 days present [DOT/1000 DP]
- Duration of therapy
- Hospital length of stay (LOS)
- CDI rates
- Cost savings

Methods

Pre-implementation period
(February 8, 2020 – April 5, 2020)

Retrospective review of patients receiving meropenem and evaluation according to criteria for use

Implementation of restriction criteria
(January 2022)

Restriction criteria created & approved by System ASP/P&T

Education to MDs and PharmDs regarding criteria

MD and PharmD documentation in EMR required

Post-implementation period
(February 8, 2022 – April 5, 2022)

Retrospective review of adherence to restriction criteria in patients receiving meropenem

Results

	Pre-implementation n=110	Post-implementation n=39	p value
Age, years [median, IQR]	61.5 [48.8, 71.0]	57.0 [49.0, 65.0]	0.29
Male	62 (56.4)	26 (66.7)	0.26
African-American	66 (60.0)	23 (59.0)	0.91
Penicillin allergy	19 (15.6)	5 (12.8)	0.68
Criteria for Use[a]			
Active ESBL infection	16 (14.5)	12 (30.8)	0.03
History of ESBL infection in previous 90 days	5 (4.5)	12 (30.8)	<0.001
Clinically worsening despite 48 hours of cefepime or piperacillin/tazobactam	40 (36.4)	8 (20.5)	0.07
Severe sepsis and high suspicion of ESBL infection	9 (8.2)	2 (5.1)	0.73
Intra-abdominal infection with anaphylactic penicillin allergy	2 (1.8)	1 (2.4)	1.0
None of the above	56 (50.9)	5 (12.8)	<0.001

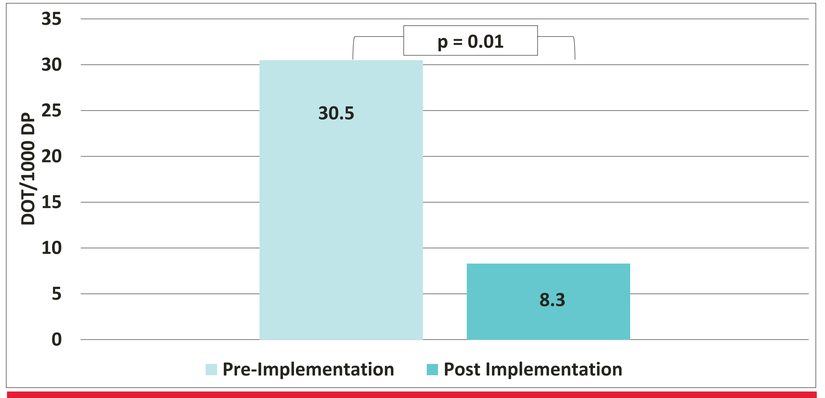
Characteristics reported as n (%) unless otherwise stated
ESBL, extended-spectrum beta-lactamase
[a]Patients may meet more than one criterion for use.

Results

	Pre-implementation n=110	Post-implementation n=39	p value
Primary Outcome			
Inappropriate utilization±	71 (64.5)	5 (12.8)	<0.001
Secondary Outcomes			
CDI SIR	0.1	0.1	0.99
LOS, days [median, IQR]	11.9 [7.8-20.4]	9.2 [5.4-15.2]	0.05
Duration of meropenem use, days [median, IQR]	5.8 [3.2-7.3]	2.4 [1.0-5.5]	<0.001

±Inappropriate utilization defined as non-adherence to the meropenem restriction criteria
CDI SIR, Standardized infection ratio

Days of Therapy per 1,000 Days Present (DOT/1000 DP) pre- vs post-implementation periods



Conclusion

- ASP-driven implementation of restriction criteria decreased inappropriate utilization of meropenem.
- Meropenem restriction may reduce the number of meropenem orders, duration of meropenem therapy, & hospital length of stay.
- Projected annual savings was estimated at $57,300 after implementation of restriction criteria.

References

1. Lee SY, Kotapati S, Kuti JL, Nightingale CH, Nicolau DP. Impact of extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella* species on clinical outcomes and hospital costs: a matched cohort study. Infect Control Hosp Epidemiol 2006;27:1226–32.
2. Zhanel GG, Wiebe R, Dilay L, Thomson K, Rubinstein E. Comparative review of the carbapenems—focus on doripenem. Chemother J 2010;19:131–49 .
3. Tian L, Tan R, Chen Y, Sun J, Liu J, Qu H, et al. Epidemiology of *Klebsiella pneu-moniae* bloodstream infections in a teaching hospital: factors related to the carbapenem resistance and patient mortality. Antimicrob Resist Infect Control 2016;5:48.

Disclosures

The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation