Poster 2430

Impact of USCAST proposed breakpoint changes to aminoglycosides, 'cyclines, and levofloxacin on carbapenem-resistant *Enterobacteriaceae* at a U.S. tertiary referral academic medical center

Brandon Kulengowski, PharmD, MS; Gretchen Ingling, PharmD candidate; Kristen E. Wilhite, PharmD candidate; David S. Burgess, PharmD, FCCP, FIDP
University of Kentucky, College of Pharmacy, Lexington, KY

Brandon.Kulengowski@uky.edu
University of Kentucky
College of Pharmacy
789 S. Limestone St.
Lexington, KY, 40508

Abstract

Background: USCAST is one of many national committees that establish standards for testing and interpreting antimicrobial susceptibility. While working closely with EUCAST, USCAST has proposed updated breakpoints for the aminoglycosides, fluoroquinolones, and tigecycline and is discussing updated breakpoints for the tetracycline antimicrobials. A majority of U.S. hospitals currently utilize FDA or CLSI breakpoints. This study sought to determine the impact of the proposed updated breakpoints on a population of carbapenem-resistant *Enterobacteriaceae* at a U.S. tertiary referral academic medical center.

Methods: Carbapenem-resistant *Enterobacteriaceae* (n=122) from January 2012 – January 2017 were identified as part of routine patient care for study inclusion. Amikacin, gentamicin, tobramycin, levofloxacin, minocycline and tigecycline were evaluated in duplicate on at least two separate occasions by broth microdilution according to CLSI guidelines. The most conservative minocycline breakpoint (≤1 mg/L) being discussed by USCAST was utilized for analysis. McNemar's test determined significant susceptibility changes between USCAST and FDA/CLSI breakpoints for all CRE and for *K. pneumoniae* and *Enterobacter spp.*

Results: *K. pneumoniae* (n=58; 48%) and *Enterobacter spp.* (n=40; 33%) comprised the majority of CRE.

Table 1: CRE susceptibility

Antimicrobials	EUCAST % Susceptibility	CLSI/FDA % Susceptibility	USCAST % Susceptibility	P-value
Aminoglycosides				
Amikacin	66%	86%	55%	<0.001
Gentamicin	21%	31%	21%	<0.001
Tobramycin	15%	18%	14%	0.063
'Cyclines				
Minocycline	-	16%	1%	<0.001
Tigecycline	43%	84%	43%	<0.001
Fluoroquinolones				
Levofloxacin	6%	15%	6%	0.001

P-values <0.05 are significant and indicate differences between CLSI/FDA and USCAST susceptibility

Conclusions: Implementation of the proposed USCAST susceptibility breakpoints will impact clinician antimicrobial choice regarding the treatment of infections caused by CRE. Amikacin and tigecycline susceptibility markedly decreased when utilizing the proposed USCAST breakpoints.

Objective

To determine the impact of the USCAST proposed antimicrobial susceptibility breakpoint changes on carbapenem-resistant *Enterobacteriaceae* at a tertiary referral academic medical center

Results

Figure 1: Carbapenem-resistant *Enterobacteriaceae* (n=122)

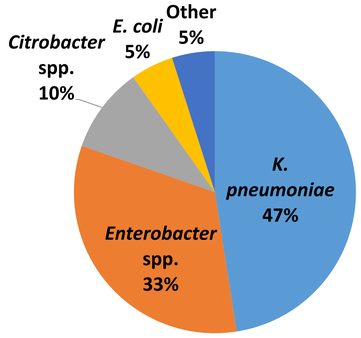


Table 2: Agency Antimicrobial Susceptibility Breakpoints

Antimicrobials	EUCAST (mg/L)	CLSI/FDA (mg/L)	USCAST (mg/L)
Aminoglycosides			
Amikacin	8	16	4
Gentamicin	2	4	2
Tobramycin	2	4	1
'Cyclines			
Minocycline	-	4	1
Tigecycline	1	2	1
Fluoroquinolones			
Levofloxacin	0.5	2	0.5

Figure 2: Antimicrobial Activity against Carbapenem-resistant *Enterobacteriaceae* (n=122)

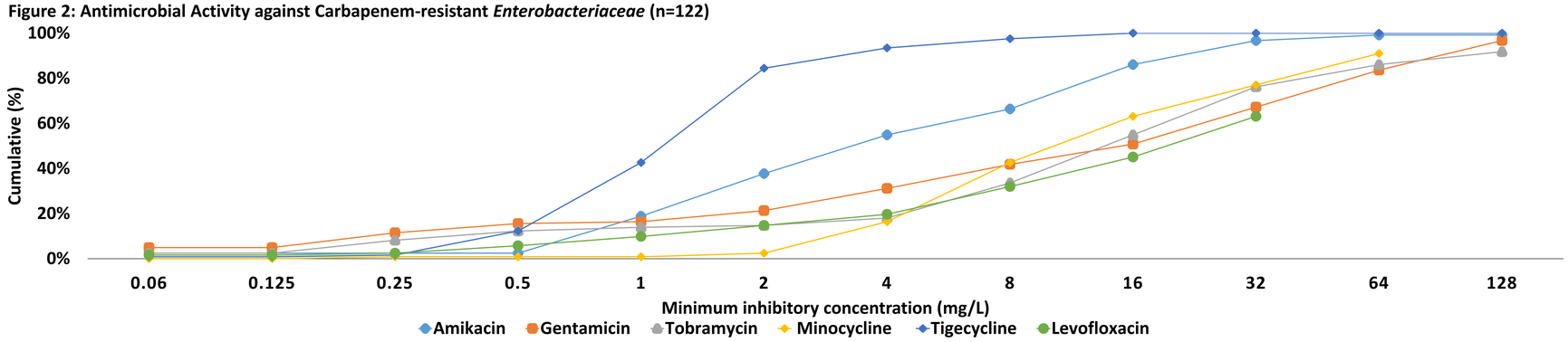


Figure 3: Susceptibility of CRE (n=122)

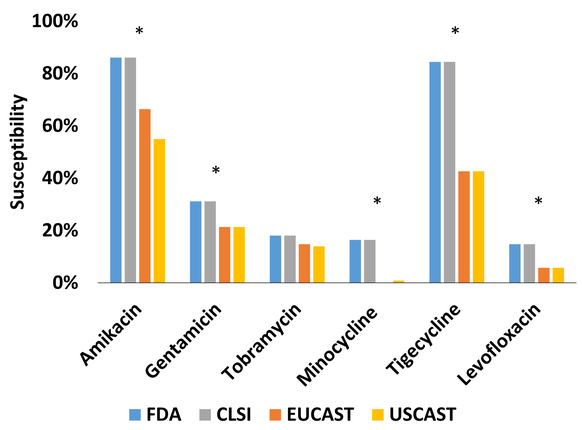


Figure 4: Susceptibility of *Enterobacter* spp. (n=40)

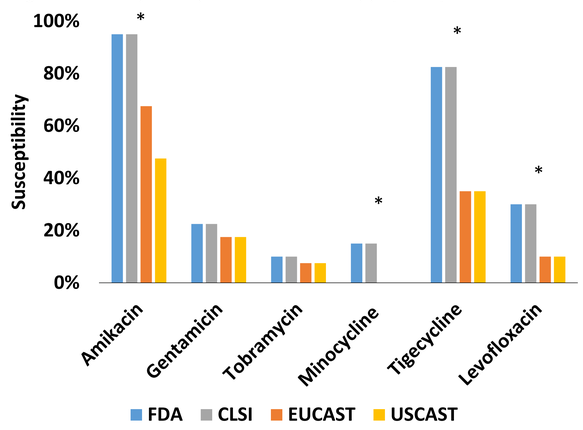
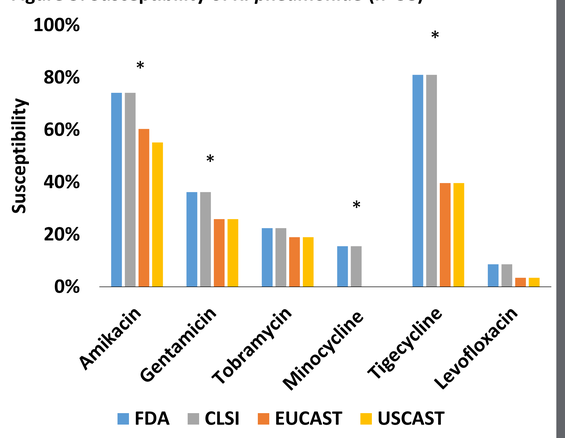


Figure 5: Susceptibility of *K. pneumoniae* (n=58)



*** Denotes *P* ≤ 0.05 when CLSI susceptibility is compared to USCAST**

Methods

- Carbapenem-resistant *Enterobacteriaceae* (CRE; n=122) were collected from 01/2012 – 01/2017 at the University of Kentucky Academic Medical Center.
- The activity of amikacin, gentamicin, tobramycin, levofloxacin, minocycline, and tigecycline were evaluated in duplicate on at least two separate occasions by broth microdilution according to CLSI guidelines.
- CLSI, FDA, EUCAST, and USCAST breakpoints for CRE were utilized for comparing susceptibility.
- McNemar's test was used to identify significant differences between USCAST breakpoints and CLSI/FDA breakpoints for all CRE.

Key Results

- Carbapenem-resistant *Enterobacteriaceae* (CRE) primarily consist of *K. pneumoniae* (47%; Figure 1) and *Enterobacter* spp. (33%; Figure 1).
- Tigecycline and amikacin are the most potent antimicrobials studied against CRE (Figure 2).
- Amikacin, gentamicin, minocycline, tigecycline, and levofloxacin are all significantly impacted by the proposed USCAST susceptibility breakpoint changes (Figure 3).
- Gentamicin and tobramycin susceptibility are not significantly impacted the USCAST proposed breakpoint changes for *Enterobacter* spp. (Figure 4).
- Tobramycin and levofloxacin susceptibility are not significantly impacted by the USCAST proposed breakpoint changes for *K. pneumoniae* (Figure 5).

Conclusions

- The USCAST proposed breakpoint changes significantly impact CRE populations. Specifically, decreased susceptibility of these antimicrobial agents will further limit antimicrobial options for patients with infections caused by CRE.
- The impact that the proposed breakpoint changes will have on patient morbidity and mortality is unknown .