Impact of Revised CLSI and Current EUCAST Carbapenem Breakpoints on Enterobacteriaceae Susceptibility Rates: Report from the SENTRY Program

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ABSTRACT

Background: In mid-2010, CLSI revised ENT CARB (ertapenem [ER], imipenem [IP], meropenem [ME]) breakpoints (CBP), as well as providing initial doripenem (DO) criteria. These reduced MIC CBPs significantly to levels like those of EUCAST. Reference S testing results from SENTRY Program (2009-2007) were used to quantify the impact of these CBP changes on perceived coverage (%).

Methods: SENTRY Program ENT (27,415 strains), tested against CBPs were tabulated using CLSI (M100-S19 [2009], M100-S20-U [2010]) and EUCAST CBPs.

Results: CLSI (2010) CARB CBPs decreased for ER (8.3x) and ME (4x) with coverage reductions of 98.3 to 94.3%, 99.0 to 93.0% and 99.1 to 98.6%, respectively. DO coverage was 98.7% for both CBP sets. CLSI results were slightly lower than EUCAST S rates for ER (96.5%), IP (97.6%) and ME (98.7%). The rank order of perceived coverage was: for CLSI – DO (98.7%) > ME (98.6%) > ER (94.3%) > IP (93.0%) and for EUCAST – DO = ME (98.7%) > IP (97.6%) > ER (96.5%). CP-S varied from 83.3% (EUCAST) to 89.1% (CLSI). CLSI CBPs detected nearly all carbapenemase-producing strains.

Conclusions: Revised CLSI and current EUCAST CARB CBPs significantly decrease perceived coverage (not rank orders); most impacted were ER (-4.0%) and IP (-6.0%) S. The new CLSI CBPs approach harmonization with EUCAST.

MATERIALS AND METHODS

Organism Collection: 27,415 Enterobacteriaceae isolates recovered from respiratory tract, skin and skin structure and bloodstream infections were collected from patients in Asia-Pacific, European, North American and Latin American medical centers between 2007 and 2009. Rank order of pathogen frequency was Escherichia coli (12,031), Klebsiella spp. (6,933), Enterobacter spp. (3,707), Serratia spp. (1,608), Proteus mirabilis (1,350), Citrobacter spp. (676), Indole positive Proteus spp. (557), Salmonella spp. (324), and other Enterobacteriaceae (229).

Susceptibility Testing: The isolates were tested for susceptibility in cation-adjusted Mueller-Hinton broth against up to 30 antimicrobial agents including multiple cephalosporins and carbapenems by reference broth microdilution methods as described by the CLSI M70-A8 (2009). Susceptibility and resistance interpretations were calculated based on the old CLSI M100-S19 breakpoints, the revised breakpoints in the M100-S20-U document, and the current EUCAST breakpoints for comparison purposes.

Concurrent testing of quality control (QC) strains assured proper test conditions were applied. The QC strains included E. coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853.

RESULTS

- The revised CLSI carbapenem susceptibility breakpoints for Enterobacteriaceae (M100-S20-U, 2010) changed most for ertapenem (eight-fold lower), and less for imipenem and meropenem (four-fold). Breakpoints were introduced for doripenem (≤1, 2, ≥4 mg/L for S, I, R), similar to imipenem and meropenem.
- Cefepime MIC distribution has been added to emphasize the wider spectrum of activity of the carbapenem class agents against this large collection of Enterobacteriaceae isolates (Tables 1-4), regardless of current breakpoints.
- Raising the carbapenem breakpoints decreases the risk of treating patient infections with KPC-producing or other carbapenem-resistant strains with carbapenem MIC results currently in susceptible or intermediate categories.
- Greatest harmonization was observed between the new M100-S20-U and EUCAST breakpoints for doripenem (0.0% difference) followed by meropenem (-0.5%), ertapenem (-4.0%) and imipenem (-6.0%; Tables 2 and 3).
- The rank order of carbapenem activity against the 27,415 Enterobacteriaceae strains did not significantly change and was doripenem (98.8%) > meropenem (98.6%) > ertapenem (94.3%) > imipenem (93.0%; Tables 1 and 4).

CONCLUSIONS

- The revised carbapenem breakpoints found in the CLSI M100-S20-U (2010) document produced modest decreases in the perceived susceptibility rates (-0.5 to -6.0%) when tested against this large world-wide collection of Enterobacteriaceae strains (SENTRY Program, 2007-2009).
- The revised CLSI M100-S20-U breakpoints (most conservative) demonstrate greater harmonization with the current EUCAST carbapenem breakpoints for susceptibility and resistance rates, thus reducing the risk of selecting carbapenem therapy against strains producing carbapenemases.

SELECTED REFERENCES