Comparison of carbapenem breakpoints in Clinical Laboratory Standard Institute and European Committee on Antimicrobial Susceptibility Testing guidelines on antibiotic susceptibility test reporting of Acinetobacter baumannii

Editor,

*Acinetobacter baumannii* has emerged as a major multidrug-resistant nosocomial pathogen.[1] Carbapenems are often the only available therapeutic option. European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical Laboratory Standard Institute (CLSI) guidelines are the widely accepted interpretative criteria for antibiotic susceptibility testing (AST).[2,3] However, the interpretation for carbapenems varies with these two guidelines. Currently, CLSI clinical breakpoints for both disc diffusion and minimum inhibitory concentration (MIC) have undergone significant revisions and doripenem breakpoints have been published recently. Consequently, AST reports in diagnostic laboratories have significant change based on the new guidelines and breakpoints.

We tested 29 isolates of *A. baumannii* from blood and urine samples by disc diffusion test[4] using imipenem (10 µg), meropenem (10 µg), and doripenem (10 µg) commercial discs (Hi-Media, Mumbai) and by MIC determination using doripenem E-strip (Hi-Media, Mumbai). The results were interpreted as per CLSI and EUCAST guidelines.[2,3,5] Table 1 shows the percentage of isolates resistant to imipenem, doripenem, and meropenem according to these guidelines. The resistance pattern of *A. baumannii* showed consensus between the two guidelines with respect to imipenem disc diffusion test. Only one isolate was identified as resistant by the EUCAST guidelines and missed using the CLSI guidelines. On the contrary, there was disagreement in results of disc diffusion for meropenem and doripenem (Table 1). The latest CLSI guidelines have altered carbapenem interpretative values for both disc diffusion and MIC testing based on the dose regimen of these antibiotics.[3] The sensitive zone size in CLSI 2014 guidelines has been revised from ≥16 to ≥22 mm for imipenem and from ≥16 to ≥18 mm for meropenem.[3,4] Furthermore, doripenem has been included as the primary test group antibiotic. Similarly, the EUCAST guidelines give sensitivity ≥23 mm for both imipenem and doripenem and ≥21 mm for meropenem. The major difference between these two guidelines is the elimination of intermediate criteria in the EUCAST guidelines.

Doripenem, a new member of carbapenem family, is less susceptible to carbapenemases and has lower MIC compared to imipenem and meropenem in *A. baumannii*.[2] Although it was in clinical use, CLSI interpretative criteria for doripenem disc diffusion (≥18 mm sensitive; 15–17 mm intermediate; ≤14 mm resistant) and MIC (≤2 µg/mL sensitive; 4 µg/mL intermediate; ≥8 µg/mL resistant) have been introduced recently. We have evaluated MIC for doripenem by E-test. The E-test for doripenem showed 65.51% (n = 19) isolates as resistant by CLSI and 86.2% (n = 25) isolates as resistant by EUCAST guidelines while disc diffusion method for doripenem showed 17.24% (n = 5) resistance by CLSI and 58.62% (n = 17) resistance by EUCAST. The discrepancy in disc diffusion and E-test for doripenem was found in 14 isolates by CLSI and 8 isolates by EUCAST (Table 1). These isolates displayed sensitive zone of inhibition in spite of their resistant MIC values. This result indicates that disc diffusion has wider variation in resistance. On the contrary, E-test results in these two guidelines showed better concurrence. Hence, MIC interpretation is more valid and gives better results compared to disc diffusion.

This study was conducted with a small sample size. The findings of this study should be further confirmed by larger multicenter studies. Since interpretive guidelines are by nature subjective, every institution should choose the most appropriate guideline as per their need. Furthermore, there is a need for uniform interpretative guidelines for susceptibility pattern of doripenem. This would help improve reporting and reduce variation of results between the laboratories.

**Table 1:** Comparison of carbapenem resistance as per Clinical Laboratory Standard Institute and European Committee on Antimicrobial Susceptibility Testing breakpoints

| Antibiotics               | Resistant (CLSI) (%) | Resistant (EUCAST) (%) |
|---------------------------|----------------------|------------------------|
| Imipenem (disc diffusion) | 17 (58.62)           | 18 (62.06)             |
| Meropenem (disc diffusion)| 5 (17.24)            | 17 (58.62)             |
| Doripenem (disc diffusion)| 5 (17.24)            | 17 (58.62)             |
| Doripenem (MIC)           | 19 (65.51)           | 25 (86.2)              |

CLSI: Clinical Laboratory Standard Institute; EUCAST: European Committee on Antimicrobial Susceptibility Testing; MIC: Minimum inhibitory concentration

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There are no conflicts of interest.
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