P0807
Paper Poster Session
Antimicrobial susceptibility testing of Gram-negative bacteria

Amoxicillin-clavulanic acid susceptibility testing: fixed ratio versus fixed concentration of clavulanic acid and clinical outcome implications in bacteraemia caused by Enterobacteriaceae

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Background: Currently, international committees EUCAST and CLSI differ in their recommendations about the microdilution methodology and susceptibility breakpoints for amoxicillin-clavulanate (AMC). Our objective was to compare susceptibility testing results when using EUCAST and CLSI recommendation, and the implications of discrepancies in clinical outcome.

Material/methods: A multicenter (13 Spanish hospitals) prospective cohort of patients with bacteraemia due to Enterobacteriaceae who received initial monotherapy with AMC was performed. Susceptibility was determined by broth microdilution according to CLSI (amoxicillin:clavulanate 2:1 ratio) and EUCAST (2mg/L fixed clavulanate concentration) recommendations. Essential agreement was calculated, considering EUCAST as the reference method. To evaluate the concordance, kappa index was calculated. For categorical agreement, clinical categories according to EUCAST and CLSI interpretative criteria were used, and very major errors, major errors, and minor error were calculated considering EUCAST recommendations as reference. Outcome variables were clinical response according to objective criteria (SOFA change) at the end of treatment (EOT) with AMC (EOT-A), at EOT with all antibiotic (EOT-B), and 30-day mortality. Clinical analysis of errors was evaluated according to outcome variables.

Results: We included 264 episodes (202 caused by *E. coli*). Fifteen (5.7%) isolates were ESBL-producers and five (1.9%) OXA-1-producers. Median age was 75 (range, 64-82). Acquisition was nosocomial in 109 (41.3%) cases. The most common source was urinary tract (171 episodes, 64.7%); 49 (18.6%) presented with severe sepsis or shock. The MIC distribution showed important differences: essential agreement between EUCAST and CLSI results was 73.1%, and categorical agreement was 34.5%; the kappa index was 0.24. Overall, 53.4% of isolates were resistant according to EUCAST and 19.7% according to CLSI. A high number of very major errors were observed (45/264, 17.0%), major error was detected in 1 case (0.4%) and minor errors in 45 (17.0%). When the clinical outcome of episodes with concordant and discrepant clinical interpretative categories was analysed, no differences were detected (Table 1).

Conclusions: Important discrepancies in MIC values and clinical categorization obtained with CLSI and EUCAST methodologies were detected. EUCAST methods showed higher resistant levels. No outcome implications were found regarding these discrepancies in this study but more clinical data are needed to evaluate the impact of these differences.

Clinical interpretative category	Failure at the EOT-A	Failure at the EOT	Mortality
$CLSI^{s}$ $EUCAST^{s}$ [n=122 (%)]	6/122 (13.1)	4/122 (3.3)	8/122 (6.6)
$CLSI^{s}$ $EUCAST^{R}$ [n=45 (%)]	6/45 (13.3)	3/45 (6.7)	4/45 (8.9)
$CLSI^{R}$ $EUCAST^{s}$ [n=1 (%)]	0/1 (0)	0/1 (0)	0/1 (0)
$CLSI^{R}$ $EUCAST^{R}$ [n=51 (%)]	12/51 (23.5)	5/51 (9.8)	4/51 (7.8)
$CLSI^{I}$ $EUCAST^{SR}$ [n=45 (%)]	10/45 (22.2)	3/45 (6.7)	3/45 (6.7)