Temocillin susceptibility testing with Vitek2® system and E-test®: Are these methods reliable to determine temocillin MIC?

INTRODUCTION

- The use of temocillin (TEM) is increasing in serious infections caused by Enterobacteriaceae, including extended-spectrum β-lactamases (ESBL), as an alternative to carbapenems (1-5).
- Therefore, accuracy of *in vitro* minimal inhibition concentration (MIC) values is of high importance in an era of antibiotic stewardship based on PK/PD.

MATERIALS AND METHODS

- 100 isolates of *Enterobacteriaceae* were collected from respiratory samples isolated from ICU patients.
- MICs of temocillin were determined in parallel by 3 methods:
  - E-test® (Biomérieux, France) (A)
  - Vitek2® (Biomérieux, France) (B)
  - BMD, following CLSI recommendations (C)

- Since no EUCAST or CLSI breakpoint guidelines exist at this time, susceptibility to temocillin was determined according to breakpoints provided by BSAC (British Society for Antimicrobial Chemotherapy) (6): (S: MIC ≤ 8 mg/L; R: MIC > 8 mg/L).
- Evaluation of categorical agreement (CA), essential agreement (EA), very major errors (VME) and major errors (ME), as defined in Cumitech 31A (7).
- The production of ESBL or carbapenemase was screened according to the antibiotic susceptibility profile.
- ESBL expression was confirmed by the double-disc synergy test.
- Carbapenemase production was established by a colorimetric test detecting the carbapenem hydrolysis or an immunochromatographic assay.

RESULTS

- 100 *Enterobacteriaceae* isolates were collected:
  - *Klebsiella pneumoniae* (KP) (34%)
  - *Escherichia coli* (EC) (23%)
  - *Serratia spp.* (18%), others (25%).
- 35 were ESBL-producers; 13 were carbapenemase-producers.
- 41 isolates were resistant to temocillin (MIC > 8 mg/L) according to BMD method (Table 1).

Table 1: Rates of temocillin Resistance (BMD)

<table>
<thead>
<tr>
<th></th>
<th>Number of isolates (%)</th>
<th>Essential agreement EA (should be ≥ 90%)</th>
<th>Categorical agreement – CA (should be ≥ 90%)</th>
<th>Very Major Errors – VME (should be ≤ 3%)</th>
<th>VME with MIC &gt; 1 twofold dilution</th>
<th>Major Errors – ME (should be ≤ 3%)</th>
<th>ME with MIC &gt; 2 twofold dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K.pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.coli</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serratia spp.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Performances per species were very different as shown in figure 1 for *K.pneumoniae* and *E.coli*.

CONCLUSION

- Compared to BMD, essential agreements are above 90%, as recommended by Cumitech 31A, for both E-test® and Vitek2®.
- Results for categorical agreement are, for both methods, beyond 90% (not acceptable Cumitech 31A), but this can be explained by BSAC breakpoints (no “intermediate” category).
- When taking the adapted definition of VME and ME with MIC > ± 1 twofold dilution, Vitek2® still seems to overestimate sensitivity (with VME rate of 7.3%).
- While E-test® seems to overestimate resistance (with ME rate of 6.8%).
- Looking at the species level, this is essentially the case for *E.coli*.
- The tested MIC range with Vitek2® is limited (≤ 4 to ≥ 32 mg/L).
- When the use of TEM is considered by the clinician, we would recommend to control TEM MIC at least with an E-test®, or, even better, by BMD, especially for *E.coli*.