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

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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 inhibitory concentration (MIC) values is of high importance in an era of antibiotic stewardship based on PK/PD.

OBJECTIVE

- **To perform and compare two antimicrobial susceptibility testing (AST) methods used routinely in many laboratories:**
  - **Vitek2®, bioMérieux France**
  - **E-test®, bioMérieux France**

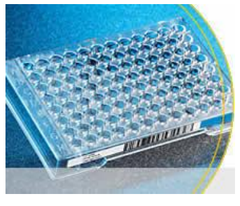
  for determination of TEM MICs with a reference broth microdilution (BMD) method.
- **To evaluate which method is reliable to determine TEM MICs.**

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)

(A)

(B)



(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 using an immunochromatographic assay.

References:
1 *Laterre P.-F.* and al. JAC 2015; 70: 891–898; **2** *Livermore DM, Tulkens PM*, JAC. 2009 Feb;63(2):243-245; **3** *Gupta ND* and al. JAC 2009 Aug;64(2):431-433; **4** *Balakrishnan I.* and al. JAC. 2011 Nov;66(11):2628-31; **5** *De Jongh R.* and al, JAC 2008 ; 61, 382–388 ; **6** BSAC. Standing Committee on Susceptibility Testing. Version 14.0, 05-01-2015; **7** *Clark, R. B.* and al. 2009. Cumitech 31A, Coordinating ed., S. E. Sharp. ASM Press, Washington, DC.

Acknowledgements: *We thank Eumedica® for providing us with E-tests®.*

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 (Table1).

Table1 : *Rates of temocilline Resistance (BMD)*

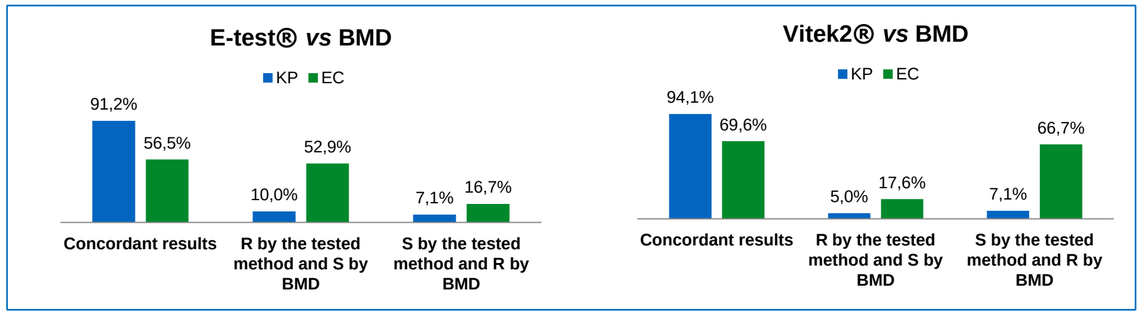
	Number of isolates (%)		
		S	R
K.pneumoniae	34	20	14 (41%)
E.coli	23	17	6 (26%)
Serratia spp.	18	4	14 (78%)
Others	25	18	7 (28%)
Overall	100	59	41

Table2 : *Overall results for agreements, major and very major errors between methods.*

	Essential agreement – EA (should be ≥ 90%)	Categorical agreement –CA (should be ≥ 90%)	Very Major Errors – VME (should be ≤ 3%)	VME with MIC > ± 1 twofold dilution	Major Errors – ME (should be ≤ 3%)	ME with MIC > ± 1 twofold dilution
E-test® vs BMD	96,0 %	82,0 %	12,2%	0,0%	22,0%	6,8%
Vitek2 ® vs BMD	95,0%	84,0%	24,4%	7,3%	10,2%	3,4%

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

Figure 1 : *Concordant and discordant results for K.pneumoniae (KP) and E.coli (EC) between methods*



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*.**