3543

Performance of the EUCAST disk diffusion method in detection of carbapenemase-producing Enterobacteriaceae (CPE) - The NordicAST 2016 CPE study

Bjørg Haldorsen[1], Christian G. Giske[2], Dennis Hansen[3], Kristjan Orri Helgason[4], Gunnar Kahlmeter[5], Iren H.Löhr[6], Erika Matuschek[5], Monica Österblad[7], Kaisu Rantakokko-Jalava[8], Mikala Wang[9], Arnfinn Sundsfjord[1], Ørjan Samuelsen[1] and the NordicAST CPE study group.

[1]Norwegian National Advisory Unit on Detection of Antimicrobial Resistance, Department of Microbiology and Infection Control, University Hospital of North Norway, Tromsø, Norway.[2]Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden. [3]Department of Clinical Microbiology, Herlev and Gentofte Hospital, Herlev, Denmark. [4]Clinical Microbiology, Landspitali University Hospital, Reykjavik, Iceland. [5]EUCAST Development Laboratory, Växjö, Sweden. [6]Department of Medical Microbiology, Stavanger University Hospital, Stavanger, Norway. [7]Bacterial Infections Unit, National Institute for Health and Welfare, Turku, Finland. [8]Clinical Microbiology Laboratory, Turku University Hospital, Turku, Finland. [9]Department of Clinical Microbiology, Aarhus University Hospital, Aarhus, Denmark.

Objective

The aim of this study was to examine the EUCAST recommended screening criteria, based on the EUCAST disk diffusion method, for detection of carbapenemase-producing Enterobacteriaceae (CPE) in a Nordic multi-laboratory study.

Methods

Sixty-one Nordic laboratories (Denmark *n*=9, Finland *n*=15, Iceland *n*=1, Norway *n*=14, and Sweden *n*=22) blindly examined a collection of CPE (*n*=21 Table 1), with reduced susceptibility to meropenem (MEM MIC 0.25 - >16 mg/L). One *K. variicola* strain with bla_{OXA-48}-like was provided in triplicate. *E. coli* ATCC 25922 was included as quality control. All laboratories were to perform the EUCAST disk diffusion method using MEM 10 µg discs, and report their results and interpretation according to EUCAST guidelines using the NordicAST algorithm.

Results

With the exception of one laboratory, all laboratories reported zone diameters for MEM within the accepted QC range for *E. coli* ATCC 25922.

All laboratories reported MEM zone diameters below the EUCAST screening cut-off of <27 mm on all strains with a MEM MIC ≥1 mg/L. For strains with a MEM MIC of 0.5 mg/L (all OXA-48-like positive) and 0.25 mg/L (NDM-positive *P. mirabilis*), eight and one laboratory, respectively reported MEM zone diameters above the EUCAST screening breakpoint (NordicAST algorithm) of <27 mm (27-28 mm). For the laboratories reporting a zone diameter ≥ 27 mm, the reported QC values were in the upper range of the QC interval.

In terms of the laboratories own interpretation of the results, differences were mainly observed based on the interpretation criteria used and the MEM MIC. Depending on the isolate, 2-11% of the laboratories using the <27 mm EUCAST screening breakpoint (*n*=44) did not suspect carbapenemase-production in the isolates with a MEM MIC of 0.25 or 0.5 mg/L. Of the laboratories that used the <25 mm EUCAST screening breakpoint (*n*=8) and clinical breakpoints (*n* =7), 13-38% and 57-86%, respectively did not suspect carbapenemase-production in these isolates.

Table 1. Carbapenemase-producing Enterobacteriaceae including carbapenemase class/gene, meropenem MIC, meropenem zone distribution reported by the participating laboratories and suspicion of carbapenemase production.

		MEM MIC	Zone diameter distribution using meropenem discs from Oxoid, BD and Mast (*n* =58) S ≥ 22 mm R < 16 mm. Screeningbreakpoint < 27 mm																						Suspect
		mg/L	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	CPE**
Class A	*n* = 4																								
KPC (*n* =3)	*K. pneumoniae*	1			1		1	1	2	1	5	6	9	13*	11	4	2		1				1			98%
	E. cloacae cplex	>16	57*	1																						100%
	E. cloacae cplex	8	7			4	3	2	4	4	14*	12	3	4	1											98%
IMI (*n* =1)	*E. cloacae cplex*	1	12		2		1	3	4	2	1	1	2		5*	5	7	3	7	2		1				89%
Class B	*n* = 9																								
NDM (*n* =5)	*K. pneumoniae*	>16	57*	1																						100%
	K. pneumoniae	>16	9		4	3	16*	16	6	2	2															100%
	P. mirabilis	0.25								1				1	3	3	11	6	12*	6	9	4	1	1		75%
	E. coli	2	9	1	1		2	1	3	3	5	8*	11	6	5	3										100%
	Citrobacter sp.	4	3		1	1		2	6	6	4	10*	8	4	1	5	1	2		2						98%
VIM (*n* =3)	*E. coli*	1								3	1	1	5	6	18*	10	8	5		1						98%
	K. pneumoniae	2	1								3	5	7	9	8*	8	2	4	7	2	2					98%
	K. pneumoniae	>16	53*	1	4																					100%
IMP (*n* =1)	*E. coli*	1								1		1		2	3	12	15*	14	6	2	2					97%
Class D (OXA-48 like)	*n = 8*																								
	K. variicola	0.5														1	3	2	9	11	19*	9	4			82%
	K. variicola	0.5	1												1		1	7	10	13*	13	9	3			84%
	K. variicola	0.5														1	3	3	6	13	11*	12	5	2	2	80%
	K. pneumoniae	2	3			2					2		2	1	7	7	17*	13	2	2						98%
	K. pneumoniae	0.5															2	2	7	12	15*	9	8	3		80%
	E. coli	1					1										6	6	15	18*	8	2	2			89%
	E. coli	0.5															2	5	6	8	18*	13	5	1		87%
	K. pneumoniae	2					1	1							2	1	4	11	12*	15	8	2	1			85%

* Median zone diameter, ** Results from participating laboratories using meroepenem discs from ROSCO also included.

Conclusions

The EUCAST disk diffusion method is a robust method to detect CPE, but isolates with low MEM MICs pose challenges to the laboratories. The study shows the importance of using the screening cut-off of <27mm to achieve the highest sensitivity and in particular for the detection of OXA-48-producing isolates. The effect on specificity of using <27 mm versus <25 mm in a low-prevalence routine setting remains to be determined.

Acknowledgements

We want to thank all the participating laboratories for their contributions to the NordicAST 2016 CPE study.

Contact information: bjorg.haldorsen@unn.no