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Evaluation of an algorithm based on faropenem and temocillin inhibition zone diameters for the phenotypic detection carbapenemase-producing *Enterobacteriaceae*

Laurent Dortet[1,2,3], Sandrine Bernabeu[1,2,3] and Thierry Naas[1,2,3]

[1] Bacteriology-Hygiene unit, Assistance Publique/Hôpitaux de Paris, Bicêtre Hospital, Le Kremlin-Bicêtre, France. [2] EA7361 "Structure, dynamic, function and expression of broad spectrum β-lactamases", Université Paris Sud, Université Paris Saclay, LabEx Lermit, Faculty of Medicine, Le Kremlin-Bicêtre, France. [3] Associated French National Reference Center for Antibiotic Resistance: Carbapenemase-producing Enterobacteriaceae, Le Kremlin-Bicêtre, France

Background

With the increasing reports of carbapenem resistance caused by the dissemination of carbapenemase-producting *Enterobacteriaceae* (CPE) several novel technologies have been implemented for the rapid detection of CPE. Currently, these techniques are most often used as complementary test after antimicrobial susceptibility testing results leading to additional cost for clinical laboratories. Accordingly it is of important to develop solution (e.g. algorithms) with high sensitivity and to negative predictive value (NPV) to discriminate non-CPE from those that require complementary testing. Here, **we develop a phenotypic algorithm based on the interpretation of two discs (faropenem and temocillin) for the early detection of non-CPE.**

Methods

Bacterial isolates

The Faropenem/temocillin based algorithm has ben first validated on **a collection of 200 well-characterized enterobacterial isolates** including 137 CPE and 63 non-CPE. Then, it has been **prospectively** compared to the three discs-based (ticarcillin-clavulanate, imipenem and temocillin) algorithm proposed by the Commitee of the Antibiogram of the French Society of Microbiology (CA-SFM) on **211 non-duplicate clinical enterobacterial isolates with reduced susceptibility to carbapenems**.

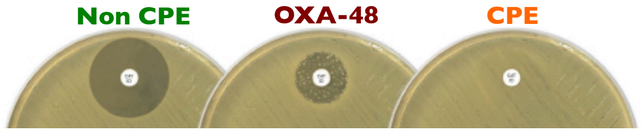
Faropenem/temocillin based algorithm

Inhibition zone diameters of a faropenem containing disc (CAT-ID™, ref D71C, MAST Diagnostic) (**Figure 1**) and a temocillin 30 µg disc (TEM 30C, MAST Diagnostic) were measured and subjected to the algorithm described in **Figure 2A**.

CA-SFM algorithm

Inhibition zone diameters of ticarcillin/clavulanate 75/10 µg, imipenem 10 µg (OXOID, Dardill, France) and temocillin 30 µg (MAST Diagnostic) were measured and subjected to CA-SFM algorithm as previously described (**Figure 2B**).

Figure 1. Representative images of CAT-ID™ disc results



*According to the manufacturer instructions
d = diameter of the inhibition zone

Results

On the collection strains (n=200) the faropenem/temocillin-based algorithm perfectly detected 66.7% of the non-CPE. No false negative was been detected. Most of the OXA-48-like producers (90.5%) have been detected with 98.6% specificity (**Table 1**).

Results of the prospective study (211 isolates) showed **that the faropenem/temocillin-based and CA-SFM algorithms were equivalent for the screening of non-CPE among Enterobacteriaceae with decreased susceptibility to carbapenems** (**Table 1**). Due to its ability to directly detected OXA-48-like producers with 96.8% specificity and 92.5% positive predictive value (PPV), implementation of the **faropenem/temocillin-based algorithm may avoid additional testing for CPE in 57.8% of the enterobacterial isolates with decreased susceptibility to carbapenems compared to 37.4% with the CA-SFM algorithm.**

Figure 2. Prospective comparison of the faropenem/temocillin based algorithm (panel A) and CA-SFM algorithm (panel B) on 211 consecutive enterobacterial isolates with reduced susceptibility to carbapenems.

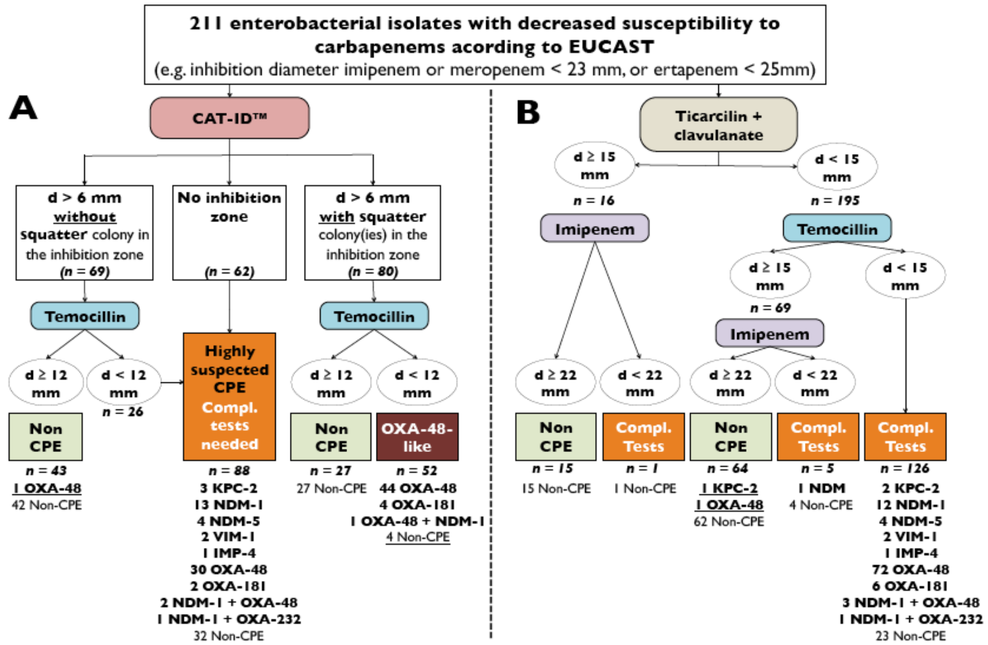


Table 1. Performances of the Faropenem/Temocillin-based algorithm and CA-SFM algorithm

[a] N, Number; [b] Compl., Complementary; [c] Se, Sensitivity; Sp, Specificity; PPV, Positive predictive value; NPV, Negative predictive value; -, can not be determined

Study type	N[a]	Algorithm used	Accurately detected isolates: non-CPE	Accurately detected isolates: OXA-48-like	Compl. tests required[b]	Performance for CPE detection[c] Se	Sp	PPV	NPV
Prospective	211	CA-SFM	73.3%	0%	62.6%	**98.1%**	73.3%	78.8%	**97.5%**
		Faropenem / temocillin	65.7%	59.0%	42.2%	**99.3%**	90.8%	95.0%	**98.6%**
Strain collection	200	Faropenem / temocillin	66.7%	90.5%	59.0%	**100%**	66.7%	-	-

Conclusion

We demonstrated that the faropenem/temocillin-based algorithm might accurately replace the CA-SFM one, resulting in a reduced cost and in a gain of time for clinical microbiology laboratories. However, these two algorithms suffer the same disadvantages: (i) the susceptibility testing has to be performed using disc diffusion methods, although most of laboratories use automated liquid methods, (ii) could not be directly applied on colonies grown on CPE selective medium.