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Evaluation of an algorithm based on faropenem and temocillin for the phenotypic detection of carbapenemase-producing Enterobactericeae

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

[1]*Imperial College London*

[2]*Ea7361,Université Paris Sud, Chu Bicetre, Aphp*

[3]*Hopital de Bicetre; Ea7361, Université Paris Sud; Service de Bacteriologie*

Background: With the increasing dissemination of carbapenemase-producting *Enterobacteriaceae* (CPE) several novel technologies have been implemented for their rapid detection. Currently, these techniques are most often used as complementary tests after initial antimicrobial susceptibility testing results. Accordingly, it is of great importance to develop algorithms based on routine antibiograms with high sensitivity and good negative predictive value (NPV) to discriminate non-CPE from those that require complementary testing. Here, we evaluated a phenotypic algorithm based on the interpretation of two discs (faropenem and temocillin) for the early detection of non-CPE.

Material/methods: The Faropenem/temocillin based algorithm is based on the recording of inhibition zone diameters of a faropenem containing disc (CAT-ID™, MAST Diagnostic) and a temocillin 30 µg disc (MAST Diagnostic). This algorithm has been 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 Committee of the Antibiogram of the French Society of Microbiology (CA-SFM) on 211 non-duplicate clinical enterobacterial isolates with reduced susceptibility to carbapenems.

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

The prospective study (n=211) 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). 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% of the

enterobacterial isolates with decreased susceptibility to carbapenems compared to 37% with the CA-SFM algorithm.

Study type	N[a]	Algorithm used	Accurately detected isolates:		Compl. tests required[b]	Performance for CPE detection[c]			
			non-CPE	OXA-48-like		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%	-	**-**

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

Conclusions: 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 require disc diffusion methods, although most laboratories use automated liquid methods, (ii) and require additional 24h for susceptibility testing on colonies grown on CPE selective medium.