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Evaluation of the Carbapenem-Inactivation Method for the detection of carbapenemase-producing Enterobacteriaceae

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Background: There is an urgent need for accurate and fast diagnostic tests to identify carbapenemase producing enterobacteria (CPE). Here, we have evaluated the Carbapenem Inactivation Method (CIM), which has been developed as a phenotypic technique for detecting carbapenemase activity from bacterial culture. The CIM, based on *in vitro* inactivation of the meropenem contained in a 10µg charged disk by carbapenemase-producing strains, was reported to be 100% sensitive and specific for CPE detection.

Material/methods: A total of 257 enterobacterial isolates were used to evaluate the performance of the CIM in comparison with the Carba NP test. Molecular detection was used as the gold standard. Ninety three well characterized isolates (including 30 non-CPE and 63 CPEs of high diversity) with decreased susceptibility to at least one carbapenem molecule were used to (i) evaluate the best substrate that have to be used in the CIM and (ii) to compare it to the Carba NP test. The CIM was then evaluated prospectively against 164 suspected CPE isolates referred to the French National Reference Center for Antimicrobial Resistance from march to april 2016.

Results: Based on the results of the retrospective study, sensitivity and specificity of the CIM and the Carba NP test were 92.1% and 100%, respectively. Five OXA-48 like enzymes, which gave uncertain or false-negative results with the Carba NP test were positive for the CIM. On the other hand, 3 NDM-1 and one VIM-1-producing *Enterobacteriaceae* were repeatedly negative for the CIM, while the Carba NP test was positive. We demonstrated that the meropenem was the best substrate to perform the CIM test since sensitivity and specificity were 81.1% and 100% using ertapenem disk, and 100% and 66.7% using imipenem disk, and respectively. Taking in account of the results of the retrospective and the prospective study CIM test and Carba NP test have quite similar parameters with sensitivity, specificity, positive predictive value and negative predictive value of 96.3%, 98.9%, 99.0% and 98.4% for the CIM test versus 96.9%, 100%, 100% and 100% for the Carba NP test.

Conclusions: Our results confirm that the CIM has high sensitivity and specificity for CPE detection. It has significant advantages, including low cost and simplicity of implementation. Above all, it is really easy to interpret. It may be a useful tool for the reliable confirmation of carbapenemase-activity in enterobacterial isolates, especially in clinical microbiological laboratories with limited resources, no trained personnel, and no specialized equipment to detect carbapenemase activity. The main disadvantage of the CIM resides in the need for a two hours incubation and a subsequent overnight culture.