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Evaluation of the beta-carbs test, a colorimetric test for the rapid detection of carbapenemase activity in gram negative bacilli

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) are most often resistant to most if not all classes of antimicrobial molecules, and thus represent a major public health concern. Since their identification based solely on antibiotic susceptibility testing is not easy, there is an urgent need for accurate and fast diagnostic tests to identify carbapenemase-producing bacteria. Various phenotypic confirmation tests for detecting carbapenemases have been developed, including detection of carbapenem hydrolysis using MALDI-TOF MS, or biochemical tests (e.g. Carba NP test and derivatives) Here, we have evaluated a novel colorimetric test (β-CARBA™ test) to detect carbapenemase-producing Gram negative bacilli from cultured colonies.

Material/methods: The commercially available β-CARBA™ test (Bio-rad) is based on the change of color of a undisclosed chromogenic substrate in presence of carbapenem-hydrolyzing enzymes. One colony is resuspended in 200 µl of reaction mixture, and incubated at room temperature for 30 minutes. A color change from yellow to orange red or purple signals the presence of a carbapenem-hydrolyzing activity. The performances of the β-CARBA™ test (Bio-rad) were compared to those of Carba NP test (or CarbAcineto NP test), and RAPIDEC® CARBA NP (bioMérieux) using a collection of 230 isolates with characterized β-lactamase content. This collection included 156 carbapenemase-producers (121 Enterobacteriaceae, 16 *Pseudomonas*, 19 *A. baumannii*) and 74 were non-carbapenemase-producers (55 Enterobacteriaceae, 10 *Pseudomonas* and 9 *A baumannii*).

Results: The β-CARBA™ test correctly detected 86.9% of the carbapenemase producers including all KPC, VIM, IMP, 91.3% of the NDM, 80.5% of the OXA-48-like, and all the *A. baumannii* related OXA-carbapenemases (OXA-23, OXA-40, OXA-58 and over-expressed OXA-51). All rare metallo-β-lactamases (SPM, AIM, GIM, DIM and SIM) were detected. Importantly, all non-KPC Ambler class A carbapenemases (GES variants, IMI-variants, NMC-A, SME, and FRI-1) were not detected including .GES-variants with carbapenemase activity (n=3), IMI (n=3), NMC-A (n=1), SME (n=2), FRI-1 (n=1)

and BIC-1 (n=1). All non-carbapenemases-producers gave a negative result except with OXA-163, OXA-405 and one TEM-3-producing *C freundii*.

The overall sensitivity and specificity of the β-CARBA™ test were 86.5% [CI95 = 80.3% - 91.0%] and 94.6% [CI95 = 86.9% - 97.9%], respectively. As comparison, the sensitivity and specificity of the RAPIDEC® CARBA NP were 97.5% [CI95 = 93.7% - 99.0%] and 100% [CI95 = 95.1% - 100%], respectively and those of the Carba NP/CarAcineto NP test were 95.6% [CI95 = 91.1% - 97.8%] and 100% [CI95 = 95.1% - 100%], respectively. This test is easy to perform and to interpret by non-specialized staff members.

Conclusions: Despite, lack of specificity towards non-KPC Ambler class and OXA-48-like carbapenemases, the β-CARBA™ test could complete the existing panel of tests available for the confirmation of carbapenemases in Gram negatives.