A practical diagnostic algorithm for screening and confirmation of carbapenemase production in Enterobacteriaceae in an OXA-48 endemic region using temocillin and ertapenem discs

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) have been increasing worldwide, and are currently endemic in many countries. Rapid detection of CPE isolates is the most important step to implement infection control measures in order to prevent further dissemination. Many phenotypic methods have been developed with this purpose, some of them based on disc diffusion using temocillin. The aim of this study is to describe an algorithm for screening and confirmation of CPE performed in an OXA-48 endemic hospital and to evaluate its efficacy.

Materials/methods: All Enterobacteriaceae recovered from samples of patients admitted to the hospital between May and November 2017 were assessed by the algorithm described in Figure 1. All isolates showing diameters less than 24 mm (or MICs higher than 0.5 mg/L) for ertapenem (criteria 1) and less than 12 mm (criteria 2) for temocillin in disk diffusion assays, were tested sequentially by a lateral flow immunochromatographic (IC) assay (OXA-48 K-SeT® Coris BioConcept, Gembloux, Belgium), a multiplex PCR with targets for VIM, KPC and OXA-48 (RealCycler, Progenie molecular, Valencia, Spain) and, if neither of these tests were positive, by the modified Hodge test.

Results: 272 isolates met criteria 1 and 2, 136 of them were confirmed as OXA-48 producers, and 131 were recovered from patients who had been previously infected/colonized with OXA-48 isolates and assumed to produce the carbapenemase based on their resistance phenotype. Four isolates were positive for VIM and a single isolate was negative for all tests, including the modified Hodge (Figure 1). The algorithm was easy to apply, reliable and, in case of OXA-48-producers, results are obtained at the same time as those of the antimicrobial susceptibility testing.

Conclusions: In geographical regions with a high prevalence of OXA-48 producers, the algorithm presented here using a combination of the modified zone diameter cut-offs for temocillin (≥12 mm) previously suggested by Huang et al., (J Antimicrob Chemother 2014; 69:445-50), with the EUCAST breakpoint for ertapenem, could save unnecessary additional testing for confirmation of carbapenemase-producing Enterobacteriaceae.
Microscan + disc diffusion assay performed in parallel in an OXA-48 endemic area

CRITERIA 1: MIC ertapenem > 0.5 or ertapenem disc diameter ≤ 24 mm

272 isolates

CRITERIA 2: temocillin < 12 mm

CPE with same resistance phenotype in last 6 months
No CPE with same phenotype in last 6 months

151 isolates

Lateral flow immunochromatographic (IC) assay OXA-48 K-Set®

130 isolates

15 isolates

Same day as AST results

24 h after AST results

CPE

Homemade PCR for other carbapenemase genes

Hodge Test

OXA-48/VIM/IMP real-time PCR

1 isolate

No CPE

CPE, carbapenemase-producing Enterobacteriaceae; AST, antimicrobial susceptibility testing

*This isolate was an Enterobacter cloacae which showed low level of resistance to ertapenem and no resistance to imipenem or meropenem