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Resistance to colistin in Gram-negative rods

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Carbapenemase-producing Enterobacteriaceae may be responsible for therapeutic failures since such strains are usually multidrug-resistant. Colistin, an antibiotic of the polymyxin family, is one of the last-resort molecules potentially active for treating patients infected with these strains. Its use is thus constantly increasing but resistances occur.

Our work contributed to improve the diagnosis of colistin resistance by developing two new diagnostic tools: a rapid test, the Rapid Polymyxin NP test and a selective culture medium, the SuperPolymyxin agar. In term of resistance mechanisms, we identified novel chromosomal mutations within the *pmrA, pmrB, phoP, phoQ, mgrB* and *crrB* genes responsible for the acquired colistin resistance and heteroresistance in *K. pneumoniae* and *K. oxytoca*. We revealed that chromosomal mutations and plasmid resistance were additional and could lead to the acquisition of a high level of colistin resistance in *E. coli*. We investigated an outbreak caused by colistin- and carbapenem- resistant OXA-48-producing *K. pneumoniae* strains in France in 2014. We also identified the low-level intrinsic resistance to colistin of *Hafnia* spp. Finally, we evaluated the usefulness of a novel therapeutic option, namely ceftazidime / avibactam, in combination or not with aztreonam, for potential treatment of infections caused by colistin-resistant and carbapenemase-producing *K. pneumoniae***.**

This work has significantly contributed to improve the knowledge of colistin resistance in Gram negatives in diagnostic, in characterization of acquired or intrinsic resistance mechanisms, and in epidemiology.

Jury :
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