TITLE: PLASMID-MEDIATED QUINOLONE RESISTANCE (PMQR) AND EXTENDED-SPECTRUM BETA-LACTAMASES (ESBL) GENES IN CHROMOSOMAL AMPC-PRODUCING *ENTEROBACTERIACEAE* ISOLATED FROM HOSPITALIZED PATIENTS: QNRD1 PREVALENCE

Authors: [1]ARAUJO, I.J.; [1]ANDRADE, L.N.; [2]MARTINEZ, R.; [1]DARINI, A.L.C.

Institution: [1] School of Pharmaceutical Sciences of Ribeirão Preto – University of São Paulo

[2] Clinical Hospital of Ribeirão Preto – University of São Paulo

ABSTRACT:
Chromosomal AmpC-producing *Enterobacteriaceae*, especially the genera *Serratia, Providencia, Citrobacter, Proteus* and *Morganella,* informally named SPACE group pathogens, are opportunistic bacteria associated to nosocomial infections. It is verified that there are few phenotypic and molecular data about antimicrobial resistance for these species, when compared to others. This study aimed the investigation of plasmid-mediated quinolone resistance (PMQR) and extended-spectrum beta-lactamases (ESBL) genes in chromosomal AmpC-producing *Enterobacteriaceae* resistant to quinolone and/or 3^{rd}-4^{th} generation cephalosporins. Bacteria were isolated from inpatients in an university hospital in two different time periods (2007, n=19 and 2016, n=48). We investigated the presence of PMQR genes (*qnrA, B, C, D, S e VC, aac(6´)-Ib-cr, qepA* and *OqxAB*) and ESBL genes ($bla_{\text{CTX-M, TEM and SHV}}$) by PCR and sequencing. In addition, plasmids replicons of the major incompatibility (Inc) groups occurring in *Enterobacteriaceae* were screened by PCR-based replicon typing (PBRT) scheme. In 19 enterobacteria (*Morganella morganii*, n=9, *Serratia marcescens*, n=5, *Citrobacter koseri*, n=2, *Citrobacter freundii*, n=1, *Providencia stuart* n=1, *Proteus mirabilis*, n=1) *qnrD1* gene was detected. Some *M. morganii* presented concomitantly other *qnr* genes (B or S). Moreover, $bla_{\text{CTX-M-2}}$ was also detected in the *Citrobacter freundii* e *Morganella morganii*. For other isolates, AmpC-overproducing was responsible to resistance to extended cephalosporins. Plasmids *colE*-like were detected in almost all isolates carrying *qnr* genes. SPACE group pathogens seem to be important reservoir of *qnr* genes in the hospital studied, highlighting *qnrD1*, little detected in other studies compared to other *qnr* genes. It was also possible to observe increase frequency of *qnr* genes in these species comparing 2007 to 2016. This knowledge becomes fundamental to trace new strategies to control antimicrobial resistance, contributing to better prognosis and management of bacterial infections in hospitals.

Keywords: *ampC*, resistance genes, plasmids, opportunistic pathogens, nosocomial infection

Acknowledgments: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP - 2014/14494-8; CAPES, PNPD/CAPES)