TITLE: CARBAPENEM RESISTANCE AND VIRULENCE CHARACTERISTICS IN *Acinetobacter baumannii* AND *Pseudomonas aeruginosa* ISOLATED FROM A TERTIARY HOSPITAL

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Abstract:

Pseudomonas aeruginosa and *Acinetobacter baumannii* are highly implicated in nosocomial infections. These species are often associated with multidrug resistance phenotypes, since they have intrinsic and acquired resistance genes to various antimicrobial drugs. The objective of this study was to evaluate physiological and molecular characteristics of carbapenem resistance in *P. aeruginosa* and *A. baumannii.* Carbapenem-resistant *P. aeruginosa* (n=19) and *A. baumannii* (n=44) were isolated from hospitalized patients. Physiological tests were performed to evaluate hemolytic activity, oxidative stress, biocides tolerance and biofilm formation, besides determination of antimicrobial susceptibility patterns. Genetic markers related to β-lactamases production (*bla*$_{KPC}$, *bla*$_{SIM}$, *bla*$_{IMP,}$ *bla*$_{SPM-1}$, *bla*$_{VIM}$, *bla*$_{GIM,}$ *bla*$_{OXA}$ and *bla*$_{NDM-1}$), efflux systems (*Ade*B*, mex*B*, mex*D*, mex*F and *mex*Y) and porin loss (*opr*D) were screened by PCR. Epidemiological data were also evaluated. Advanced age, predominance of intensive care patients, use of invasive medical devices (such as venous catheter), previous treatment with fluoroquinolones or β-lactams in combination with β-lactamase inhibitor and prolonged stay in hospital were predisposing factors for infection by these microorganisms. No resistance was observed against colistin and tigecycline. Hemolytic activity was not observed in carbapenem-resistant *P. aeruginosa*. These bacteria were less tolerant to oxidative stress and biocides, but they showed increased ability of biofilm formation. Genes encoding efflux pumps (MexAB-OprM, MexCD-OprJ, MexEF-OprN, MexXY-OprM), SPM-1 and *opr*D were found in *P. aeruginosa*. The major molecular mechanisms of carbapenems resistance present in *A. baumannii* strains were oxacilinases synthesis (OXA-23, OXA-51 and OXA-143) and efflux pump (*Ade*B*)*. These results may suggest that carbapenem-resistance is truly a complex phenomenon related not only to drug-resistance genetic markers, but also, to structure modifications and alterations in bacterial physiology. As an ecological consequence, carbapenem-resistance may be associated to the infection prognosis, not only related to the patients' health status, but also to the alterations in bacteria structure and physiology.

Keywords: resistance, carbapenem, porin, efflux, β-lactamases

Financial support: CAPES, CNPq, FAPEMIG