TITLE: HIGH GENETIC DIVERSITY OF CARBAPENEM-HYDROLYZING CLASS D ß-LACTAMASES-PRODUCING *Acinetobacter baumannii* ISOLATED FROM BLOODSTREAM INFECTIONS OVER TEN YEARS

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ABSTRACT

Multidrug-resistant *Acinetobacter baumannii* (MRAB) are considered one of the major threats in hospital settings owing to its significant genomic plasticity in acquiring antibiotic determinants of resistance (ADR). The aim of this study was to investigate the ADR and the clonal relatedness of MRAB isolated from bloodstream of patients admitted in University Hospital of Londrina (UHL) from 2006 to 2016. The identification and the antimicrobial susceptibility tests of clinical isolates were performed by biochemical tests, disk diffusion method, and different automatized systems, and interpretation followed Clinical and Laboratorial Standards Institute guidelines. Molecular identification of isolates as *A. baumannii* was defined by the presence of $bla_{\text{OXA-51}}$. The production of carbapenemases was investigated by CarbAcineto NP test and the ADR were detected by PCR. The genetic similarity of the MRAB was determined by ERIC-PCR, and the clonal analysis was conducted using the BioNumerics software with a 90% cutoff. A total of 103 MRAB isolates collected from inpatients in all units of UHL were studied. The antibiotic susceptibility profile of MRAB revealed high rates of resistance to all groups of antimicrobials: cefotaxime (100%), cefepime (100%), imipenem (92,2%), meropenem (93,2%), ciprofloxacin (100%), levofloxacin (100%), sulfamethoxazole/trimethoprim (87,4%), gentamicin (72,8%), and amikacin (48,5%). Among the 94 carbapenem-non-susceptible MRAB, 93 (98,9%) were carbapenemase-producers. All isolates were positive for $bla_{\text{OXA-51}}$ confirming the *A. baumannii* species. The majority of the MRAB harbored $bla_{OXA\text{-}23}$ (90,3%), except for 2 isolates that harbored $bla_{\text{OXA-143}}$ (1,9%). None of the MRAB were positive for $bla_{\text{OXA-24/40}}$, $bla_{\text{OXA-58}}$, bla_{SHV}, $bla_{\text{CTX-M}}$, bla_{GES}, bla_{IMP}, bla_{SIM}, bla_{GIM}, bla_{VIM}, *mcr*-1, and *qnr* genes. The dendrogram analysis identified twenty clones, where five of them, M (23,3%), J (17,5%) P (11,6%), K (10,7%) and R (9,7%), represented the majority of the isolates. The MRAB of these main clones were detected in inpatients from all units of UHL in different years, indicating persistence of endemic clones adapted to selective pressure of antimicrobials in the UHL as well as suggesting intra-hospital transmission by medical staff and patient transfer. This work demonstrates that typing and molecular epidemiology studies of MRAB provide useful information to surveillance programs aiming controlling the spread and potential outbreaks by MRAB in UHL.

Keywords: *Acinetobacter baumannii*, ß-lactamases, bloodstream infections, genetic diversity, multidrug-resistant

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