TITLE: CLONAL EXPANSION OF POLYMYXIN-RESISTANT *Acinetobacter baumannii* IN A TEACHING HOSPITAL

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ABSTRACT:
Acinetobacter baumannii (AB) is an opportunistic pathogen often multidrug-resistant and associated with hospital infections, for which polymyxins (PLM) are last resource treatment. We characterize 16 AB strains isolated from Aug-Oct/2016 in a Brazilian hospital and present the genetic basis for five PLM resistant strains. We identified AB species amplifying $bla_{\text{OXA-51-like}}$ and assessed the genetic similarity by *Apa*I DNA macrorestriction followed by PFGE. We typed each pulsotype representatives by MLST. The results showed a clonal similarity in five out of six strains resistant to PLM (PLM-R), which was of 100% in three of them. Our findings indicate a cross-transmission, either by the healthcare staff or contaminated equipment, suggesting pulsotype A-ST1 as an endemic clone that expanded with recent mutations leading to PLM resistance (possibly selected by the polymyxin B use). All antimicrobial categories plus chlorhexidine gluconate (CHG) had their MIC determined either by broth microdilution or disk diffusion. We observed a 37.5% incidence of PLM resistance. All the strains were extensively drug-resistant and four were pan drug-resistant. CHG MICs were lower than the patient bathing solution concentration, which could be an effective spread control measure. Because some of the isolates were from catheter tips, we wanted to assess their biofilm formation, and indeed all strains form biofilm, but only a PLM-S was a good former; it seems AB biofilms could be a survival mechanism, especially when resistance is not high enough. Draft genome of some isolates was obtained on Illumina systems and submitted to ResFinder 3.2 and CARD to search for acquired resistance genes. The *mcr* and *eptA* genes were absent. Instead, amino acid substitutions in PmrCAB, known to confer colistin resistance, are likely the reason for the PLM resistance in these strains. PmrB substitution T232I was present in the three resistant strains that had lower polymyxin B MICs (16-64 mg/L). The other three (MIC >128 mg/L) had a P170L substitution in the same protein. Colistin MICs of these strains were all ≥128 mg/L. All the PLM-R isolates had a mutation leading to R125H replacement in PmrC. We compared a PLM-S to a PLM-R strain, both ST1, detecting variants by CLC Genomics and besides *pmrB* and *pmrC*, we observed 28 ORFs mutated. The high incidence of PLM resistance among the AB isolates highlights the need for constant resistance vigilance, particularly regarding drugs used as last resources.

Keywords: *Acinetobacter baumannii*, multidrug resistance, polymyxins

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