Title: EVALUATION OF PERSISTENCE PHENOTYPE IN Acinetobacter baumannii – Acinetobacter calcoaceticus COMPLEX ISOLATES AFTER MEROPENEM EXPOSURE

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Abstract: Acinetobacter baumannii - Acinetobacter calcoaceticus complex is an important bacterial group responsible for several healthcare-associated infections. Although much has been elucidated about resistance in this complex, very little is known about the persistence phenotype. Bacterial persisters comprise a small subpopulation of susceptible cells able to survive to lethal concentrations of bactericidal antimicrobials or other stressors. Persistence is associated to failures in the antimicrobial therapy, especially of the chronic and recurrent infections. Therefore, the aim of this study was to evaluate the formation of persister cells in clinical A. baumannii-calcoaceticus complex isolates in planktonic culture after exposure to different concentrations of meropenem, a carbapenem widely used to treat infections caused by this bacterial complex. Twenty non-duplicate clinical A. baumannii-calcoaceticus isolates were obtained from different clinical specimens from university hospital in Porto Alegre - RS, and previously characterized as susceptible to meropenem by the assessment of Minimum Inhibitory Concentration (MIC). The isolates were cultivated in LB broth at 37°C until the late exponential growth phase and exposed to 15 µg/mL or 30 µg/mL of meropenem (15x and 30x the highest MIC found among the isolates, respectively) for 48 h. In order to determine the number of Colony Forming Units per milliliter (CFU/mL) of the surviving fraction, aliquots were removed after 6, 24 and 48 h of meropenem exposure, serially diluted and drop plating on nutrient agar. All isolates when cultured under planktonic condition produced persister cells after exposure to 15 μg/mL or 30 μg/mL of meropenem, however in different fractions, ranging from 0.0035% to 0.7214% and 0.0009% to 0.2412% of the original population, respectively. This is the first report of persister cells occurrence in A. baumannii-calcoaceticus after a carbapenem exposure. Our data suggest that persistence phenotype is widely distributed among A. baumanniicalcoaceticus complex isolated from healthcare-associated infections, and the presence of this phenotype may result in ineffectiveness of the antimicrobial therapy.

Keywords: persistence, *Acinetobacter baumannii-Acinetobacter calcoaceticus* complex, meropenem

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