Clonal Expansion of Acinetobacter baumannii Strains Displaying Elevated Tigecycline MIC Values Responsible for Increasing Resistance Rates in Latin America

**Objectives**: To evaluate the high prevalence of Acinetobacter spp. (ASP) displaying elevated tigecycline MICs (≥2 mg/L) in Latin American hospitals and its correlation with the presence of active efflux systems (AdeABC) and possible horizontal gene transfer (HGT) events.

**Methods**: 1,950 ASP isolates were tested for MIC values ranging to 4 to 8 mg/L and the isolates were all resistant to tigecycline as shown on the CLSI breakpoints. The expression of the AdoABC efflux pump was confirmed by measuring \\(^{14}\)C-leucine uptake in the presence of inhibitors and geometric analysis (MALDI-TOF MS). Molecular typing using PFGE showed that 15/29 isolates from Sao Paulo belonged to a major clone and the remaining 4 strains belonged to other PFGE types.

**Results**: Isolates were genetically related. Expression results of AdeABC and AdeFHG were also evaluated.

**Conclusion**: Tigecycline-resistant strains in Brazil and Mexico are associated with the overexpression of two resistance-nodulation-cell division (RND) multidrug transporters, AdeABC and AdeFHG. AdeABC overexpression contributes to resistance to various antimicrobial classes, including β-lactams, antimycotics, quinolones and tigecycline. A. pittii and A. genomic species 2 isolates are reported to synthesize an orphan that is a two-component regulation system and mutations on the orphan gene del1 altered the expression of AdoABC efflux pump. AdeABCá and AdeFHG overexpression could lead to the overexpression of rpoB, chloramphenicol and clindamycin as well as decreased susceptibility to commonly used antibiotics without affecting 8-lactams and antimycotics.

**Materials and Methods**: A total of 1,080 ASP isolates from Latin America were selected in 2011 and high-quality DNA-free RNA preparations and measured by quantitative RT-PCR, normalized using 18S rRNA (Acinetobacter) and 16S rRNA (Escherichia coli) as housekeeping genes. The expression of adeABC and adeFHG were determined using a real-time PCR method described as the Clinical and Laboratory Standards Institute (CLSI, M07-A9) with a few modifications to generate results of AdeABC and AdeFHG tested for 18 strains with MIC values ranging to 4 to 8 mg/L and the isolates were all resistant to tigecycline as shown on the CLSI breakpoints (M07-S2). PCR, gel electrophoresis, and sequencing were used to identify the isolates.

**Introductions**: AAC-6’-Ia and AAC-6’-Ib are the two main families of the AAC-6’ class of acetyltransferase that are involved in resistance to aminoglycosides, sulfonamides, and tetracyclines. AAC-6’-Ia and AAC-6’-Ib are involved in the overexpression of efflux pumps, which can lead to the extrusion of compounds and it may occur due to horizontal acquisition of genetic elements.

**Results**: In this study, we evaluated a total of 1,950 ASP isolates collected in 2011 to 2015 from Latin American hospitals and the isolates were genetically related. Expression results of AdeABC and AdeFHG were also evaluated.

**Conclusions**: Tigecycline-resistant strains in Brazil and Mexico are associated with the overexpression of two resistance-nodulation-cell division (RND) multidrug transporters, AdeABC and AdeFHG. AdeABC overexpression contributes to resistance to various antimicrobial classes, including β-lactams, antimycotics, quinolones and tigecycline. A. pittii and A. genomic species 2 isolates are reported to synthesize an orphan that is a two-component regulation system and mutations on the orphan gene del1 altered the expression of AdoABC efflux pump. AdeABCá and AdeFHG overexpression could lead to the overexpression of rpoB, chloramphenicol and clindamycin as well as decreased susceptibility to commonly used antibiotics without affecting 8-lactams and antimycotics.

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