TITLE: EFFECTS OF SUB-INHIBITORY CONCENTRATIONS OF POLYMYXIN B ON PATHOGENICITY FACTORS OF MULTIDRUG RESISTANT *Acinetobacter baumannii* STRAINS

AUTHORS: Costa, P. S.; Rezende, I.; Mendes, T. A. O.; Farias, L. M.; Nobre, V.; Gonçalves, R.; Santos, S. G.

INSTITUTION: INSTITUTO DE CIÊNCIAS BIOLÓGICAS, UFMG, BELO HORIZONTE, MG, BRASIL.

ABSTRACT:

The high frequency of *Acinetobacter baumannii* in health care-related infections (HAI), currently around the world, is mainly due to its ability to invasion, colonization and tissue destruction, which are associated to the presence of several pathogenicity factors found in this microorganism, in addition to its resistance to multiple antimicrobials agents. Studies have shown that subinhibitory (sub-MIC) concentrations of antimicrobials may alter the transcriptional and phenotypic response of bacteria, but little is known about how sub-MIC of Polymyxin B (sub-MIC PolyB) can affect these processes. Thus, this study evaluated the sub-MIC PolyB influence in the growth curve, biofilm formation, resistance to oxidative stress and the expression of regulatory genes related to virulence in the *A. baumannii* reference strain (ATCC 19606) and in four clinical strains (numbered as 05, 06, 10 and 32). Biofilm formation was evaluated by the crystal violet method and the oxidative stress was screened by resistance to hydrogen peroxide with the disc diffusion test. The expression of genes *bap, recA, adeR, oxyR, bfmR* and *abaI* obtained from the strains submitted to sub-MIC PolyB conditions were performed by quantitative real-time PCR. It was verified that sub-MIC PolyB reduced the formation of biofilm in a concentration-dependent manner and the resistance to oxidative stress was affected only with ½ MIC, which led to a lower response of the bacteria to exposure to hydrogen peroxide. Expression of the regulators, *bap* and *recA* were significantly increased in the presence of sub-MIC PolyB in reference strain and in one clinical strain (number 05). For strain 10, all these genes did not undergo expression alteration; and for the strain 32 all the genes had their expression diminished. These results indicate that sub-MIC PolyB may reduce biofilm formation and bacterial resistance to hydrogen peroxide, as well as affect the expression of important genes related to pathogenicity in *A. baumannii* multidrug resistant. Our results confirm that residual amounts of Polymyxin B can regulate positively or negatively important pathogenicity factors in *A. baumannii*, which can contribute to the success of the infectious diseases by these bacteria. In addition, these data alerts the monitoring of patients under antimicrobial therapy, aiming at their increasingly rational use.

Keywords: Patogenicity; Biofilm; Polimylyxin B; *Acinetobacter baumannii*

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