ANTI-BIOFILM CATIONIC PEPTIDES POTENTIATE THE ACTION OF BETA-LACTAM ANTIBIOTICS AGAINST MULTI-DRUG RESISTANT K. PNEUMONIAE

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Multi-drug resistant carbapenemase-producing Klebsiella pneumoniae (KpC) are becoming a common cause of infections in health care centers. This bacterium can develop multicellular biofilms, which lead to adaptive antibiotic resistance. Here we accessed the ability of KpC strains isolated of patients from Brasilia hospitals to form biofilm in nutrient rich medium and nutrient poor media and evaluated the effect of cationic peptides (alone or combined with conventional antibiotics) against those strains. Using microplates assays we observed that KpC stains form a thicker biofilm in BM2 minimal medium when compared at rich media. Through this assay, we also found that the small cationic peptides 1018, DJK-5 and DJk-6 inhibit planktonic growth and prevent biofilm formation of different KpC strains. The concentration of peptides to prevent biofilm formation was lower than that one required inhibiting planktonic cells of most tested strains. Using flow cell experiments, we observed that 1018 and DJK-6 were able to disturb 2-days old biofilms of different KpC strains. In some cases, the peptides induced significant biofilm cell death. The peptide DJK-6 increased the action of β-lactam antibiotics, including the carbapenem meropenem, a last resource antibiotic against KpC strains. Combinations between DJK-6 and meropenem prevented planktonic growth, biofilm formation and leaded the eradication of 2-days old biofilms. Interestingly, peptide DJK-6 was able to enhance, by at least 32-fold the ability of meropenem inhibit biofilm growth of the strain 1825971 and at least 16-fold the ability of meropenem eradicate pre-formed biofilm of this strain. Using peptide DJK-6 to potentiate the activity of β-lactams, including meropenem, represents a promising strategy to treat infections caused by KpC isolates.

Keywords: biofilms, carbapenemase-producing K. pneumonia, cationic peptides.

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