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ePoster Viewing

Antimicrobials: in vitro antibacterial susceptibility

Acquisition of *Acinetobacter baumannii* colistin resistance due to loss of lipopolysaccharide results in increased susceptibility to clinically relevant antibiotics without altering susceptibility to antimicrobial peptides

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Objectives: The acquisition of colistin resistance in multidrug resistant *Acinetobacter baumannii* can complicate the effective treatment of infections caused by these strains. The objective of this study was to characterize how the acquisition of colistin resistance in multidrug resistant *A. baumannii* due to loss of lipopolysaccharide (LPS) affected susceptibility to clinically relevant antibiotics and cationic antimicrobial peptides.

Methods: Colistin resistant, LPS deficient derivatives of clonally distinct multidrug resistant clinical isolates with mutations in the LPS biosynthesis genes *lpxA*, *lpxC*, and *lpxD* were employed. MIC values for 14 antibiotics and bacterial killing assays for six cationic antimicrobial peptides were determined for both the parental strains and their LPS deficient derivates by broth microdilution. Ethidium bromide accumulation assays were performed in order to characterize differences in membrane permeability between LPS replete and deficient strains.

Results: Susceptibility was unchanged or varied minimally for gentamicin, ciprofloxacin, ticarcillin, ampicillin, tigecycline and sulbactam upon LPS loss. Moderate increases in susceptibility were seen for amikacin (4-16 fold), ceftazidime (4-64 fold), imipenem (4-32 fold) and meropenem (4-64 fold) between LPS deficient strains and their parental counterparts. Dramatic increases were observed upon LPS loss for azithromycin (>32 fold change, all MIC values ≤ 0.25 mg/L for all strains), rifampicin (>32 fold change, all MIC values ≤ 0.125 mg/L for all strains) and for vancomycin (64-512 fold change). However, doses ranging from 8 to 32 mg/L of the six antimicrobial peptides were able to kill bacteria, reducing more than 6 log the bacterial viability.

Conclusions: These results indicate that the acquisition of colistin resistance through LPS loss in multidrug resistant *A. baumannii* can result in increased susceptibility to clinically relevant antibiotics without altering the susceptibility to cationic antimicrobial peptides. The increased susceptibility to antibiotics may, in part, be due to increased membrane permeability.