INFLUENCE OF POLISACCHARIDE CAPSULE AND PNEUMOCOCCAL SURFACE PROTEIN A (PspA) ON THE BACTERICIDAL ACTIVITY OF INDOLICIDIN AGAINST *Streptococcus pneumoniae*

WAZ, N. T.; FRÓES, B. M.; OLIVEIRA, S.; DARRIEUX, M.

UNIVERSIDADE SÃO FRANCISCO (AV. SÃO FRANCISCO DE ASSIS, 218, CEP 12916-900, BRAGANÇA PAULISTA – SP, BRASIL)

ABSTRACT

Streptococcus pneumoniae is responsible for high morbidity and mortality worldwide. The polysaccharide capsule confers protection against phagocytosis and influences many aspects of pneumococcal pathogenesis. The capsular polysaccharides (CPS) are highly immunogenic and exhibit great structural variability, with more than 100 serotypes described so far. Antimicrobial peptides (AMPs) are an important innate defense mechanism against many pathogens. An example of AMP is indolicidin, a cationic peptide produced by bovine neutrophils, with bactericidal effects against bacteria. CPS has been shown to interfere with the ability of AMPs to kill pneumococci, but the effects of capsule variability in susceptibility to indolicidin have not been explored. The present work aimed to determine the effects of capsule and PspA – another important virulence factor of pneumococci – on resistance to indolicidin *in vitro*. A bactericidal plate assay was designed to determine the susceptibility of pneumococci to killing by indolocidin, comparing wild type x mutant strains lacking PspA or capsule. Different pneumococcal serotypes exhibited variable resistance to indolicidin, which appears to be correlated with the capsule net charge. Interestingly, the effect of capsule expression on resistance to indolicidin was dependent on the serotype; bacteria with lower zeta potential were more resistant to indolicidin when capsule was present, while those with less negative surface charge were more resistant in the absence of capsule. Finally, mutant strains lacking PspA showed reduced resistance to indolicidin, an effect that was reproduced by incubating wild type bacteria with anti-PspA antiserum. The addition of purified CPS had a protective effect, increasing bacterial resistance to indolicidin. Taken together, the results indicate that CPS and PspA play an important role in modulating bacterial resistance to indolicidin, with the effects of capsule varying among different serotypes. These results may contribute to elucidate the protective role of CPS and PspA against pneumococcal diseases, leading to development of alternative vaccines against this pathogen.

Keywords: Capsular polysaccharide, Indolicidin, PspA, *Streptococcus pneumoniae*.

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