ALTERATIONS IN PRODUCTION OF BIOFILM AND HYDROLYTIC ENZYMES IN STRAINS OF *Staphylococcus aureus* ISOLATED IN HIGH CONCENTRATIONS OF VANCOMYCIN

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ABSTRACT: *Staphylococcus aureus* is one of the most important human pathogens, responsible for a huge number of infections worldwide. Vancomycin (VC) is the antimicrobial choice for empirical therapy to treat *S. aureus* in hemodyalisis patients. Studies have shown that dosages with the minimum serum concentration ≤10µg/mL are associated with therapeutic failures and may promote the emergence of *S. aureus* strains with a phenotype of intermediate resistance for VC (hVISA - "heterogeneous Vancomycin-Intermediate *S. aureus*"). This relationship between staphylococcal pathogenesis and susceptibility to vancomycin has been investigated, but more studies are needed to understand this relationship. The aim of this study was to verify changes in biofilm expression and in the production of hydrolytic enzymes in 15 *S. aureus* subpopulations isolated in 16 µg/mL vancomycin (derivative strain) in relation to its original (parental) strain. Fifteen strains isolated from bacteremia in hemodyalisis patients were exposed to a selective pressure assay in increasing concentration of VC (0,5 until 16 µg/mL). The MIC for VC was determined by broth microdilution. Analysis of the autolytic profile, the production of biofilm and, hydrolytic enzymes was performed in derivatives strains isolated in 16 µg/mL of VC with their respective parental strains. Strains Mu50 and Mu3 were used as control in the tests. Statistic test used was T paraded. Results: The MIC of the parental strains ranged from 0,5 to 1,5 µg/mL VC, whereas in derivatives strains from 1,0 to 2,0 µg/mL. In three (20%) strains the MIC was increased in two dilutions. Note that all strains showed MIC in the susceptibility range. In eight strains derivative (53%) the production of biofilm was decreased in comparison with their parental strain and in seven strains (47%) the production was the same in parental and derivative strain. Of five hydrolytic enzymes tested only two were significant hemolisin and dnase (p=0,0002 and 0,0021, respectively). In 10 strains (67%) the production was decreased or did not show any production of hemolisin in derivative strain and, in five strains (33%) the production was equal in parental and derivative strain. The production of dnase was equal in all strains. Our results showed that the physiological changes necessary to survive in high concentration of vancomycin have an impact on virulence, probably due to reducing of expression the some virulence factors like biofilm and production of hydrolytic enzymes.

Key-words: *Staphylococcus aureus*, resistance, virulence, MIC, vancomycin

Financial support: CAPES, CNPQ

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