TITLE: ANTIMICROBIAL MODULATION OF BIOFILM FORMATION AND PRESENCE OF RELATED GENES AMONG *Staphylococcus aureus* ISOLATES CARRYING *pvl* GENES FROM DIFFERENT GENETIC BACKGROUNDS

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ABSTRACT

Staphylococcus aureus isolates cause a wide range of infections and the presence of Panton-Valentine leukocidin (PVL) may lead to clinical complications. Moreover, the ability of some isolates to form biofilm is related to an increase of bacterial pathogenicity, and the presence of sub-minimum inhibitory concentrations (sub-MICs) of antimicrobials can modulate the bacterial virulence expression. A collection of 12 *S. aureus pvl* positive isolates, previously characterized in relation to their clonal lineage and SCC*mec* types was selected: USA1100/type IV (5 isolates), USA400/IV (2) and USA400/MSSA (2), USA300/IV (1), USA800/IV (1) and ST30/SCC*mec* V (1). The isolates were analyzed as the presence of *icaA* and *sasG* genes by PCR, and the MIC in TSB with 1% of glucose was determined for oxacillin, cefalexin, linezolid and vancomycin. The modulation of biofilm production in the presence of ¼ and ½ of MICs was accessed in polystyrene plates and stained with safranin. The optical densities at 492nm (DO_{492nm}) were measured and compared to the biofilm formation in absence of antimicrobials. All isolates presented the *icaA* gene, and seven (58%) (USA300, USA400, USA800 and one isolate from USA1100 clone) were *sasG* positive. Sub-MICs of oxacillin and cefalexin induced the biofilm formation in MRSA isolates, being the opposite observed for the MSSA isolates, irrespective of presence of *icaA* or *sasG* genes. However, linezolid and vancomycin sub-MICs reduced the biofilm formation in USA300 and USA400 isolates (*sasG*+), but not in USA1100 isolates (*sasG*-), which had their DO_{492nm} values increased, except for one USA1100 isolate tha twas *sasG*-positive and presented a reduction of their values for both antimicrobials. Therefore, β-lactams can induce the biofilm formation among MRSA, but this fact was not found among MSSA isolates, irrespective of the clonal lineage. Under action of linezolid, biofilms of *sasG*-positive isolates suffered a reduction, which can be related with the protein synthesis inhibition by this antimicrobial. On the other hand, among *sasG*-negative USA1100 isolates, linezolid and vancomycin sub-MICs induced the biofilm formation. The role of antimicrobials sub-MICs in the modulation of biofilm production by different *S. aureus* lineages and the presence of *sasG* gene as a predictor of the outcome of the biofilm modulation needs to be further investigated.

Keywords: *S. aureus;* biofilm; *sasG;* sub-MICs.

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