

**TITLE:** ISOLATION OF *Staphylococcus aureus* STRAINS FROM HIGH CONCENTRATIONS OF VANCOMYCIN

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**ABSTRACT:**

Bacteremia are the second cause of mortality in hemodialytic (HD) patients. Vancomycin (VC) is the antimicrobial choice for empirical therapy with a average dose of 25 mg/kg of body weight being applied every 72 hours, always after the hemodialysis session. The minimum serum concentration (MSC) of VC desirable for effective action against *S. aureus* should be 10-20 µg/mL. Studies have shown that dosages with MSC ≤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*"). Despite the many reports of isolation of these strains, the clinical implications of this phenotype are not yet well understood. The aim of this work was to select *S. aureus* subpopulations capable of growing at high VC concentrations. Forty-nine *S. aureus* strains isolated from bacteremia in HD patients were exposed to a selective pressure assay in increasing concentration of VC (0,5 until 16 µg/mL). The strains grown in the highest VC concentration were isolated and called derivative, while its original strain called parental. The MIC for VC was determined by broth microdilution. Analysis of the autolytic profile was performed in derivatives strains isolated in 16 µg/mL of VC with their respective parental strains to verify possible changes related to the thickening of the cell wall. *S. aureus* strains Mu50 and Mu3 were used as control in the tests. All *S. aureus* strains were able to grow at a minimum concentration of 4 µg/mL and a maximum of 16 µg/mL: 17 (35%) strains grew in 4 µg/mL, 8 (16%) strains in 6 µg/mL, 9 (18%) strains in 12 µg/mL and 15 (31%) strains in 16 µg/mL of VC. 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. No significant increase was observed in the MICs between the derivatives strains and its parental strains, except three (20%) strains that the MIC was increased in two dilutions. Note that all strains showed MIC in the susceptibility range. Seven strains (70%) isolated in 16 µg/mL of VC showed lower autolytic activity than their respective parental. All strains were able to grow at high VC concentrations indicating a relatively rapid physiological adaptation suggesting a mechanism of tolerance rather than resistance. MIC determination does not appear to be a good predictor of the *S. aureus* ability to grow at high VC concentrations.

**Keywords:** Bacteremia; hVISA; Vancomycin; Hemodialytic Patients

**Development Agencies:** CAPES, CNPq, FAPES