

TITLE: COMPARATIVE EVALUATION BETWEEN METHODS FOR DETERMINATION OF MINIMUM INHIBITORY CONCENTRATION OF VANCOMYCIN IN *Staphylococcus aureus* ISOLATED FROM BLOODSTREAM INFECTIONS

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ABSTRACT:

Staphylococcus aureus is a microorganism associated with a variety of nosocomial and community-acquired infections. Currently, vancomycin is the main choice for the treatment of infections by methicillin-resistant *S. aureus* (MRSA). According to the Clinical and Laboratory Standards Institute (CLSI), broth microdilution (BMD) is considered the gold standard for measuring vancomycin MIC in *S. aureus*. However, BMD is laborious and expensive method. Thus, most clinical laboratories employ practical methods in the routines, such as automated systems or gradient MIC strips, but these methods may not determine accurate vancomycin MIC values. The aim of this study was to carry out a comparative analysis between commercial methods (Etest® strips, Phoenix® and VITEK® 2 systems) with the standard BMD method. A total of 78 clinical strains of *S. aureus* were isolated from bloodstream infections of patients admitted to a university hospital in Rio de Janeiro, Brazil. Fifty-one isolates were classified as MRSA and 27 as methicillin-susceptible *S. aureus* (MSSA). Following CLSI and the manufacturers' recommendations, vancomycin MIC was determined using BMD, Etest®, Phoenix® and VITEK® 2; and the results were compared through statistical analysis. The characterization of the mobile genetic element Staphylococcal Cassette Chromosome *mec* (SCC*mec*) was carried out for all MRSA isolates. The BMD and Phoenix® tended to determine values of MIC= 1 µg/mL (83.3% and 87.2%, respectively), while Etest® and VITEK® 2 determined the majority with MIC= 1.5 µg/mL (41%) and 0.5 µg/mL (83%), respectively. Thus, Etest® and VITEK® 2 tended to overestimate and underestimate, respectively, the MIC values of vancomycin when compared to BMD. The absolute agreement ($0 \pm$ dilution) with BMD was highest for Phoenix® (78.2%), followed by Etest® (26.9%) and VITEK® 2 (23.1%). There was not statistical difference ($P > 0.05$) among Phoenix® and BMD results. The results indicate that Phoenix® to be a better method for determination of vancomycin MIC, as compared to Etest® and VITEK® 2. Of the five types of SCC*mec* found (I - V), SCC*mec* II (39%) and IV (51%) were the most frequent. The results of the current study showed that vancomycin MICs vary according to the test method. It is essential that clinicians take into account the differences in MIC results determined by different methods, since the MIC value is generally the parameter used by clinicians to select the appropriate therapy.

Keywords: *Staphylococcus aureus*, vancomycin, minimum inhibitory concentration, automated systems, Etest®

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