VANCOMYCIN INTERMEDIATE RESISTANCE AND HETERORESISTANCE IN *Staphylococcus aureus* ISOLATES FROM BLOODSTREAM INFECTION IN AN UNIVERSITY HOSPITAL IN RIO DE JANEIRO, BRAZIL

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Abstract:

Approximately 40% of all *Staphylococcus aureus* isolates from bloodstream infections (BSI) are resistant to methicillin at Brazilian hospitals. In this context, vancomycin and others antimicrobial agents are important to therapy. The aim of the present study was to determine the resistance to vancomycin and other antimicrobials and characterize the type of *mec* cassette in *S. aureus* isolates from BSI. Consecutive *S. aureus* isolates from patients with BSI attended in a university hospital between 2011 and 2013 were analyzed. One isolate by episode was considered. The isolates were analyzed by the cefoxitin disk diffusion test. The Minimum Inhibitory Concentration (MIC) for vancomycin, teicoplanin, linezolid, daptomycin, tigecycline (all from Sigma®) and ceftaroline, the active metabolite of ceftaroline fosamil, (donated by AstraZeneca Pharmaceuticals) was determined by the broth microdilution method (BMD). Isolates with vancomycin MIC ≥2µg/ml were tested for heteroresistance (hVISA) using BHI agar supplemented with 3, 4 or 6µg/ml (BHIa3, BHIa4 or BHIa6) of vancomycin, and BHIa4 containing casein (BHI4ca) was also used. The macromethod Etest (MET) and Etest GRD was also performed. Population analysis profile (PAP) was used to confirm hVISA and VISA isolates. All cefoxitin-resistant isolates (MRSA isolates) were subjected to PCR for detection of the SCC*mec* type. Among 110 isolates, 31 (28%) were MRSA: 15 (48%) carried the SCC*mec* II and 16 (52%) the SCC*mec* IV. The vancomycin MIC50 and MIC90 were 1 and 2, respectively. Six isolates showed intermediate resistance to vancomycin (VISA isolates) and four of them were MRSA SCC*mec* types II (n=3) and IV (n=1). MRSA isolates were more likely to be resistant to daptomycin (p = 0.0003). All isolates were susceptible to teicoplanin, linezolid and tigecycline. One isolate presented intermediary resistance to ceftaroline (MIC = 2 µg/mL - SCC*mec* II). Among 25 isolates with vancomycin MIC≥2 mg/L, three grew on BHIa3, including one MRSA-IV. Other three isolates grew on MET, being one MRSA-II that also grew on agar BHIa4 and BHIa4ca and was confirmed as hVISA. Among VISA isolates 5 (83%) grew on BHIa4. No isolate grew on agar BHIa6 or Etest GRD. Among two MRSA presumed to be hVISA only one, presenting the SCC*mec* II, was confirmed as hVISA. The results showed the presence of hVISA and VISA isolates related to BSI in our hospital harboring emerging types of SCC*mec* II and IV.

Keywords: Bloodstream infections*;* heteroresistance; *Staphylococcus aureus;* vancomycin; VISA.

Agências de fomento: CNPq, FAPERJ, CAPES