EVALUATION OF THE SYNERGISTIC POTENTIAL OF ANTIMICROBIALS AGAINST *STAPHYLOCOCCUS AUREUS* ISOLATES FROM BLOODSTREAM INFECTIONS

AUTHORS: RIBEIRO, V.N.[1]; DAMASCO, A.P.[1]; DA COSTA, T.M.[1]; FERREIRA, R.B.R.[1]; NOUÉR, S.A.[2]; DOS SANTOS, K.R.N.[1]

INSTITUTION: [1]INSTITUTO DE MICROBIOLOGIA PAULO DE GÓES, UNIVERSIDADE FEDERAL DO RIO DE JANEIRO (AV. CARLOS CHAGAS FILHO, 373, CCS, SALA I2-010, CEP 21941-902, RIO DE JANEIRO – RJ, BRAZIL).

HOSPITAL UNIVERSITÁRIO CLEMENTINO FRAGA FILHO, RJ (R. PROF. RODOLPHO PAULO ROCCO, 255 - CIDADE UNIVERSITÁRIA, RIO DE JANEIRO - RJ, CEP: 21941-913)Although new antimicrobials (ATBs) have been used to treat infections caused by *Staphylococcus aureus*, the mortality associated with this pathogen has not been reduced. In addition, there is an increased resistance to the majority of ATBs currently used in the therapy of bloodstream infections (BSI). Combination of drugs can be used as an alternative. This study evaluated the effect of ATB combination against *S. aureus* isolates from BSI. Fourteen isolates showing different minimum inhibitory concentrations (MIC) for vancomycin were selected. The MIC by broth microdilution was determined for daptomycin (DAP), rifampin (RIF) and trimethoprim/sulfamethoxazole (TSX), and for ceftaroline (CEF) by Etest method. Synergism was evaluated by Checkerboard between VAN + TSX; VAN + RIF; DAP + TSX; DAP + RIF and by the Etest method for VAN + CEF for isolates with MIC ≥ 2 μg/mL for vancomycin. Time kill was performed for the best combinations in the checkerboard. Pulsed field gel electrophoresis determined the clonality of the isolates. Among the 14 isolates, six had vancomycin MICs of 4 μg/mL (VISA isolates), three had MIC 2 μg/mL, including one with vancomycin heteroresistance (hVISA) and other five isolates had MIC 1 μg/mL. Six isolates were daptomycin non-susceptible (MIC > 1 μg/mL). One isolate was resistant to SXT (MIC ≤ 38/2 μg/mL), as well as one demonstrated intermediate resistance to CEF (MIC = 2 μg/ mL). Eleven isolates were sensitive to RIF. All antimicrobial combinations showed additive effects (fractional inhibitory concentration index, FICI >0.5 - <2) against all isolates. DAP + RIF, DAP + TSX and VAN + RIF presented better FICI results for some isolates, which were selected for the time kill method. Additive effect was observed in all combinations tested by the time-kill. The combination VAN + CEF showed synergistic effect against the isolates, including VISA isolates. Although the presence of different lineages tested, such as USA100 (MRSA-VISA and hVISA), USA400 (MSSA and MRSA), USA800 (MRSA and MSSA) and Brazilian endemic clone (BEC) the study did not find correlation between clonality and values of FICI. The combinations VAN + RIF and VAN + CEF can be a good alternative for BSI therapy caused by VISA and isolates with vancomycin MIC ≥ 2 μg/mL. In addition, additive effect combinations may mean a good option in infections where treatment failure occurs, decreasing adverse effects and preventing the emergence of antimicrobial resistant subpopulations.

KEYWORDS: *S. aureus*, synergism, checkerboard, vancomycin, VISA.

DEVELOPMENT AGENCY: FAPERJ, CNPq, CAPES

.