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Abstract (poster session)

Comparative activity of various antibiotics alone and in combination against high inocula methicillin-resistant Staphylococcus aureus with reduced susceptibilities to vancomycin

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Background: Methicillin-Resistant Staphylococcus aureus (MRSA) is endemic worldwide, with increasing vancomycin (V) heteroresistance. Many new antibiotics (abx) developed are active against MRSA but the optimal chemotherapy is not well defined in endocarditis & osteomyelitis (high inocula infections). We aim to examine the utility of various abx alone & in combination (combi) at high inocula for potential clinical use against a variety of well characterized MRSA with vancomycin heteroresistance. Methods: 10 well-known MRSA clones [ST239 V-intermediate, UK-EMRSA-15, ST30 community-associated (CA) & ST8 USA300 CA) were selected for the study. Minimum inhibitory concentrations (MIC) were determined according to reference broth-dilution methods. Time-kill studies (TKS) were performed with 8 log CFU/ml at baseline using maximum achievable, clinical, unbound concentrations (mg/L) of linezolid (L) (19), daptomycin (D) (5), rifampicin (R) (2), tigecycline (T) (2) & V (12) alone & in combi against the test strains. Bactericidal (>= 3log CFU/ml drop from baseline inocula) activity & synergism (>=2 log CFU/ml drop from most active abx) were evaluated at 24h. Results: The test strains had T MICs of 0.06 – >=8 mg/L, R MICs of <=0.06 mg/L, V MICs of 1 – 4 mg/L, D MICs of 0.5 – >=16 mg/L & L MICs of 0.06->=16 mg/L. In single TKS, there were at least 1 abx alone that exhibited bactericidal activity in 4/10 strains; D,L & V was bactericidal against strain 1(4.29 log), 2(4.85 log) & 7(4.48 log) respectively, while T & R individually was bactericidal against strain 6(4.95 log & 4.74 log respectively). In combi TKS for these 4 strains, only L+R was bactericidal against strain 1(5.00 log) & D+T was bactericidal against strain 2(3.51 log) at 24h. In 6/10 strains (3, 4, 5, 8, 9, 10) where no abx alone exhibited bactericidal activity, the combi TKS showed that only D+T was bactericidal against strain 9(4.52 log), D+T & T+R were bactericidal against strain 8(4.42 log & 4.79 log respectively), D+R & D+V were synergistic against strain 3 (5.90 log for both combi). Conclusions: Combi therapy may be useful against MRSA infections with reduced susceptibilities to V based on the encouraging in vitro activity. However, 2-drug abx combi may not be sufficient to totally eradicate the infection. Our approach may be used to identify abx combi that can be used for long-term adjuvant antibiotic therapy in clinical situations like osteomyelitis. Further research is warranted.