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Comparative pharmacodynamics of ceftobiprole, daptomycin, linezolid, telavancin, tigecycline, and vancomycin in the treatment of methicillin resistant *staphylococcus* aureus: a monte carlo simulation Analysis

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Background/Objectives: Appropriate initial treatment choices for methicillin resistant Staphylococcus aureus (MRSA) infections are very critical. The aim of this study was to compare the ability of Ceftobiprole, Daptomycin, Linezolid, Telavancin, Tigecycline, and Vancomycin to achieve their requisite pharmacokinetic/pharmacodynamic (PK/PD) target against clinical MRSA isolates.

Methods: Monte Carlo Simulations were performed to simulate the PK/PD indices of the investigated antimicrobials. Population Pharmacokinetic data and Pharmacodynamic indices were integrated into Monte Carlo Simulation routine with 10,000 iterations. Probability of target attainment (PTA) was estimated at MIC values ranging from 0.03-32 μg/ml to define the PK/PD susceptibility breakpoints. Cumulative fraction of response (CFR) was computed using MIC data from the Canadian National Ward (CAN-Ward) study collected in 2007, 2008 and 2009.

Results: Analysis of the simulation results suggested the breakpoints of 8μg/ml for Ceftobiprole, 0.12 μg/ml for Daptomycin and Tigecycline, 0.5 μg/ml for Telavancin and 1 μg/ml for Linezolid and Vancomycin. The estimated CFR were 100, 66.5, 84, 89.1, 98.2, 60, 97.5 % for Ceftobiprole, Daptomycin (4mg/kg/day), Daptomycin (6mg/kg/day), Linezolid, Telavancin, Tigecycline, Vancomycin (2gm/day) and Vancomycin (3gm/day), respectively.

Conclusions: Ceftobiprole and Telavancin have the highest probability of achieving favorable outcome against MRSA infections. The susceptibility results suggested a further reduction of the vancomycin breakpoint to 1 μg/ml.