Pharmacodynamic Profiling of Antibiotics Used in the Treatment of MRSA-Infected ICU Patients

Background: Appropriate initial treatment choices for methicillin resistant Staphylococcus aureus (MRSA) infections are very critical especially in the intensive care units (ICU) settings. The aim of this study was to compare the ability of ceftobiprole, dalbavancin, daptomycin, tigecycline, linezolid and vancomycin to achieve their requisite pharmacokinetic/pharmacodynamic (PK/PD) targets against MRSA isolates collected from ICU settings.

Methods: Monte Carlo Simulations were performed to simulate the PK/PD indices of the investigated antimicrobials. 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 Intensive Care Unit (CAN-ICU) study.

Results: Analysis of the simulation results suggested the breakpoints of 8 μg/ml for ceftobiprole, 0.12 μg/ml for dalbavancin, daptomycin and tigecycline, and 1 μg/ml for linezolid and vancomycin. The estimated CFR were 100, 100, 70.8, 87.6, 88.7, 82.4, 89.4, 98.3 % for ceftobiprole, dalbavancin, daptomycin (4mg/kg/day), daptomycin (6mg/kg/day), linezolid, tigecycline, vancomycin (1gm BID) and vancomycin (1.5gm BID), respectively.

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

Keywords: MRSA, Monte-Carlo simulation, ceftobiprole, dalbavancin, vancomycin

Biography
Ayman M Noreddin received his PhD in Pharmaceutical Sciences from the University of the Pacific, California and received research training as a visiting scholar at the Department of Medicine, Stanford University. He had Post-doctoral fellowship (Pharmacokinetics and Pharmacodynamics of Antimicrobials), Department of Medical Microbiology, University of Manitoba followed by an American College of Clinical Pharmacy postdoctoral fellowship (Infectious Diseases). His research interest includes Pharmacokinetic/Pharmacodynamic modeling of anti-infective and anti-cancer therapy, clinical simulation and Monte Carlo analysis and bacterial resistance in biofilm studies. He has outstanding records of scientific and academic accomplishments with multiple research funding, numerous publications in highly prestigious journals and various presentations in both national and international conferences. He served as a Scientific Reviewer for the NIH as well as other national and international research institutions.

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