P1201
Paper Poster Session
PK/PD of agents against Gram-positives

Vancomycin continuous infusion dose optimization for the treatment of "MIC Creep" methicillin-resistant Staphylococcus aureus infections in critically-ill Thai patients

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Background: Giving vancomycin to a patient with rapidly changing physiologic conditions that will affect its pharmacokinetics (PKs), such as critically-ill patient, is challenging. Moreover, the shifting phenomenon of vancomycin's MIC of MRSA strain to the higher value, also known as "MIC Creep", will escalate the difficulty to determine the optimum dose of vancomyin. Owing to the vancomycin's desired pharmacokinetic-pharmacodynamic (PK-PD) indices affording good clinical outcome for the treated patients, i.e AUC_{0-24}/MIC ≥400mg.hr/L, extending the infusion was expected to ensure the achievement of this intended PK-PD indices. The objective of the present study was to determine the most appropriate continuous infusion vancomycin dosage regimen to treat "MIC Creep" MRSA infections in critically-ill Thai patients.

Material/methods: Monte Carlo simulation by using 10,000 replications was performed for several vancomycin continuous dosage regimens with or without loading dose (LD). For dosage regimens without LD, the simulated vancomycin dose was ranging from 2g, 3g, and 4g every 24h. Loading dose ranging from 1-5g were simulated to the continuous infusion 2g as a maintenance dose (MD). While, LD ranging from 1g-4g and 1g-3g were simulated to the MD 3g and 4g, consecutively. Vancomycin concentrations were estimated from population PK study conducted in 212 Thai patients. The probability of target attainments (PTAs) of each dosage regimen were calculated from the number of simulated patients who achieved AUC_{24}/MIC ≥400 for MIC 1.5mg/L and 2.0mg/L divided by total number of replication.

Results: If PTA at least 80% was allowed as the threshold, continuous dosage regimen of 4g every 24h without LD, MD 3g with LD 2g-4g, and MD 4g with LD 2g-3g could afford the desired PTA for MRSA with MIC 1.5mg/L. No any continuous dosage regimen without LD and only dosage regimen given as MD 4g with LD 3g could afford PTA >80% for MRSA with MIC 2mg/L. However, if particular conditions required PTA >90%, only continuous dosage regimen of 4g every 24h without LD, MD 3g with LD 3g-4g, and MD 4g with LD 2g-3g could afford the desired PTA for MRSA with MIC 1.5mg/L. No any continuous dosage regimen with or without LD could afford PTA >90% for MRSA with MIC 2mg/L. All PTA achievement represented the PTA at steady state condition.

Conclusions: Continuous dosage regimen of 4g/day without LD or at least 3g/day with LD 2g were needed to afford particular intended PTA achievement for MRSA with MIC 1.5mg/L. Continuous dosage regimen was not effectively used to treat MRSA with MIC 2mg/L. Finding of the present study could be used as a guidance in determining the best continuous dosage regimen in documented vancomycin treatment. Further study was needed to identify the risk of nephrotoxicity afforded by each dosage regimen.