"THE IMPACT OF PK/PD INDICES

ON THE SELECTION OF THE RIGHT ANTIMICROBIAL AGENT"

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INTRODUCTION:

An understanding of the pharmacokinetic (PK) and pharmacodynamic (PD) principles that determine response to antimicrobial therapy can guide clinicians to choose better dosing regimens. Factors influential on antibiotic disposition and clinical outcome are presented, with a focus on the duration of infusion, dose intervals, MIC value, primary site of infection.

MATERIALS:

PubMed (2000-2019) was reviewed for relevant publications assessing antimicrobial dose regimen according PK/PD indices and clinical outcomes for various sites of infection.

RESULTS:

Major PK/PD indices for antimicrobial agents form three types: Type I with best PK/PD parameter the 24h-AUC/MIC & Peak/MIC for Concentration-dependent killing and Prolonged persistent effects antibiotics, Type II with Time>MIC for Time-dependent killing and Minimal persistent effects antibiotics and Type III with 24h-AUC/MIC for Time-dependent killing and Moderate to prolonged persistent effects antibiotics. Drug solubility, volume of distribution, extent of protein binding in addition to the major clearing pathway of the agent provide significant PK influences. PD indices derived from in vitro and animal models determine the optimal magnitude and frequency of dosing regimens for patients. PK/PD modeling and simulation has been shown an efficient means of assessing these PD endpoints according the above PK determinants which guide tissue penetration and effectiveness in the site of infection.

DISCUSSION AND CONCLUSION:

Knowing PK properties of an antibiotic and its PD measure of efficacy can maximize the use of these drugs in case where clinical data remains limited for a number of infection site-antibiotic exposure relationships. Modeling and simulation can bridge preclinical and clinical data for the prescription of optimal antibiotic dosing regimens in favor of personalized medicine.