PHARMACOKINETIC AND PHARMACODYNAMIC PROPERTIES OF ANTIMICROBIALS IN THE CORRECT THERAPY OF INFECTIONS

FRANCESCO SCAGLIONE MD, PhD

Department of Pharmacology, Chemotherapy and Toxicology
Faculty of Medicine, University of Milan

Pharmacodynamics examines the relationship between an antimicrobial and organism over time, determining the effects of variations in drug concentrations on organism killing and growth dynamics . Specific pharmacokinetic/pharmacodynamic (PK/PD) indices, such as the area under the serum concentration time curve (AUC) over minimum inhibitory concentration (MIC) ratio (AUC/MIC), peak serum level/MIC ratio (Peak/MIC), or time that serum levels remain above the MIC (T>MIC), have been shown to be the primary determinants of in-vivo efficacy and to vary in importance for different classes of drugs. These characterizations have proven invaluable for predicting therapeutic outcome against multiple resistant pathogens and more recently have provided insight into preventing the emergence of drug resistance . The time course of antimicrobial activity is dependent on the drug's pharmacokinetics and two major pharmacodynamic characteristics. The first is the rate of organism killing and whether increasing drug concentrations enhance the rate and extent of killing. The second is the presence or absence of inhibitory effects on organism growth which persist after drug levels have fallen below the MIC. These drug-organism dynamics are important determinants of optimal dosage regimens. For example, pharmacodynamic characterization of the b-lactam class has shown no enhancement in killing with increasing concentrations and short or no persistent effects. Dosing regimens which prolong the duration of exposure enhance the activity of these drugs. Frequent dosing or continuous infusion is the most efficacious dosing strategy for these agents. For antimicrobial agents with time-dependent killing and minimally or moderately prolonged postantibiotic effects, such as b-lactams, macrolides, and oxazolidinones, T >MIC is the most useful predictor of efficacy . AUC/MIC and Peak/MIC ratios are predictive for agents with concentration-dependent killing and prolonged postantibiotic effects. These PK/PD parameters best describe the activity of the aminoglycosides, fluoroquinolones, and ketolides . The AUC/MIC ratio can also be used to predict the efficacy of antibiotics with time-dependent killing and prolonged effects, such as azithromycin, tetracyclines, and streptogramins .