Pharmacodynamics of Antibacterial Agents

Introduction

- The pharmacodynamic (PD) effect of an antibiotic is the result of the exposure of bacteria to the unbound fraction of antibiotic at the site of infection. In contrast, pharmacokinetics (PK) characterizes the time course of drug (antibiotic) concentrations in body fluids as a result of absorption, distribution, and elimination after the drug is administered. In simple terms, pharmacodynamics is what a drug does to the body, whereas pharmacokinetics is what the body does to a drug.
- Antibacterial drugs can be broadly divided into two groups, bactericidal and bacteriostatic. Bactericidal drugs kill bacteria; bacteriostatic drugs only inhibit bacterial growth and thus depend on the host immune system to clear the infection.
- Concentration-dependent killing means that the rate and extent of killing correlate with drug concentration. Therefore, Cmax and AUC are important determinants.
- Time-dependent killing means the the extent of bactericidal activity depends mainly on the duration of drug exposure. For maximal killing, the free (unbound) concentration of drug should be maintained above the MIC for a drug-specific percentage of the dosage interval: Penicillins: 50% Cephalosporins: 50-70% Carbapenems: 40%
- Penicillins: 50%
- Cephalosporins: 50-70%
- Carbapenems: 40%
- Post-antibiotic effect (PAE) refers to persistent suppression of bacterial growth following limited exposure to an antibiotic. The mechanism of the PAE is unclear. It may be the time required for bacteria to restore vital proteins before growth can continue, or alternatively it may reflect persistence of an antibiotic at its binding site.
- Knowledge of PK/PD principles can provide for more rational selection of dosing regimens.
- References: Infect Dis Clin North Am 2009;23:791; Infect Dis Clin North Am 2003;17:479.

Pharmacodynamics of antibacterial drugs

Antibacterial activity	Post-antibiotic effect (PAE)	Drugs	Goal of therapy	PK/PD parameter
Bactericidal, time-dependent	Short for gram-positive cocci, none to short for gram-negative bacilli (except carbapenems, which have a PAE against many gram-negative bacilli)	Beta-lactams, vancomycin	Enhance duration of exposure	Time above MIC
Bactericidal, concentration-dependent	Prolonged (also concentration-dependent)	Aminoglycosides, fluoroquinolones, daptomycin, colistin, metronidazole, azithromycin (?), ketolides	Enhance antibiotic concentrations	Cmax/MIC, AUC24/MIC

Bacteriostatic	Moderate to prolonged	Macrolides, clindamycin, streptogramins, tetracyclines, tigecycline, linezolid	Enhance amount of antibiotic	AUC24/MIC