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Pharmacokinetic and Pharmacodynamic Considerations of Antimicrobial Use

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The purpose of antimicrobial chemotherapy is to eliminate the invading pathogen(s) from the site of infection by providing adequate levels of effective antibiotics. The pharmacology of antimicrobial therapy can be divided into two distinct components: pharmacokintics and pharmacodynamics. The former refers to what we do to the drug such as absorption, metabolism, distribution, and elimination, while the latter refers to what the drug does to the host or bacteria including pharmacologic and/or toxicologic effects and bactericidal or bacteriostatic effects.

Although minimal inhibitory concentration (MIC) or minimal bactericidal concentration (MBC) describes antimicrobial activity at one point in time, they do not provide any time course of the antimicrobial activity. To this end the persistent antibacterial effect on removal of antibiotics after brief contact is known as the postantibiotic effect (PAE), this led to discovery of the postantibiotic sub-MIC effect (PAE-SME), and the postantibiotic leukocyte enhancement (PALE), giving us dynamic concept for the pharmacologic action.

The bactericidal activity of antibiotics can be divided into two different types, the concentration- dependent and the time-dependent. In case of the first pattern, the higher the concentration, the greater the killing effect and this is true with aminoglycosides, fluoroquinolones, and metronidazole. In the second pattern, maximal bactericidal activity is achieved by raising antibiotic concentrations several fold higher than MIC above which no further killing effect is obtained, thus bactericidal activity in this pattern is largely dependent on the time of exposure. Examples belonging to this category include β-lactam antibiotics including carbapenems, monobactam, macrolides, and clindamycin. In case of the time-dependent antibiotics, adequate levels of antibiotics (4-5 fold higher than MIC) should be maintained as much as possible. The animals infected with *Streptococcus pneumoniae* treated with penicillins or cephalosporins,, survival data indicate that the time above MIC should be 340% to predict excellent survival.

In the concentration-dependent category highest dose without causing toxic effect to the host should be given intermittently; not only animal data but some human data confirm the theory. Recently pharmacokinetic/ pharmacodynamic parameters such as AUIC (AUC/MIC) and C_{max}/MIC have been applied to predict therapeutic efficacy and emergency of bacterial resistance, respectively, with quinolone antibiotics. It was discovered that quinolones with AUIC of >30 and >100, for Gram-positive and Gram-negative infections, respectively, show good therapeutic outcome, while C_{max}/MIC of >10 predicts low incidence of resistance.

In summary, many different pharmacokinetic and pharmacodynamic parameters have been introduced in recent years and they seem to contribute to the therapeutic outcome significantly when used wisely. However much more study is needed to understand precise mechanisms applicable to individual antibiotics. In the future as we produce more antimicrobials of different mechanisms and as we study them more in detail, much more precise use of pharmacokinetic and pharmacodynamic parameters will lead to good therapeutic outcome.