PK/PD VARIABLES IN RELATIONSHIP TO PATIENTS AND ORGANS

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It is important to consider the pharmacodynamic/pharmacokinetic (PK/PD) characteristics of an antibiotic when selecting the proper drug and posology for therapy, especially in patients with serious infections or risk factors such as reduced immune function (i.e. age, diabetes, trauma), organ dysfunction or in intensive care, since PK/PD can help predict a drug's efficacy. In general, antibiotics acting on DNA or protein synthesis, such as fluoroquinolones or aminoglycosides, have concentration-dependent activity. Especially fluoroquinolones should have AUC/MIC ratios over 100-125 for good bacterial eradication and clinical outcome, at least for serious infections due to Gram-negative rods. On the other hand, for some Gram-positive species such as *Streptococcus pneumoniae*, an AUC/MIC ratio of about 50 is usually sufficient, even though this might lead to suboptimal antibiotic levels. The optimal posology for these antibiotics involves reaching maximum concentrations since their bactericidal activity is directly proportional to peak concentrations and all possess a prolonged postantibiotic effect (PAE).
Antibiotics such as beta-lactams and glycopeptides, active against the bacterial wall, have time-dependent efficacy meaning that serum levels of most beta-lactams (penicillins, cephalosporins and monobactams) must be maintained over the MIC for the maximum time. Although carbapenems and glycopeptides must have extended exposure time, their serum levels can go below the MIC during the interdose interval because of their prolonged PAE. However, T>MIC values for beta-lactams may vary according to bacterial species, being higher for *Enterococcus* spp. and *Pseudomonas aeruginosa* than for *Escherichia coli* or *S. pneumoniae*. PK/PD characteristics are usually correlated with antibiotic plasma levels but can be lower for some sites which are difficult to reach such as bone, CNS, lungs. In these cases special posologies must be devised, either increasing the dose or altering the interdose interval or, in the case of beta-lactams even administering the antibiotic by continuous infusion. On the contrary, antibiotic concentrations in some sites such as the lower urinary tract, can be much higher than plasma levels. In conclusion the pharmacologist should have a role in antimicrobial therapy, by defining the PK/PD characteristics and how they are correlated with both bacterial susceptibility and infection site, to reduce the risk of suboptimal exposure and increased resistance.