Designing a Dosing Regimen

Ideally, a dosing regimen is based on the minimal inhibitory concentration (MIC) or even the minimal antibiotic concentration (M particular pathogen. Depending on the antimicrobial, plasma or tissue drug concentrations should either markedly exceed the concentration-dependent antimicrobials, such as the aminoglycosides and the fluorinated quinolones) or be above the MIC for (time-dependent antibiotics, such as β-lactams and most “bacteriostatic” drugs). To compensate for drug disposition to tissue antibiotics, dosages for most drugs should result in plasma drug concentrations that are several times higher than the calcula MIC in the infected tissues or fluids. For dose-dependent drugs, efficacy is enhanced by increasing the dose; for time-depende enhanced by shortening the dosing interval.

In today's infectious disease environment, appropriate design of a dosing regimen should depend not on labeled doses, but ra regarding the current pharmacodynamics of the infecting microbe (ie, MIC from the pathogen cultured from the patient, or the M pathogen collected from the target animal). This information must be integrated with the pharmacokinetics of the drug measur species of interest. Appropriate pharmacokinetic parameters upon which the dosing regimen should be designed include max C_{max} for concentration-dependent drugs and C_{max} and drug elimination half-life for time-dependent drugs. Supportive informa often can be acquired from the literature. For example, if the MIC of a *Pseudomonas aeruginosa* isolate for amikacin is 4 µg/mL peak plasma drug concentrations achieve 40–48 µg/mL. The dose should be adjusted further if the infection is in a tissue not v in the presence of marked inflammatory debris. Cephalexin is a time-dependent drug. If *Staphylococcus intermedius* cultured f of 2 µg/mL, then the dosing regimen should be designed to assure that drug concentrations are above 2 µg/mL for at least 50% interval. This may be difficult, because cephalexin's half-life is only 1.5 hr. Using data reported in the literature for dogs, an oral achieve a C_{max} of 25 µg/mL. In one half-life, concentrations (µg/mL) will decline to 12.5; in the second, to 6.25, in the third to 3.1 the fourth half-life, or 6 hr. Thus, 3 elimination half-lives, or 4.5 hr can elapse before the target MIC is reached and the next dose interval is generally more cost effective than increasing the dose, particularly for drugs with a short half-life—for each 2 half-live dose must be doubled.

The integration of pharmacokinetics and pharmacodynamics can also be accomplished based on package insert information example, for concentration-dependent drugs, the C_{max} should be at least 10 × the MIC_{90} of the target microorganism for that d drug concentrations should be above the MIC_{90} of the infecting microbe for ≥50% of the doing interval.