Pharmacokinetics is the study of the change in concentration of a drug, such as that of an antibiotic in a particular tissue over time. In the case of systemic antibiotics, this change can be measured. For example, physicians can administer a particular antibiotic to a subject in pill form and afterward draw blood at different time periods for measurement. This information alone, however, is not enough to predict the success or failure of an antibiotic in eradicating bacteria from a particular tissue in the body.

**PREDICTING PHARMACEUTICAL EFFECTIVENESS**

Certain pharmacokinetic parameters can predict an antibiotic’s ability to eliminate pathogenic organisms. These parameters include (1) the time at which the concentration of the antibiotic is higher than the mean inhibitory concentration (MIC) of the organism, (2) the area between the curve of the concentration of antibiotic, (3) the MIC of the organism, and (4) the maximum concentration of the antibiotic (Cmax).

Because different antibiotics work by different mechanisms, the parameters describing their efficacy vary. For example, in the case of bacteriostatic antibiotics such as vancomycin, the important parameter is the time at which the concentration of the antibiotic is higher than the MIC of the organism. Similarly, fluoroquinolones work more effectively if the concentration of the antibiotic is significantly higher than the MIC of the organism for an extended period of time.1,2 Additionally, the efficacy of the antibiotic relates to the Cmax of the antibiotic in the target tissue.3

**PHARMACODYNAMICS**

Pharmacodynamics describes the efficacy of an antibiotic based on the total exposure of the pathogenic organism to the antibiotic. Three parameters describe the pharmacodynamic characteristics of an antibiotic: (1) the ratio of the area under the concentration-time curve to the MIC of the organism (area under the inhibitory curve), (2) Cmax, and (3) the duration of time that the concentration of the antibiotic exceeds the MIC of the organism. Much of the research on pharmacodynamics has concentrated on fluoroquinolones, and, in those cases, the effectiveness of the antibiotic has been shown to be related to the Cmax and the area under the inhibitory curve.4-6

As stated earlier, in the case of other antibiotics such as vancomycin, the time that the concentration of the antibiotic is above the MIC of the organism relates to the effectiveness of the antibiotic. In the case of vancomycin, it is not important to maintain an extremely high level of antibiotic, but rather to maintain the concentration of the antibiotic above the MIC of the organism for an extended period of time.

Regarding ocular disease or ocular infection prophylaxis,
it has been difficult to obtain information that demonstrates the kinetics of antibiotics in ocular tissues for logistical reasons. My colleagues and I have recently presented this type of study at the Ocular Microbiology and Immunology Group meeting during the 2003 AAO annual meeting. In this study, patients undergoing cataract surgery were dosed with moxifloxacin 0.5% at 15, 30, 60, 120, and 180 minutes prior to removing an aqueous sample at the commencement of cataract surgery. With this process we were able to construct a concentration-time curve that included the Cmax of the antibiotic. We were able to obtain extremely high levels of moxifloxacin in the aqueous humor, levels that remained high and beneficial during the entire course of the study. In fact, the ratio of Cmax to MIC, using an MIC value obtained from actual endophthalmitis isolates of *Staphylococcus epidermidis*, was approximately 30:1. We are in the process of repeating this study with other antibiotics.

**LOOKING AHEAD**

The type of information presented here is very exciting and offers a new way of analyzing the effectiveness of antibiotics in both the treatment of ocular infections and for the purpose of preoperative prophylaxis. When used topically, moxifloxacin 0.5% appears to have favorable pharmacokinetic characteristics, which, based on previous literature, should translate into pharmacodynamic parameters that will determine success in the treatment and prevention of infection.

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