



INTERNAL MEDICINE:

Ciprofloxacin – A wise choice for use in dogs and cats?

Overview

Ciprofloxacin is increasingly being prescribed for antimicrobial therapy as a substitute for veterinary approved fluoroquinolones in dogs and cats. Unfortunately this practice is largely being directed by generic pricing rather than sound pharmacokinetic principles.

Problems with usage

1. The oral bioavailability of fluoroquinolones varies significantly both among different species and also between different fluoroquinolone compounds. Ciprofloxacin has been shown to have poor and variable oral bioavailability in dogs and cats. For example, although enrofloxacin is structurally similar to ciprofloxacin, with the only difference being the addition of an ethyl group on the piperazine ring, this modification turns out to be critically important for the difference in oral bioavailability of these drugs. Ciprofloxacin's oral bioavailability is approximately 70% in humans, whereas that reported in dogs is about 40% and in cats is about 33%. In contrast, the oral bioavailability of enrofloxacin (and marbofloxacin) is between 90-100% for dogs and cats. Mean peak serum concentrations of enrofloxacin in dogs are four-fold higher than those of ciprofloxacin following administration of each drug at a dosing rate of 5 mg/kg per os. As the oral dosage of ciprofloxacin is increased, rates of absorption are nonlinear with absorption prolonged and variable.
2. Fluoroquinolones are concentration (dose) dependent antibiotics. For optimal clinical efficacy, fluoroquinolones should achieve high maximum concentration values (C_{max}). The rate and extent of bacterial killing and clinical efficacy increases as the concentration of the drug increases. For dogs and cats, ciprofloxacin demonstrates inferior pharmacokinetic properties to achieve desirable C_{max} values to maximize clinical efficacy.
3. Resistance protection is an important goal of antimicrobial therapy. During acute infections, bacterial loads may exceed 10^9 cfu/ml (colony forming units per ml). The frequency with which a spontaneous mutant that confers drug resistance is estimated at 1 spontaneous mutant for every 10^7 to 10^9 bacterial cells. As such, an acute infection with $\geq 10^9$ cfu is likely to harbour one or more resistant cells and in the presence of an antimicrobial agent, may allow for the selective amplification of the resistant subpopulation as the susceptible population is being eliminated by therapy. High drug concentrations are required to block all growth, including those of mutants. Given the high oral bioavailability of the veterinary approved fluoroquinolones, when these antibiotics are used appropriately, they would likely minimize emergence of such mutant populations. Concern should be made that with the use of ciprofloxacin in dogs and cats as there is high likelihood of suboptimal dosing which may lead to the selective amplification of mutant subpopulations in high density bacterial populations.

Conclusions

Ciprofloxacin is not an appropriate antibiotic for use in bacterial infections in dogs and cats due to its variable and poor oral bioavailability, and concern for inadvertent mutant bacterial population selection due to unpredictable peak serum drug concentrations. Only veterinary approved fluoroquinolones should be used in dogs and cats due to their superior and reliable oral bioavailability.

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