ADVANCES IN AVIAN CLINICAL THERAPEUTICS

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Abstract

This article reviews advances in the pharmacokinetics and pharmacodynamics of therapeutic agents used in avian medicine. There has been a significant body of work published within the last 5 years that has helped provide a scientific basis for drug treatment in avian patients. This concise article of different studies on antibacterial, antifungal, analgesic, sedative and anesthetic, hormone (e.g., deslorelin), psychotropic, antiepileptic, and cardiovascular drugs provides evidence of the advancements in this area of companion exotic animal medicine. Copyright 2014 Published by Elsevier Inc.

Key words: analgesic; antibiotic; antifungal; birds; anesthetic agent; antiepileptic drug; hormones; psycotropic agent; sedative

This article reviews advances of the pharmacokinetics and pharmacodynamics of drugs used to treat avian species. The information presented provides evidence of the significant advancement that the field of avian medicine and surgery has experienced. New studies have evaluated drugs in avian species for which there was only dosages a frequency of administration recommendation available from extrapolation from other species or scaling methods. A few of the studies have shown great differences between the empiric dosages used for years and those recommended from the results of the scientific studies, thereby indicating the need for species-specific pharmacokinetic and pharmacodynamic studies. There is also information on readily available recently released drugs, providing treatment options for the clinician in the management of infectious and noninfectious diseases. New routes (e.g., intranasal [IN]) and methods of administration (e.g., medicated food and medicated water) have also been evaluated for some therapeutic agents, expanding the options available for minimally invasive routes of drug administration in patients. Slow-release formulations for antimicrobials and analgesic drugs have also been investigated and will likely be an area of research in the near future to improve the veterinarian's ability to treat avian species. The results from these studies are the starting point for the scientific basis of avian therapeutics. Ultimately, it is the clinician's responsibility to exercise caution when administering drugs to an avian patient, making individual adjustments when needed, and evaluating the therapeutic response and the presence of adverse effects.

ANTIBIOTIC AGENTS

Enrofloxacin

Enrofloxacin is a fluoroquinolone antimicrobial with bactericidal activity against Gram-negative organisms; less activity against Gram-positive organisms; minimal activity against anaerobic bacteria; and occasional therapeutic activity against other organisms, such as *Chlamydia* spp., *Mycoplasma* spp., and *Mycobacterium* spp.[1] The pharmacokinetics of enrofloxacin has been investigated in a variety of avian species, with varied oral bioavailability. Recently, enrofloxacin was evaluated in African penguins (*Spheniscus demersus*),[2] and it was determined that a dose of 15 mg/kg every 24 hours orally, whether in fish or

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pilled, is expected to achieve the surrogate markers of efficacy for bacteria with a minimum inhibitory concentration (MIC) of 0.5 μg/mL or less. Mean terminal elimination half-life was 13.79 hours pilled and 11.93 hours when administered in fish.

The lack of a commercially available oral enrofloxacin suspension has resulted in a variety of compounded suspension that use several enrofloxacin formulations mixed with flavoring agents and vehicles to facilitate oral administration to exotic animals. The stability of 3 extemporaneous oral suspensions of enrofloxacin mixed with readily available flavoring vehicles when stored at room temperature (22°C or 72°F) has recently been evaluated.[3] Commercially available enrofloxacin tablets were compounded with a mixture of distilled water and corn syrup (Karo dark corn syrup; ACH Food Co Inc, Memphis, TN USA) (formulation A) or cherry syrup (Cherry syrup; Humco Holding Group Inc, Texarkana, TX USA) (formulation B) flavoring vehicles to create suspensions with a nominal enrofloxacin concentration of 22.95 mg/mL, and 2.27% enrofloxacin injectable solution was compounded with a liquid sweetener (Ora-Sweet; Paddock Laboratories Inc, Minneapolis, MN USA) (formulation C). Results indicated that when stored in amber-colored vials at room temperature for 56 days, the enrofloxacin concentration strength in all 3 formulations was retained within acceptance criteria of 90% to 110%. Subjectively, cherry syrup flavoring was better at masking the smell and taste of enrofloxacin than were the other mixing vehicles.[3]

Marbofloxacin

Marbofloxacin is a fluoroquinolone with a similar bactericidal spectrum to that of enrofloxacin,[4] but offers some advantages, such as a longer elimination half-life, greater tissue-penetrating ability, and a higher bioavailability.[5] The pharmacokinetics of marbofloxacin have been investigated in a variety of avian species, most recently in ducks.[6-8] In Muscovy ducks (*Cairina moschata*), marbofloxacin had a good oral bioavailability (72% to 88%) and the recommended dosages from those studies were 2 to 2.5 mg/kg every 24 hours orally for the treatment of most Gram-negative bacteria (MIC <0.20 μg/mL).[7,8] In mallard ducks (*Anas platyrhynchos*), intravenous (IV) administration appeared to have high total plasma clearance, consequently a higher dosage of 10 to 15 mg/kg IV was recommended in that study.[6]

Orbifloxacin

Orbifloxacin is another fluoroquinolone with a similar antimicrobial spectrum as that of enrofloxacin and marbofloxacin.[9] Recently, pharmacokinetic and pharmacodynamic studies were completed in birds using Japanese quail (*Coturnix japonica*) as a model for small granivourous birds.[10] The results of this study suggested that orbifloxacin is a potentially useful antimicrobial for small granivorous birds with infections caused by susceptible bacteria.[10] Orbifloxacin appeared to be completely absorbed when orally administered to the Japanese quail, which resulted in an excellent oral bioavailability (102%), wide tissue distribution, and good penetration through biological membranes, similar to distribution determined for other fluoroquinolone agents in birds.[10] The dosages for orbifloxacin recommended from this study were 15 to 20 mg/kg orally every 24 hours.

Doxycycline

Doxycycline, a semisynthetic tetracycline, is considered the drug of choice for treating avian chlamydiosis. This antibiotic inhibits protein synthesis by reversibly binding to 30S ribosomal subunits, and it has numerous pharmacologic advantages compared with other tetracyclines.[11] Doxycycline is considered a bacteriostatic antibiotic and is presumed to be active only during the replication phase in the life cycle of chlamydiae. As the organism is intracellular and unsubstantiated historic observations with marginally effective antimicrobials suggested posttreatment persistence of infection, prolonged treatment periods of 30 to 45 days have been recommended.[12,13] In a recent study where cockatiels (*Nymphicus hollandicus*) were experimentally inoculated with doxycycline, the drug was effective in eliminating *Chlamydia psittaci* infection following administration of 35 mg/kg orally of the drug via feeding tube into the crop every 24 hours for 21 and 45 days. The governmental regulations in some countries may require longer treatment than the 21 days suggested from the results of this study. The compendium of measures to control *C. psittaci* infection among humans (psittacosis) and pet birds (avian chlamydiosis) should be followed in the United States, and governmental regulations might guide treatment in other countries.

Doxycycline has also been evaluated in naturally infected cockatiels for the treatment of spiral bacterial infection.[14] Results suggested that