A Cat is Not a Dog: Specific Therapeutic Considerations
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In the past, cats have been treated very often as if they were small dogs. However, cats and dogs are quite different species regarding therapeutic considerations because of biological/physiological but also psychological differences. The cat is generally considered as a more difficult species in terms of handling and drug administration than the dog. Analgesics tend to be less frequently prescribed in cats than in dogs after traumatic injury (Armitage et al., 2005). Therapeutic management of a feline patient should be based on specific considerations. Although major differences exist between cats and dogs in drug safety and toxicology, only pharmacokinetics and pharmacodynamics will be considered here.

Choice of Formulations and Route of Administration

Oral formulation—Oral administration is a very convenient route for treatment of chronic diseases. Swallowing of liquid formulations is easier than that of tablets. For tablets, small-size tablets are needed. The tablet can be inserted in some appetent food (fish or liver). The broken surface a secable tablet should be covered with butter to mask the taste of the medication. After tablet administration, a water bolus is recommended to facilitate oesophageal transit (Westfall et al., 2001). This procedure may prevent oesophageal stricture or oesophagitis observed with some caustic compounds (e.g., doxycycline) and due to oesophageal retention of the tablet. Because of the greater issue in dosing cats, palatable feline formulations represent a current challenge for drug industries. A taste which is desirable in dogs and humans does not make it desirable to feline patients. For example, cats did not like the taste of some sweeteners like saccharin, but are highly responsive to amino acids. Cats exhibit no preference for salt solutions over tap water (Thombre, 2004). Medications are sometimes smeared onto fur for ingestion during self-grooming but such an approach is not appropriate.

Injectable formulation—When possible, intravenous administration should be preferred in cats. Feline post-vaccinal fibrosarcomas due to
subcutaneous inflammatory reactions at sites of injection have been largely described over the last decade and are mainly associated with the injection of inactivated virus vaccines containing aluminium-based adjuvants (Hendrick, 1998).

The practitioner should be aware that administration-induced stress can affect blood glucose, but also neutrophil, eosinophil, and lymphocytes counts.

**Pharmacokinetic Differences Between Cats and Dogs**

**Absorption**

Oral absorption may differ between cats and dogs because of gastrointestinal anatomical and physiological differences. The absolute gastric and intestinal volumes are larger in the dog. The relative volumes of the stomach and large intestine are similar, but the relative size of the feline small intestine is shorter than that of the dog. In fasting conditions, beads (1.5-5 mm) empty similarly from the stomach in dogs and cats. In the fed state, their residence time is higher in the stomach of the cat. A delay in gastric emptying may alter drug absorption. Gradual emptying of drug into the duodenum may indeed allow the complete dissolution of the total dose (Sutton, 2004). The small intestinal transit times of small beads was reported slightly longer in the cat than in the dog (Chandler et al, 1997). The small intestinal permeability may be different in cats compared to dogs. For lactulose, it is 3-4 times higher in cats than in dogs (Johnston et al, 2001). For ciprofloxacin, the mean oral bioavailability in dogs approximate 40% whereas in cats, it was 0-20% (Albarellos et al, 2004). Oral formulations of selamectin show a higher bioavailability in cats (109%) compared to dogs (62%) (Sarasola et al, 2002). This may result from lower P-glycoprotein concentrations in the cat.

Oral mucosal administration has been also proposed in cats as an alternative for injections. For buprenorphine, the maximal concentration was observed 15 min after dosing. The oral bioavailability by this route is 100%. This high value by comparison with other species could be explained by the alkaline pH (8 to 9) of the cat’s mouth, as buprenorphine is a weak base. The same study demonstrated that most of the owners consider this route highly acceptable or acceptable (Robertson et al, 2003).

Topical formulations may be also absorbed quite differently between cats and dogs because the cats skin appears to be thinner than the dog skin (Monteiro-Riviere et al, 1990). For example, the bioavailability of topical formulations of selamectin in cats (74%) was higher than that in dogs (4.4%), which could be explained by greater transdermal flux (Sarasola et al, 2002). After fentanyl transdermal patch placement, cats achieve steady
state plasma concentration faster than dogs (6-12 h vs 18-24 h) (Riviere and Papich, 2001).

Distribution

Total body water contents in dogs and cats are very similar (66 and 64%, respectively) (Culebras et al., 1977). Differences in drug distribution between dogs and cats may also exist although underlying mechanisms remain unknown. For example, doxycycline is more extensively bound to serum proteins of cats (98%) than to those of dogs (91%). Binding to feline albumin is also more important (76 vs 54%). Volume of distribution of doxycycline was approximately 3 times lower in cats (340 mL/kg) than in dogs (930 mL/kg) (Riond et al., 1990).

Metabolism

Drug metabolism represents the most important pharmacokinetic difference between cats and dogs. Cats are relatively deficient in their ability to conjugate xenobiotics with glucuronic acid, and consequently the clearance of drugs which biotransformation depends mainly on glucuronidation is decreased and half-life is prolonged. Recently, a molecular genetic basis for this deficiency has been identified (Court and Greenblatt, 2000). Such a deficiency explains the feline susceptibility to the toxic effects of phenolic drugs (e.g., paracetamol) and delayed elimination of other drugs such as aspirin (its half-life is about 37.6 h in cats and 8.6 h in dogs) or carprofen (the half-life of carprofen in cats is 20 h (Taylor et al., 1996), twice that of the dog). Morphine also is poorly biotransformed in cats in morphine-6 glucuronide, a metabolite with analgesic properties, which explains that morphine appears to be less effective in cats than in other species. Inversely, acetylation is deficient in dogs but apparently not in cats, and clearance of drugs which metabolism depends on acetylation is higher in cats than in dogs (e.g., hydralazine, diltiazem) (Boothe, 1990).

Renal and Biliary Elimination

Renal elimination may also differ. Creatinine is essentially cleared by glomerular filtration in both species and therefore an indicator of glomerular filtration rate. Its plasma clearance in cats (about 2.3 mL/min/kg (Le Garrereres et al., 2007)) however is smaller than that in small-breed dogs (3.5-4 mL/min/kg). As both species are carnivorous, the urine pH is very similar and acid. Consequently, interspecies difference in tubular reabsorption according to the pKa of the drug is probably of limited importance. Bromide is also essentially cleared by the kidney but its elimination half-life in cats is approximately one third (1.6 weeks) of that reported in dogs (5.3 weeks) (Boothe et al., 2002). In contrast, prevalence of
adverse effects (especially bronchial asthma) seems to be higher in cats and bromide appears not to be a safe drug to use in cats.

Biliary excretion is not well documented in cats. Sulfobromophthalein and indocyanine green clearances are higher in cats than in dogs (Center et al, 1983).

Pharmacodynamic Differences

Pharmacodynamics may differ independently of pharmacokinetic differences. The example of morphine is well known in small animal pharmacology. It causes CNS stimulation and pupillary dilation in cats, contrary to what is observed in dogs. Because of mydriasis, the cat should be approached very slowly and kept away from bright light. Excitation at the dose currently recommended (0.1-0.2 mg/kg) is extremely rare. Furosemide efficacy is different between cats and dogs. A dose of 0.625 mg/kg is effective in the dog but not the cat. Urine potassium excretion was relatively dose-independent in the cat, whereas it increases in dogs with increasing doses (Klatt et al, 1975). Specific dosage regimen should be defined for the feline and canine patients in conditions such as congestive heart failure. Differences in response to isoflurane for dogs and cats were also described (Steffey and Howland, 1977).

Conclusion

Dosage regimen in small dogs should not be extrapolated to cats. Specific information in pharmacokinetics but also pharmacodynamics is still needed for many drugs used in feline medicine.

References


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