New developments in diagnostics, management, and treatment options for feline diseases have occurred over the last few years. Cats are a unique species, and drug dosages, efficacy, and safety cannot always be extrapolated from other species. Differences in absorption, metabolism, and elimination between cats and dogs can affect clinical outcomes and the potential for toxicities. Some of the recent developments in feline therapeutics include:

- Pain management in cats
- Drug delivery methods to address administration and compliance issues
- A new antimicrobial for cats
- New research into anticonvulsant options for cats

Within this manuscript, recommendations for medical treatment may be covered that are not labeled for use in dogs and cats. Whether these are products developed for use in humans or are extra-label use of veterinary products, the recommendations are based on medically recognized standards of care.

**Pain Management in Cats**

Very few analgesic drugs are approved for use in cats in the United States, and there are no FDA approved analgesic drugs labeled for long-term management of chronic pain in cats. Oral analgesic drug options are limited in the cat due to drug formulations, lack of approved drugs, and minimal safety and efficacy studies. Many practitioners have used analgesics off label in cats, for example transmucosal buprenorphine, NSAIDS, transdermal narcotics, tramadol, gabapentin, and narcotics. Unfortunately, very little is known about the pharmacokinetics, appropriate dose, toxicity, and analgesic response in cats.

**NSAIDs**

Meloxicam is approved for use in cats in the United States as a single 0.3 mg/kg SQ injection for the control of postoperative pain and inflammation associated with orthopedic surgery, ovariohysterectomy, and castration when administered prior to surgery. Some specialists have recommended various NSAID off-label protocols for acute and chronic pain management in cats using a reduced dose and/or frequency. Despite anecdotal reports of efficacy, none of the protocols have efficacy studies to prove the benefit outweighs the risk.

**Opioids**

Since most opioids have erratic and poor absorption after oral administration, their clinical use is limited by this route of administration. Transmucosal administration of buprenorphine has shown to be effective and well tolerated in cats (Robertson et al. 2005). The alkaline pH of cat saliva favors absorption of the drug into systemic circulation with median bioavailability reported as 116% (Robertson et al. 2005). Advantages of this administration route include: small volume, low potential for side effects, duration of action (up to 6 hours), convenient administration, and well-accepted administration.

**Tramadol**

Research has provided new information on the pathophysiology of pain and treatment options. Tramadol is a centrally acting human analgesic drug that interacts with opioid, adrenergic, and serotonic receptors. (Raffa et al. 1992). Tramadol has been used extensively by veterinarians in a multimodal approach for the management of chronic pain in dogs with osteoarthritis. Tramadol pharmacokinetics was first described by Kukanich & Papich (2004), where it showed good absorption in dogs after oral administration. Tramadol is metabolized to the active metabolite O-desmethyltramadol (M1), which is reported in people to have more potent mu receptor binding than the parent compound (Poulsen et al. 1996). The half life of tramadol and the M1 metabolite is 0.8 and 2.18 hours after a single oral dose of 5 mg/kg in healthy dogs. Based on these pharmacokinetic studies a dose of 5 mg/kg every 6 hours in dogs achieves plasma concentrations associated with analgesia in humans (Kukanich & Papich 2004). To date, there have not been pharmacodynamic studies to determine plasma concentrations that correlate with analgesia in dogs.

Tramadol pharmacokinetic studies have recently been conducted in the cat (Pypendop & Ilkiw 2008; Papich & Bledsoe 2007). In cats, oral absorption can be variable but bioavailability as high as 93% has been reported (Pypendop & Ilkiw 2008). Compared to dogs, tramadol has shown to have longer elimination half life and greater
M1 to tramadol ratio after oral administration of an immediate release tablet (Pypendop & Ilkiw 2008; Papich & Bledsoe 2007). Similar to dogs, the active metabolite, O-desmethyltramadol, is produced after oral administration, but the half life in cats is longer than in dogs (4.81 hr vs. 2.18 hr) (Pypendop & Ilkiw 2008). These differences may support less frequent administration in cats, but pharmacodynamic studies are needed to compare efficacy with the pharmacokinetics. Tramadol was well tolerated in cats, with infrequent neurological side effects reported (Papich & Bledsoe 2007). One disadvantage of using tramadol in cats is the bitter taste of the tablet.

**Alpha 2 Agonists**

In 2008 dexmedetomidine was approved for use in dogs and cats in the United States. Dexmedetomidine is a purified form of medetomidine, containing only the active dexmedetomidine enantiomer. Dexmedetomidine is a selective alpha 2 adrenergic agonist indicated for use as a sedative and analgesic in dogs and cats to facilitate clinical examinations, clinical procedures, minor surgical procedures, and minor dental procedures. In dogs, dexmedetomidine is also indicated for use as a preanesthetic to general anesthesia. In a study using label intramuscular doses in cats, sedation and analgesia were achieved within 5 minutes, peak effects were seen within 30 minutes, and sedation/analgesia was sufficient to perform minor procedures in the cats (US FOI, 141–267, 2007). Reduced doses of medetomidine are often given to animals when used in combination with opioids (Tranquilli et al. 2004).

**Drug Delivery Methods to Address Administration and Compliance Issues**

Oral administration of drugs to cats can be a challenge for pet owners. The burden of administering drugs either daily or multiple times a day often results in reduced compliance. Multiple alternative drug delivery techniques have been investigated to ease administration and improve compliance. One of the first publications on the use of transdermal gels (PLO) in cats was in 2002 with methimazole (Hoffmann et al. 2002). Since then, numerous researchers have investigated the use of transdermal gels in the delivery of multiple drugs (amlodipine, atenolol, fluoxetine, dexamethasone, glipizide, buspirone, narcotics, diltiazem). Results from these studies show variable absorption and inconsistent plasma concentrations. Compounding pharmacies continue to advertise the ability to formulate a wide variety of drugs into transdermal gels, but scientific evidence does not support efficacy or safety for the majority of these claims. Most recently, pharmacokinetics and pharmacodynamic response (ECG measurements) were determined after oral and transdermal administration of atenolol to healthy cats (Macgregor et al. 2008). Results showed subtherapeutic concentrations after transdermal administration compared to oral administration in the majority of cats. In addition, heart rates were not reduced below baseline in the transdermal treated group (Macgregor et al. 2008).

**A New Antimicrobial for Dogs and Cats**

Up until 2008, all companion animal antimicrobials approved in the United States required administration at least once a day. In a study evaluating compliance of owners administering antimicrobials to their pets, only 64% of doses were administered at the prescribed frequency (Adam et al. 2005). Compliance rates were higher for clients administering antimicrobials prescribed once or twice daily compared to those prescribed more frequently (Adam et al. 2005). Cephalosporins have been used successfully in the management of skin infections for many years. In May 2008, the new cephalosporin, cefovecin, was approved in the United States for the treatment of skin infections in dogs and cats. Cefovecin has been approved in Europe since 2006 and in several other countries since 2007. Convenia is a unique cephalosporin providing up to 14 days of antibiotic treatment after a single injection in dogs and cats. Cefovecin is administered by subcutaneous injection at a dose of 8 mg/kg and is labeled for the treatment of superficial pyoderma, abscesses, and wounds caused by susceptible strains of *S. intermedius* and *S. canis* (Group G) in dogs and for the treatment of abscesses and wounds caused by susceptible strains of *P. multocida* in cats. Activity of cefovecin against other pathogens is discussed in a publication by Stegmann et al. (2006a). A second subcutaneous injection may be administered in dogs if the response to therapy is not complete. In the U.S. field efficacy studies a single injection of cefovecin was clinically equivalent to a 14-day dosing regimen with cefadroxil (Six et al. 2008). Cefovecin is not a depot or sustained release formulation but an aqueous solution that is completely and rapidly absorbed after subcutaneous administration. The time to peak concentrations (Tmax) is approximately 6 hours in the dog and 2 hours in the cat after an 8 mg/kg SC injection (Stegmann et al. 2006b; Stegmann et al. 2006c). The long half life (5.5 days in the dog and 6.9 days in the cat) is primarily attributed to the drugs’ high protein binding (Stegmann et al. 2006b). The most common side effects reported in the efficacy studies were gastrointestinal signs (nausea, vomiting, diarrhea), and the incidence was similar to the positive control, cefadroxil (Six et al. 2008). No adverse effect required prolonged treatment.
Cefovecin is not for use in dogs or cats with a history of allergic reactions to penicillins or cephalosporins. Similar to other cephalosporins, side effects for both dogs and cats include vomiting, diarrhea, decreased appetite/anorexia, and lethargy. The safety of cefovecin has not been determined in lactating or breeding animals.

New Research into Anticonvulsant Options for Cats

In dogs, multiple human drugs have been investigated as potential add-on therapy when phenobarbital and/or bromide therapy is insufficient in controlling seizures, causes intolerable adverse effects, or is discontinued because of underlying conditions. In cats, use of additional anticonvulsant therapy is limited by a lack of information on safety and efficacy, adverse effects, and frequency of dosing. Currently, the drug of choice for treatment of epilepsy in cats is phenobarbital (Quesnel 2005). In cases where response to phenobarbital is inadequate or contraindicated, alternative or additional therapies are pursued. Diazepam and bromide have been investigated for use as either add on therapy to phenobarbital or replacement therapy; however, both have been associated with adverse effects in cats (diazepam and hepatotoxicity and potassium bromide and allergic pneumonitis) (Center et al. 1996; Boothe et al. 2002).

Levetiracetam is a human antiepileptic drug. Recent studies on the use of levetiracetam in dogs and cats with idiopathic epilepsy have been presented at major scientific meetings and published in journals. The small number of studies performed with levetiracetam in dogs has shown it to be well tolerated when combined with other anticonvulsants (Patterson et al. 2008; Volk et al. 2007). A recent study found levetiracetam administered at 20 mg/kg PO every 8 hours as an adjuvant to phenobarbital in cats with idiopathic epilepsy was well tolerated, with only rare reports of inappetence and mild lethargy (Bailey et al. 2008). Concentrations were within the therapeutic range determined for humans (Bailey). Further efficacy, safety, and pharmacokinetic studies are required.

References


