Outpatient Oral Analgesics in Dogs and Cats Beyond Nonsteroidal Antiinflammatory Drugs: An Evidence-based Approach

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KEYWORDS

• Polysufated glycosaminoglycans • Amantadine • Tramadol • Gabapentin
• Pregabalin • Opioids • Antidepressants • Glucosamine

KEY POINTS

- Nonsteroidal antiinflammatory drugs are effective analgesics in dogs and cats, but adverse effects, preexisting conditions, and severity of pain may limit their use in some patients.
- Although many recommendations exist for additional analgesic use in dogs and cats, few of these recommendations are supported by controlled clinical trials.
- An injectable formulation of polysulfated glycosaminoglycans that is approved by the US Food and Drug Administration is an effective drug for controlling signs of arthritis in dogs, and amantadine in combination with meloxicam has shown efficacy in dogs with osteoarthritis.
- Oral tramadol was significantly better than placebo in controlling pain in dogs with arthritis, but the power of the study was low.
- Some data support further studies of gabapentin, pregabalin, hydrocodone, codeine, amitriptyline, and venlafaxine as analgesics in dogs and cats, but none of these drugs have shown efficacy in controlled clinical trials.
- Current data do not support the use of the oral opioids morphine, oxycodone, and methadone in dogs and cats because of low oral bioavailability.

INTRODUCTION

Treatment of outpatient pain in dogs and cats can be rewarding for the owners and veterinarians. Nonsteroidal antiinflammatory drugs (NSAIDs) are commonly administered to dogs and occasionally cats for controlling pain in an outpatient setting. There

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are several NSAIDs approved by the US Food and Drug Administration (FDA) for dogs, with label indications of postoperative pain relief and management of osteoarthritis and there are a few that are FDA approved for cats for postoperative pain. Meloxicam is also approved by the European Medicines Agency for long-term control of musculoskeletal disorders in cats. Most animals tolerate NSAIDs well, with an expected 5% to 10% of patients having to discontinue treatment because of adverse effects, and up to 10% to 12% of patients potentially not responding to therapy. Adverse effects such as vomiting, diarrhea, gastrointestinal (GI) erosion/ulceration, nephropathy, or hepatopathy can occur. In addition, contraindications/precautions such as underlying renal disease, underlying hepatic disease, corticosteroid administration, or Cushing disease may preclude the use of NSAIDs. Therefore it is important to have knowledge of potential alternate therapeutics available and an understanding of the amount of information available supporting their use in dogs in cats (**Table 1**).

PHARMACOKINETICS AND THEIR APPLICATION TO ANALGESIC DOSAGE DESIGN

Pharmacokinetic studies are performed to describe the disposition of a drug in a particular species, after specific routes of administration, and at specific doses. Changes in route of administration, species, and dose can result in changes in the pharmacokinetic parameters. Therefore extrapolation of pharmacokinetic parameters to other species, routes of administration, or doses may not be accurate. In addition, many studies assess the pharmacokinetics of a drug after a single dose, but the pharmacokinetics may change with repeated doses, so extrapolating to multiple doses may not be accurate.[1,2]

Some drugs are metabolized to produce active metabolites that can contribute to the beneficial (and adverse) effects of the drug.[3] Some studies include the measurement and pharmacokinetics of active metabolites, but not all studies measure active metabolites and as such are incomplete descriptions of the potential factors contributing to the effects of the drugs.

Pharmacokinetic studies are useful in describing the extent and duration of drug exposure after an administered dose. Data derived from pharmacokinetic studies may be used to generate dose and interval recommendations to achieve and maintain desired concentrations, but that may not confer efficacy because there may be species-specific differences in the concentration or dose response to the drug. However, these recommendations are useful for designing experimental model studies, case studies, or controlled clinical trials.

Pharmacokinetic data are often used as a method of determining drug dosages. However, without corresponding data associating plasma concentrations with a clinical effect, the predictions may not be accurate because of differences in response to the drug. Pharmacokinetic studies provide a basis for potential effects or for dosages used in experimental study designs and controlled clinical trials.

Because many drugs are administered orally to dogs and cats, oral bioavailability is an important pharmacokinetic parameter. Oral bioavailability is the rate and extent of drug absorption after oral administration. However, bioavailability is often used to express only the fraction of dose absorbed, and it is used in that context in this article. High oral bioavailability implies that a large fraction of the dose is absorbed intact into systemic circulation after oral administration. Low oral bioavailability implies that a small fraction of the drug is absorbed.

Some factors affecting bioavailability include absorption of the drug from the site of administration (eg, a drug that is not absorbed has a low bioavailability), active efflux of the drug back into the lumen of the intestines after absorption, and presystemic