Toxicology of Frequently Encountered Nonsteroidal Anti-Inflammatory Drugs in Dogs and Cats

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• Toxicology • NSAIDs • Incidents • Dogs • Cats

The nonsteroidal anti-inflammatory drugs (NSAIDs) are a group of heterogeneous compounds other than steroids that suppresses one or more substances produced during inflammatory reactions. NSAIDs are extensively used in both human and veterinary medicine for their antipyretic, anti-inflammation, and analgesic properties. Chemically, most NSAIDs are substituted organic acids. Although most NSAIDs consist of a wide range of pharmacologically active agents with diverse chemical structures and properties, they have similar therapeutic and adverse effects associated with their use. Each year the ASPCA Animal Poison Control Center (APCC) receives hundreds of cases involving acute accidental ingestion of human and veterinary approved NSAIDs in dogs and cats. The purpose of this article is provide a brief overview on the classification, mechanism of action, and pharmacologic and toxicologic properties of most commonly encountered human and veterinary NSAIDs in dogs and cats. For this purpose, the top 10 most frequently reported NSAIDs, as reported to the APCC in dogs and cats from 2005 to 2010, were selected. The article discusses general information about NSAIDs—classification, uses, pharmacokinetics, mechanisms of actions, and treatment followed by specific toxicity information involving the top 10 NSAIDs reported to the APCC.

GENERAL USES AND CLASSIFICATION

NSAIDs are used to treat a variety of conditions, including headaches and migraines, rheumatoid arthritis, osteoarthritis, inflammatory arthropathies, acute gout, dysmenorrheal, metastatic bone pain, postoperative pain, mild-to-moderate pain due to inflammation and tissue injury, pyrexia, ileus, and renal colic. In dogs, NSAIDs are approved for osteoarthritis and postoperative pain. Along with their benefits, NSAIDs

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also have some undesirable effects that can be seen both with therapeutic use and in overdose situations.

The first NSAID discovered in 1897 was acetylsalicylic acid, or aspirin. In 1961, ibuprofen was discovered after scientists had been searching for an option that had less risk for adverse gastrointestinal (GI) effects compared to aspirin. Ibuprofen became available on an over-the-counter basis in the United States in 1984. In 1999, in a continued attempt to discover an NSAID with even less risk for side effects, the first selective cyclooxygenase (COX)-2 inhibitor was approved by the Food and Drug Administration (FDA). Most NSAIDs are substituted organic acids classified into 3 main groups: carboxylic acids, enolic acids, and the newer COX-2 inhibitors (**Table 1**). The carboxylic acids can be further divided into salicylic acids, acetic acids, propionic acid, and fenamic acid. The enolic acid group can be further divided into pyazolones and oxicams. NSAIDs are placed in each of these groups based on their mechanism of action or chemical structure if the mechanism of action is not, or was not, known at the time of classification. Some veterinary approved NSAIDs (approved by the FDA) for use in dogs include Etogesic (etodolac), Rimadyl (carprofen), Metacam (meloxicam), Deramaxx (deracoxib), Previcox (firocoxib), and Zubrin (tepoxalin). Meloxicam is also approved for postoperative pain relief in cats (0.3 mg/kg SC once).

INCIDENT DATA

The widespread availability of NSAIDs has resulted in a marked increase in the number of overdose cases in humans. During 1985 to 1988, 55,800 cases of ibuprofen exposure were reported to the American Association of Poison Control Centers (AAPCC). In 1994 alone, the total number of NSAID exposures was 50,154, of which 35,703 were related to ibuprofen exposure. Despite their widespread use, the adverse effects associated with NSAID use are relatively few. One report suggests the incidence of adverse drug reactions associated with NSAID use is 24.4 per 1 million prescriptions. The fatal adverse reactions are estimated at 1.1 per 1 million prescriptions.[1] According to more recent information compiled by the AAPCC from 2003 to 2007, approximately 4% of all human incidents reported to AAPCC involved exposure to an NSAID. This translates to about 90,000 to 100,000 calls annually. The fatality review board of the AAPCC in their annual report during 2006 and 2007 assigned 5 fatalities and 107 life-threatening manifestations to NSAID exposures.[2]

Although there are several case reports that discuss toxicity reactions resulting from exposure to different NSAIDs in dogs and cats, the total incidence of adverse effects resulting from NSAID ingestion in dogs and cats is not known. Data from the ASPCA Animal Poison Control Center (APCC) electronic medical record database involving exposure to different NSAIDs (human and veterinary approved NSAID) was reviewed from 2005 to 2010. This review included information retrieved from the APCC public database. During this time period, the APCC received 22,206 reports of animals exposed to different types of NSAIDs in dogs and cats. These cases accounted for approximately 3% of the total cases called into the APCC. Of 22,206 incidents, 17,193 involved exposure to one agent only (1 NSAID). The dog was the most commonly reported species (15,823 dogs), followed by the cat (1244 cats). The other animals exposed to NSAIDs included birds, horses, ferrets, and pigs. The most common NSAID involved was ibuprofen (10,763 incidents) followed by aspirin (4170 incidents), naproxen (2690 incidents), deracoxib (1683 incidents), meloxicam (609 incidents), diclofenac (506 incidents), piroxicam (217 incidents), indomethacin (201 incidents), nabumetone (134 incidents), and etodolac (93 incidents). Of the 3 classes of NSAIDs, exposures to carboxylic acid–derivative was most commonly reported, with ibuprofen being the most commonly reported ingredient, followed by aspirin and naproxen.