

# Naproxen Toxicosis in an Elderly Greyhound

A 13-year-old, 63-lb, spayed greyhound presented after ingesting 220 mg of naproxen the previous evening.

## HISTORY

The dog had seemed uncomfortable after being exercised the previous evening; she had a history of degenerative joint disease but was not on medication. The owner had administered a single naproxen tablet (220 mg, 7.7 mg/kg), after which the dog began vomiting with increasing frequency during the night. Streaks of frank red blood were eventually noted in the vomitus.

## EXAMINATION

The dog was quiet but alert and responsive on examination. A mildly elevated heart rate of 140 beats/min (range, 80–120 beats/min) was noted. In addition, the dog was panting and demonstrated pain on abdominal palpation.

CONTINUES

## ? Ask Yourself...

Based on the information provided by the owner, which of the following effects may be expected from this naproxen exposure?

- A. GI upset
- B. GI ulceration
- C. GI ulceration & renal failure
- D. None, as the dose of naproxen is below toxic level



## **CORRECT ANSWER**

### **C. GI Ulceration & Renal Failure**

Naproxen has been used therapeutically in dogs at 2 mg/kg PO q48h. ASPCA Animal Poison Control Center (APCC) data suggest that in young, healthy dogs a one-time dose of 5 mg/kg or higher can cause GI ulceration and renal insult is possible at doses of 10 to 20 mg/kg or higher. The risk for GI or renal effects increases with concurrent use of other NSAIDs or steroids, and elderly patients may be at increased risk for renal effects if renal insufficiency is already present. The dose administered to this elderly patient was 7.7 mg/kg, and for this patient, renal effects were also possible at this dose.

### **MECHANISM OF ACTION**

Naproxen is an NSAID, and like other NSAIDs it decreases inflammation by blocking the synthesis of prostaglandins, which function as inflammatory mediators. Prostaglandins protect gastric mucosa by secretion of mucus and bicarbonate, increased mucus production and maintenance of a good mucous layer, maintenance and improvement of GI tract blood flow, reduction in stomach hydrochloric acid secretion, and promotion of epithelial cell repair and turnover.

Naproxen acts by inhibiting cyclooxygenase, which prevents arachidonic acid from converting to various prostaglandins; loss of these protective prostaglandins can lead to GI tract irritation and ulceration.

In the kidneys, prostaglandins act as vasodilators. They modulate the pressor effects of vasoactive substances (including norepinephrine, angiotensin II, and antidiuretic hormone), maintain adequate renal blood flow and glomerular filtration rates, mediate renin release, and are involved in electrolyte transfer. Therefore, decreased prostaglandin synthesis can lead to adverse kidney effects from decreased renal blood flow and glomerular filtration rate.

In dogs, naproxen is eliminated primarily in the feces and has a prolonged half-life of 72 hours, which may result from extensive enterohepatic recirculation.

### **CLINICAL SIGNS**

The most common clinical signs of naproxen toxicosis are vomiting, lethargy, and anorexia. Melena, diarrhea, hematemesis, anemia, abdominal pain, and depression are also possible. Clinical signs of azotemia, isosthenuria, uremic ulceration, halitosis, and hyperphosphatemia may be seen with kidney damage.

### **DIFFERENTIAL DIAGNOSIS**

Differentials include nephrotoxins and nephrotoxicants (eg, veterinary or human medicine NSAIDs, ethylene glycol, grapes, raisins, cardiac medication). Nontoxin-related causes of azotemia (eg, pyelonephritis, chronic renal insufficiency) should also be ruled out.

### **DIAGNOSTICS**

The baseline chemistry panel demonstrated a mildly elevated blood urea nitrogen (BUN) of 30 mg/dL (range, 7–26 mg/dL), which may have been the result of GI bleeding or prerenal dehydration. The creatinine concentration was normal at 1.4 mg/dL (range, 0.6–1.4 mg/dL); greyhounds and other sighthounds may have slightly higher creatinine concentrations than other breeds do. The urine specific gravity was 1.056, packed cell volume (PCV) 65% (range, 37%–55%), and total protein (TP) 8.3 g/dL (range, 5.8–7.2 g/dL). Sighthounds can have a higher PCV than other breeds, so the elevation may have been a normal breed variation. However, an elevated TP value suggested some level of dehydration.

The remainder of the CBC and urinalysis was unremarkable.

### **TREATMENT**

In this patient, emesis was not induced because naproxen exposure had occurred the previous night. Activated charcoal, which is contraindicated if gastric perforation is suspected or confirmed, was not administered, as the dose of naproxen had been less than 10 mg/kg and gastric bleeding was present. The clinician did not believe that the benefits of giving activated charcoal outweighed the risks.

Maropitant at 1 mg/kg SC was administered to control vomiting, along with sucralfate at 1 g PO

APCC = Animal Poison Control Center, BUN = blood urea nitrogen, PCV = packed cell volume, TP = total protein



q8h, famotidine at 0.5 mg/kg PO q12h, and misoprostol at 3.5 µg/kg PO q12h. IV fluids were initiated at 1.5 times maintenance levels because of the patient's advanced age, dehydration, and possible GI ulceration.

## PROGNOSIS

Recovery from GI irritation or ulceration is usually complete with appropriate treatment. Patients with GI ulceration are at risk for perforation and death from GI bleeding or sepsis. Medications to protect the GI tract should be continued for 7 to 10 days or beyond if ulceration has developed.

The APCC recommends fluid diuresis for a minimum of 72 hours if a nephrotoxic dose has been

ingested and subsequent weaning from fluids if kidney values remain normal. In general, renal effects of NSAIDs are considered reversible if discovered early and treated aggressively.

## FOLLOW-UP

The patient had one episode of melena in the afternoon. Her vomiting resolved within a few hours. The BUN, PCV, and TP values were normal after 24 hours of fluid therapy. The patient was discharged 36 hours after presentation and was continued on GI-protective medications for an additional 14 days. A recheck renal panel 2 days later was normal.

See **Aids & Resources**, back page, for references & suggested reading.



## Take-Home Messages

### NAPROXEN TOXICOSIS OVERVIEW

#### Decontamination

- Decontamination may not be required for a dose <5 mg/kg but may be needed to lower the risk for GI irritation.
- With toxic ingestion of naproxen, appropriate decontamination should be initiated if ingestion was recent (<2 hours). If the patient exhibits no clinical signs, emesis can be induced using apomorphine or hydrogen peroxide. If emesis is unproductive, the use of activated charcoal should be considered (1–3 g/kg PO).
- If the patient exhibits no clinical signs and NSAID ingestion occurred more than 2 hours before presentation, consider administering activated charcoal (1–3 g/kg PO).
- For ingestion of naproxen at >10 mg/kg, an initial dose of 1–3 g/kg PO activated charcoal should be followed with half the original amount q4–8h for 24 to 48 hours after ingestion, as naproxen undergoes extensive enterohepatic recirculation.
- Ideally, the first dose of activated charcoal should contain a cathartic. However, with repeated doses, a cathartic should not be used, particularly if the patient is dehydrated or has diarrhea. While rare, life-threatening hypernatremia may occur with administration of activated charcoal.

#### Laboratory

- Obtain a baseline chemistry panel and electrolytes, including serum sodium, CBC, and urinalysis (particularly specific gravity) before administering fluids.
- Repeat a renal panel (BUN, creatinine, electrolytes, albumin) at 24, 48, 72, and 96 hours.
- Monitor serum sodium regularly, since administration of activated charcoal has been associated with hypernatremia.
- Repeat CBC and urinalysis if indicated.

#### Treatment

- Monitor for signs of GI ulceration and initiate GI protection. Continue GI-protective medications for at least 7 to 10 days.
- Patients should be started on aggressive IV fluid diuresis if nephrotoxic doses of naproxen are ingested. Depending on the time to decontamination or exposure, therapy for 3 to 5 days may be necessary, based on the severity of azotemia and signs.
- Control vomiting as needed with antiemetics (eg, maropitant, dolasetron, ondansetron).
- Rarely, with life-threatening severe GI ulceration, the use of more aggressive therapy may be necessary (eg, colloid therapy, blood transfusion).