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Intoxication by Lornoxicam in Two Dogs

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ABSTRACT

Background: The indiscriminate use of drugs is routinely observed in the field of veterinary medicine. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the class of drugs that most commonly cause intoxication in pet animals. Lornoxicam, an NSAID, is a cyclooxygenase COX-1 and COX-2 inhibitor and is only recommended for human treatment. Here we present cases involving two dogs who presented with Lornoxicam intoxication following administration without veterinary prescription.

Cases: 1) - A 1-year-old female Rottweiler was presented for clinic with claudication, profuse vomiting, and fetid blackish diarrhea. The owner reported administer two tablets of oral Lornoxicam. Physical examination revealed lethargy, a bulging abdomen and pale mucous membranes. Contrast-enhanced imaging of the gastrointestinal tract revealed decreased stomach flow. The ultrasound revealed predominantly gaseous contents in the stomach with normal walls, a large amount of accumulated gas in the pyloric region. Therefore, exploratory laparotomy was held and a nonperforated ulcer was observed in the pyloric region. There were hemorrhagic areas in the stomach mucosa and enlarged lymph nodes in the duodenum. The ulcer was resected without complications. Medications included after surgery were intravenous fluid, antibiotic, analgesic, antiemetic, histamine H2-receptor antagonist and Cytoprotective drugs. The day after the surgical procedure, no episode of vomiting or diarrhea was observed and the food and water were introduced gradually in the following days. 2) - An 11-year-old male Old English Sheepdog came to the clinic with a history of vomiting, blackish diarrhea, and loss of appetite. The owner reported that first was administered deltamethrin for tick infestation and approximately 3 days after, the amitraz. The animal began vomiting, limping, and lost its appetite. Because of the limping, the owner administered Lornoxicam in a single dose and the animal start vomiting and manifested fetid, blackish diarrhea. On physical examination, the patient showed 7.0% dehydration and tenderness on palpation in the epigastric region. For diagnostic screening was performed: hematological and biochemical evaluation; the Canine Test SNAP 4DX; and total abdominal ultrasound. The results only showed leukocytosis and predominantly gaseous contents in the stomach. Then, pyrethroid and formamidine intoxication with hemorrhagic gastroenteritis secondary to Lornoxicam administration was suspected. Intravenous fluid therapy was performed with Ringer's lactate solution. In addition, metoclopramide, ranitidine, sucralfate and sulfamethoxazole/trimethoprim were administered along the gradual insertion of food and water. The patient showed complete clinical recovery after 7 days of hospitalization and was discharged.

Discussion: The clinical signs presented by the both cases were similar to those described in the literature on NSAID intoxication in animals. In the two cases, none of the exams confirmed the presence of the ulcer, but they helped to suspect. Blood tests performed for the second animal revealed findings similar to previously reported nonspecific laboratory findings for gastric ulcers. In both cases, ultrasound did not identify any changes that proved the existence of gastric ulcers. However, this test is necessary to rule out complications such as perforation or peritonitis. In the first case, exploratory laparotomy was required for a definitive diagnosis because of suspected obstruction in the pyloric region. For the second animal, surgery was not planned because all the performed tests only raised a suspicion of hemorrhagic gastritis, and the suspected diagnosis was confirmed by the positive response to the treatment. The underlying etiology in both cases was identified as Lornoxicam intoxication due to administration without veterinary medical prescription

Keywords: nonsteroidal anti-inflammatory drug, gastritis, gastric ulcer.

INTRODUCTION

The indiscriminate use of medications in animals is a routine observation. Owners' lack of knowledge, easy access to drugs in human and veterinary pharmacies, and the habit of self-medication result in drug intoxication to be one of the most important reasons for poisoning in dogs and cats [12].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the class of drugs that most commonly cause intoxication in pet animals. Drug intoxication in animals may occur through accidental ingestion or administration without professional guidance or veterinarian prescription. The availability of numerous medications in the market and their sale without professional prescription explains why intoxication with NSAIDs, antibiotics, and topical products is often observed in routine clinical practice [4,12].

NSAIDs prolong bleeding time by blocking the production of thromboxane A₂ in platelets, and it plays an important role in the activation of platelet aggregation. Other effects include gastrointestinal ulcers, which develop because of the inhibition of gastrointestinal PG synthesis. Lornoxicam is a COX-1 and COX-2 inhibitor drug belonging to the oxicam class, and there is no recommended dose for animals [1].

The present work aimed to report the first two cases of intoxication with associated gastric ulcers following administration of Lornoxicam in Brazil, emphasizing the effects of indiscriminate NSAID use without prescription and on the lack of a recommended dose for dogs.

CASES

1)- An 1-year-old female Rottweiler weighing 26 kg was brought to a veterinary clinic in the city of Ilheus, Bahia, with claudication, profuse vomiting, and fetid, blackish diarrhea. According to the reported by the owner, the animal was playing at home and began limping for no apparent reason. Therefore, the owner administered two tablets of oral Lornoxicam (Xefo®)¹ 8 mg, with an interval of 12 h between each tablet. Following the second administration, the animal began to show the abovementioned clinical signs and symptom and was brought to the veterinary clinic. On physical examination, the patient exhibited lethargy, a bulging abdomen, pale mucous membranes, and a temperature of 37.5°C. Cardiopulmonary auscultation revealed no abnormalities.

On the basis of the medical history and an abnormal appetite reported by the owner, the veterinarian suspected a gastrointestinal foreign body. Contrast-enhanced imaging of the gastrointestinal tract with image acquisition at 15, 30, and 45 min revealed decreased stomach flow. Subsequently, ultrasound was performed to confirm the presence of the suspected foreign body.

Ultrasound revealed predominantly gaseous contents in the stomach with normal walls, a large amount of accumulated gas in the pyloric region, and bowels without evidence of dilatation. No changes were observed in the other examined organs. Exploratory laparotomy was subsequently scheduled.

Pre anesthetic medication (PAM) included 0.5 mg/kg intramuscular (IM) of diazepam (Diazepam®)² and 0.5 mg/kg of chlorpromazine (Clorpromaz®)². Anesthesia was induced with 5 mg/kg of propofol (Propovan®)³ and maintained with inhalational isoflurane 2V% (Isoforine®)³.

During surgery, a nonperforated ulcer measuring approximately 3 cm in its major axis was observed in the pyloric region (Figure 1). In addition, there were hemorrhagic areas in the stomach mucosa and enlarged lymph nodes in the duodenum.

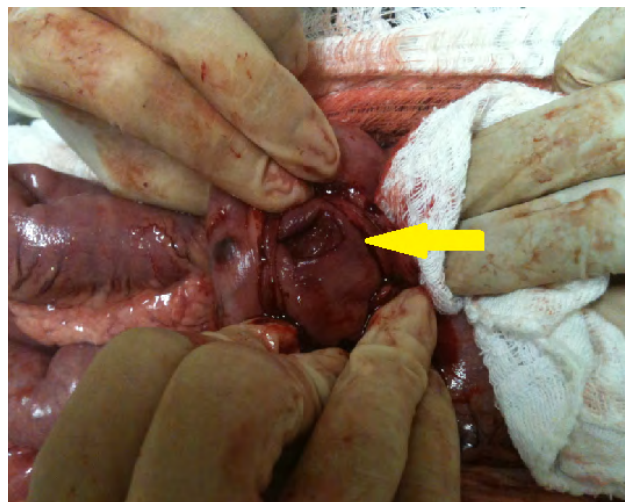


Figure 1. Photographic image of the surgery showing a nonperforated ulcer (yellow arrow) in the pyloric region.

The ulcer was resected without complications. After surgery, the patient was restrained from any type of medication, hydration, or oral feeding during the first 24 h. After that, it received 3,000 mL/EV/24 h for 3 days of ringer's lactate solution, 390 mg/EV/BID/7 days of metronidazole (Flagyl®)⁴, 0.25 mL/IM/SID/3 days of morphine sulfate (Dimorf®)³, 1.5 mg/kg/SC/TID/7 days of antiemetic metoclopramide (Plasil®)⁴, 2 mg/kg/SC/BID/7 days of the antacid ranitidine

(Antak®)⁵, and 1 g/VO/TID/7 days of the mucosal protective agent sucralfate (Sucrafilm®)⁶.

The day after the surgical procedure, no episode of vomiting or diarrhea was observed. The animal was active and showed interest in water. Water intake at a dosage of 130 mL/q 2 h, which corresponds to 60 mL/kg/day, was then permitted. From day 3, its diet was gradually replaced with wet feed therapeutic for the gastrointestinal tract for 7 days (Gastro Intestinal Royal Canin®)⁷, following which dry feed therapeutic for the gastrointestinal tract (Gastro Intestinal Royal Canin®) was administered.

Based on the medical history, imaging findings, and the findings of exploratory laparotomy, a clinical diagnosis of gastric ulcer secondary to Lornoxicam intoxication was made.

After treatment completion, the sutures were removed and the animal was discharged. There was no episode of recurrence, although the owner was educated about the dangers and consequences of medication without a prescription and veterinary guidance.

2)- An 11-year-old male Old English Sheepdog weighing 43 kg was brought to the veterinary clinic with a history of vomiting, blackish diarrhea, and loss of appetite. According to the anamnesis reported by the owner, after bathing was administered solution of deltamethrin (Butox®)⁸ at the dose of 20 mL/5L for the treatment of tick infestation. Because the infestation persisted, the owner administered solution of amitraz (Triatox®)⁸ also in the dose of 20 mL/5L approximately 3 days after deltamethrin (Butox®) administration. Subsequently, the animal began vomiting, lost its appetite, and began limping. Therefore, the owner administered Lornoxicam (Xefo®) bought from a human pharmacy without veterinary prescription, at a dose of 8 mg/VO, two tablets in a single dose. The appetite loss and vomiting exacerbated and fetid, blackish diarrhea manifested. The dog was eventually brought to the clinic after three days of clinical sign deterioration.

On physical examination, the patient was alert and showed normal mucous membranes, 7.0% dehydration, and tenderness on palpation in the epigastric region.

Because of epigastric tenderness and the gastrointestinal signs and symptoms, hematological and biochemical evaluation [blood count, blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST)] were per-

formed, besides total abdominal ultrasound and the Canine Test SNAP 4DX for ehrlichiosis, anaplasmosis, heartworm, and Lyme disease.

Hematological evaluation majorly revealed no abnormalities: red blood cells (RBCs), 5.78/mm; hematocrit, 36%; platelet count, 31,8000/mm³; and total protein, 6.8 g/dL. However, leukocytosis (28,800/mm) was apparent.

Biochemical tests also showed normal values (Table 1), and the Canine Test SNAP 4DX showed negativity for all diseases. Ultrasound showed predominantly gaseous contents in the stomach, normal walls, and bowels without evidence of dilatation. There were no abnormalities in the other examined organs.

Based on the medical history, blood tests, and imaging findings, pyrethroid and formamidina intoxication with hemorrhagic gastroenteritis secondary to Lornoxicam (Xefo®) administration was suspected. Surgery was ruled out because imaging did not reveal signs of severe ulceration in the stomach, and pharmacological treatment was planned.

Intravenous fluid therapy was performed with 3,500 mL/24 h Ringer's lactate solution. In addition, 0.5 mg/kg/SC/TID/7 days of metoclopramide (Plasil®), 1mg/kg/SC/BID/7 days of ranitidine (Antak®), 1g/VO/TID/10 days of sucralfate (Sucrafilm®), and 15/3 mg/kg/BID/7 days of the antibiotic sulfamethoxazole/trimethoprim (Afectrim®)⁹ were intramuscularly administered for the first 3 days. After 4 days, oral administration was initiated after the suppression of vomiting. Furthermore, water intake at a dose of 130 mL every 2 h was initiated, which corresponded to 60 mL/kg/day. From day 3, its diet was gradually replaced with dry feed therapeutic for the gastrointestinal tract (Gastro Intestinal; Royal Canin®). The patient showed complete clinical recovery after 7 days of hospitalization and was discharged.

However, the animal returned after 7 days with anorexia and vomiting, loss of appetite, and 7.0% dehydration. Blood tests were repeated, and mild anemia (RBCs, 4.54/mm; hematocrit, 34%) and a normal white blood cell count (7,500/mm) were observed. The other parameters were normal. This time, the owner reported that he was trying to feed the dog with homemade food (pizza and ice cream).

The animal was readmitted for dehydration management with fluid (replacement volume of 70 mL/kg/8h and maintenance with 20 mL/kg/24h).

Furthermore, 0.5 mg/kg/SC/TID of metoclopramide (Plasil®), 40 mg/kg/VO/SID of omeprazole (Petprazol®)¹⁰, and 1 g/VO/TID/10 days sucralfate (Sucrafilm®) were administered. After 3 days, it showed remission of clinical signs and was discharged with a prescription of

the same previous drugs at the same oral dose. Metoclopramide was continued for another 7 days, omeprazole and sucralfate for 20 days, and 20 mL/day of vitamin and mineral supplements (Glicopan Pet®) 10 for 30 days. The animal showed complete recovery after treatment.

Table 1. Biochemical parameters for Case Report 2.

Blood urea nitrogen	17 mg/dL (21.4-59.9 mg/dL)
Creatinine	06 mg/dL (0.5-1.5 mg/dL)
Aspartate aminotransferase	23 U/L (8.2-57 U/L)
Alanine aminotransferase	29 U/L (8.2-57 U/L)

DISCUSSION

Here we reported Lornoxicam intoxication in two dogs. These cases are important because, to the best of our knowledge, they are the first national reports on the effects of Lornoxicam in dogs. Because this medication is not recommended for animals, there are few studies on its effects and recommended doses in veterinary medicine. The low cost and ease of acquisition in human pharmacies without veterinary prescription result in indiscriminate and unsafe administration to animals. In the two cases reported here, the owners did not seek medical care for limping, the initial symptom for which Lornoxicam was administered.

There are no reports of animal predisposition to gastric ulcers according to race, age, and sex, because NSAIDs directly damage the gastric mucosa and inhibit gastrointestinal PG production [2].

The clinical signs presented by the present cases were similar to those described in the literature on NSAID intoxication in animals, including profuse vomiting, diarrhea, loss of appetite, and pain on abdominal palpation [10]. Furthermore, some authors [12] confirmed NSAIDs to be the most common self-administered drugs in animals, probably because of the low cost, ease of acquisition, and the habit of self-medication by humans.

Blood tests performed for the second animal revealed findings similar to previously reported non-specific laboratory findings for gastric ulcers. Neutrophilic leukocytosis is reportedly a common side effect of Piroxicam [10], which also belongs to the oxicam class. Assessment of renal function (BUN and creatinine) and liver function (ALT and AST) is also necessary [10], who explained the necessity of ruling

out other causes and predisposing factors for gastric ulcers, such as kidney failure and liver diseases.

The Canine Test SNAP 4DX was performed for Case 2 to rule out ehrlichiosis, a common disease in the gastrointestinal region, because the animal had a history of tick infestation and clinical features of blood loss, consistent with features of the disease. We used the blood sample collected for CBC for the SNAP 4DX test, the results of which were negative.

In both cases, ultrasound did not identify any changes that proved the existence of gastric ulcers, obstruction by a foreign body, and ulcer was suspected from the excessive accumulation of gas in the pyloric region and within the stomach. These were similar to the findings of some authors who experienced difficulty in visualizing gastric changes or gastric ulcer, even with high-resolution equipment of ultrasound [3, 6]. The common findings include generalized thickening or localized mucosal thickening associated with a large amount of hyperechoic gas. However, this test is necessary to rule out complications such as perforation or peritonitis [11].

In the first animal, exploratory laparotomy was required for a definitive diagnosis because of suspected obstruction in the pyloric region with excessive hyperechoic gas. For the second animal, surgery was not planned because all the performed tests only raised a suspicion of hemorrhagic gastritis. In this case, the suspected diagnosis was confirmed by the positive response to the treatment instituted, and the underlying etiology in both cases was identified as Lornoxicam intoxication due to administration without veterinary medical prescription.

During surgery, PAM was used to calm the patient, prevent emesis, produce analgesia and relax-

ation, facilitate induction, and provide better anesthetic recovery [5]. The choice of administering a benzodiazepine (diazepam) with a tranquilizer (chlorpromazine) is attributed to the reassurance effect and analgesia. Diazepam decreases aggression, promotes muscle relaxation, and provides discrete analgesia, while chlorpromazine shows antiemetic and analgesic effects [8]. Induction and recovery with propofol are quiet and smooth, which was observed in the anesthetized animal [5]. The use of isoflurane maintenance was for anesthetic safety, because this drug is not nephrotoxic, causes fewer cardiac abnormalities, and promotes total elimination by the lungs with rapid induction and recovery [8].

In both cases, pharmacological treatment was as per that reported in the literature. The H2 receptor antagonist is used to suppress the secretion of gastric HCl to inhibit histamine receptors. Among the drugs in this class, ranitidine was selected because it is powerful and acts rapidly, causing 90% inhibition of acid 1 h and 30 min after administration. Omeprazole was used to block the proton pump in the gastric parietal cell membrane. By decreasing the acidity of the gastric lumen, it decreases the concentration of hydrogen ions (H⁺), thereby decreasing the natural attack by the acid on the injured mucosa. Cytoprotective drugs such as sucralfate also help in protecting the gastric mucosa and promote re-epithelialization [9,10].

Metoclopramide is a centrally acting antiemetic indicated for animals that present with acute vomiting and its sequelae, including discomfort and excessive loss of fluids and electrolytes. Both animals presented with these symptoms, and this drug was considered essential for treatment success. Furthermore, the choice of subcutaneous administration was also in accordance with previously reports; oral administration is indicated only for patients with mild symptoms [9].

Gastric ulcers and gastrointestinal bleeding are widely described in the national literature, although they have never been described in association with

Lornoxicam. There is only experiment reported from Germany, where gastrointestinal bleeding was induced with this medication in six dogs and the severity of clinical symptoms was evaluated. At the end of the experiment, the authors concluded that Lornoxicam could cause severe and prolonged bleeding from the gastrointestinal tract, which requires immediate intensive care [7].

In conclusion, Lornoxicam is a drug for humans, and there are no indications or doses established for use in veterinary medicine. The lack of knowledge and the habit of owners to self-medicate, sometimes to cut the cost of veterinary consultations, leads to NSAIDs being one of the most common medications to cause intoxication in dogs.

The cases reported here contribute to national and international literature because they demonstrate the severity and intensity of clinical symptoms, which, if neglected or not diagnosed quickly and efficiently, affect the prognosis and can lead to death. Therefore, veterinarians should be aware of the side effects of NSAIDs and exercise caution with their use; furthermore, they should play an important role in guiding clients and pet owners about the risks of self-medication.

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