Suspected carprofen toxicosis caused by coprophagia in a dog

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Case Description—A 1-year-old spayed female mixed-breed dog was evaluated because of urinary incontinence, polyuria, polydipsia, and minimally concentrated urine.

Clinical Findings—Markedly high circulating alanine transaminase activity, mildly high circulating alkaline phosphatase activity, and low urine specific gravity were detected for the dog during the initial examination, and alkaline phosphatase activity was within the reference range 5 weeks after discontinuation of consumption of feces. Alanine transaminase activity was substantially lower than the value determined during the initial examination, and alkaline phosphatase activity was within the reference range 5 weeks after discontinuation of consumption of feces by the dog.

Treatment and Outcome—Access to feces of other dogs in the household was prevented; no other treatment was initiated. Urinary incontinence, polyuria, and polydipsia resolved, and urine specific gravity increased within 7 days following discontinuation of consumption of feces. An episode of inappropriate urination approximately 2 months prior to referral, which resolved 4 hours later also had a low specific gravity (1.016). Results of aerobic bacteriologic culture of this urine sample indicated no growth after 72 hours.

Abdominal ultrasonography revealed the urinary bladder was distended and located in the pelvic canal. The ultrasonographic appearance of other abdominal structures, including liver parenchyma, was unremarkable. Samples of the liver were obtained via ultrasonographically guided fine-needle aspiration. Results of cytologic examination of liver samples indicated small clusters of well-differentiated hepatocytes; these findings were unremarkable.

At this time, inadvertent exposure to carprofen via ingestion of feces was suspected on the basis of persistently low urine specific gravity and markedly high alanine transaminase activity. Total carprofen concentrations in serum and plasma samples obtained from the dog were determined via high-pressure liquid chromatography with UV detection by use of a modification of a previously described method;1 the limit of quantitation of the assay for detection of carprofen was 0.1 µg/mL. Carprofen concentrations were similar in the serum (0.59 µg/mL) and plasma (0.62 µg/mL) samples obtained from the dog. Assays for detection of carprofen in those samples were performed by personnel of the Clinical Pharmacology Analytical Laboratory at North Carolina State University.

Recommendations for the dog included prevention of access to feces of other dogs in the household;...
no other treatments were initiated. The owner reported that the dog had complete resolution of polyuria, polydipsia, and urinary incontinence within 1 week after discharge from the hospital. Results of analysis of a voided urine sample collected midstream 1 week after discharge indicated adequate urine concentration (specific gravity, 1.040). Results of serum biochemical analyses performed at this time indicated alanine transaminase activity had decreased substantially (335 U/L). All other serum biochemical analysis values were within reference ranges, including alkaline phosphatase activity (122 U/L). Serum carprofen concentration determined at this time was lower than the limit of quantitation of the assay (0.1 µg/mL).

Five weeks after the initial evaluation, the owner reported that the dog had no recurrence of urinary incontinence or polyuria and polydipsia. However, the dog occasionally consumed feces of other dogs in the household. Results of serum biochemical analyses performed at this time indicated progressively decreasing alanine transaminase activity (222 U/L). All other serum biochemical analysis values were within reference ranges at this time, including alkaline phosphatase activity (66 U/L). Plasma carprofen concentration for the dog of the present report at this time was 0.24 µg/mL; plasma carprofen concentration for the other dog in the household that was receiving carprofen was 8.39 µg/mL.

Discussion

Carprofen is an NSAID that is commonly administered to dogs to alleviate signs of pain. Carprofen is effective for treatment of animals with clinical signs attributable to osteoarthritis, and no adverse effects are detected in dogs receiving a total daily dose ≤ 2 mg/kg (0.91 mg/lb). Although the mechanism of action of carprofen is unknown, that drug inhibits both cyclooxygenase pathways and has anti-inflammatory, analgesic, and antiplatelet activities. At clinically effective doses, carprofen is a poor inhibitor of prostaglandin syntheses but does prevent CNS sensitization in response to a surgical stimulus when administered before or after surgery. In dogs, carprofen is typically metabolized by means of glucuronidation and subsequently excreted in bile. When administered to dogs IV, approximately 70% of carprofen is excreted in bile as glucuronide metabolites and recovered in the feces and 8% to 15% of the drug is excreted in urine. Carprofen metabolites may be hydrolyzed to form the parent compound, which can be detected in feces.1

Results of other studies indicate a low incidence of adverse effects in dogs that receive clinically effective doses of carprofen for a short (perioperative analgesia) or long (management of chronic signs of pain associated with osteoarthritis) duration. Vomiting and diarrhea are the most common adverse effects of carprofen in dogs. Reduced appetite and lethargy are also adverse effects of carprofen in dogs. Less common adverse effects of the drug include hypoalbuminemia, weight loss, and high circulating liver enzyme activities. Although high circulating liver enzyme activities are not commonly reported as adverse effects of carprofen in dogs, this drug can cause idiosyncratic hepatocellular cytotoxic effects. Hepatotoxic effects of carprofen are most commonly detected in spayed female dogs that receive a dosage of 1.57 to 3.10 mg/kg (0.714 to 1.41 mg/lb) twice daily. Clinical signs of dogs associated with hepatotoxic effects secondary to carprofen administration include lethargy, inappetence, diarrhea, vomiting, polyuria, polydipsia, and hematuria. The most common clinicopathologic abnormalities caused by toxic effects of carprofen in dogs include high circulating total bilirubin concentration and alanine transaminase, alkaline phosphatase, and aspartate transaminase activities. Circulating activities of alanine transaminase are typically higher than those for alkaline phosphatase in affected dogs. Results of CBCs and abdominal imaging are typically unremarkable for such dogs. Clinical signs of carprofen toxicosis typically develop between 5 and 30 days after initiation of treatment and resolve 1 to 5 days after discontinuation of administration. Clinicalopathologic abnormalities improve markedly in affected dogs within 3 weeks after discontinuation of carprofen administration.

Carprofen inhibits both cyclooxygenase pathways, which have activities in physiologic processes in various organs including the kidneys. Vasoconstriction induces activation of cyclooxygenases, resulting in production of prostaglandins that cause vasodilation and maintenance of renal blood flow. Also, prostaglandins partially antagonize the effects of antidiuretic hormone in kidneys; that hormone increases water resorption from collecting tubules. Elimination of the inhibitory effect of prostaglandins on antidiuretic hormone activity can therefore diminish free water excretion in the urine via increasing water resorption through increased activity of antidiuretic hormone. During certain conditions, administration of NSAIDs may also induce a decrease in renal blood flow and glomerular filtration rate secondary to inhibition of activity or decreased production of prostaglandins. Results of another study indicate anesthetized dogs undergoing castration that received 1 dose of carprofen (4 mg/kg [1.82 mg/lb], IV) have significantly lower glomerular filtration rates, compared with those of control dogs. Dose-dependent nephrotoxic effects of carprofen are distinct from idiosyncratic hepatotoxic effects of that drug. These findings support the possibility that NSAIDs, including carprofen, may cause adverse effects on renal function, potentially leading to acute kidney injury and impaired ability of kidneys to concentrate urine. In the dog of the present report, the clinical signs of urinary incontinence and polydipsia, high circulating liver enzyme activities, and low urine specific gravity were most likely caused by ingestion of carprofen. This conclusion was supported by the findings of high circulating carprofen concentrations in the dog and resolution of clinical signs and improvements in clinicopathologic abnormalities after prevention of exposure to carprofen. Interestingly, the only owner-reported exposure of this dog to carprofen was ingestion of feces of another dog in the household that was receiving the drug. Approximately 70% of carprofen is excreted in bile and, subsequently, feces of dogs; therefore, ingestion of feces of another dog that was receiving carprofen may have caused adverse effects in this dog of the present report.

Plasma concentrations of carprofen detected for the dog of the present report were markedly lower.
than mean plasma concentrations of that drug for dogs receiving clinically effective doses IV or orally. 2,3 The amount of carprofen ingested by the dog of the present report could not be determined. Moreover, the timing of exposure to carprofen was unknown for the dog. The half-life of a formulation of carprofen intended for oral administration is short (approx 8 hours). 15,16 Plasma and serum samples of the dog of this report were only analyzed to detect carprofen. Unmeasured metabolites of the drug may have contributed to clinical signs of carprofen toxicosis; however, the effects of metabolites of carprofen on toxic effects in dogs are unknown, to the authors’ knowledge. The adverse effects in the dog of this report could not be directly attributed to the total circulating concentrations of carprofen that were detected. However, the circulating carprofen concentration in the dog was less than the limit of quantitation of the assay and clinical signs resolved after prevention of ingestion of feces of the other dog in the household that was receiving the drug.

To the authors’ knowledge, this is the first report of suspected carprofen toxicosis in a dog attributable to consumption of feces of another dog receiving the drug. Carprofen is commonly prescribed for management of signs of pain in dogs, and it is not unusual for a dog in a multidog household to receive this drug. Findings for the dog of the present report suggested that consumption of feces of another dog receiving carprofen may cause adverse effects. This cause of adverse effects should be a differential diagnosis for dogs with clinical signs and clinicopathologic abnormalities consistent with carprofen toxicosis. A thorough history should be obtained for dogs regarding potential exposure to toxins.

References