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CASE REPORT

Use of Intravenously Lipid Emulsion for Treatment of Baclofen Toxicosis in a Cat

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A B S T R A C T

A 1-year-old female domestic shorthair cat ingested about 1.6 mg/kg body weight of baclofen. Hyperexcitability, disorientation and ataxia followed by severe central nervous system depression were noted. Hypothermia, bradycardia and tachypnea were developed. Therapy with an intravenous emulsion of 20% soybean oil in water was started because conventional therapies did not control clinical signs. A bolus of 2 ml/kg in 15 minutes following by constant rate infusion of 0.05 ml/kg/min for 4 hours was administered. Within one hour of starting the lipid administration, the cats' breathing, heart rate and patient mental state improved. Rectal temperature normalized. At the end of lipid infusion heart and respiratory rate were in the reference range as well as neurological signs resolved. The cat was discharged after 5 days of hospitalization. No recurrence of clinical signs was reported.

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INTRODUCTION

Baclofen is a centrally acting skeletal muscle relaxant. It mimics y-aminobutyric acid within the spinal cord and works by depressing monosynaptic and polysynaptic afferent reflex activity. Baclofen is used in people with multiple sclerosis, cerebral palsy and spinal cord disorders to treat muscle spasticity and pain (Khorzad *et al.*, 2012; Edwards *et al.*, 2014). Several cases of baclofen intoxication have been reported in dogs due to ingesting their owners' medication (Robben and Dijkman, 2017) but few cases of cats have been reported (Edwards *et al.*, 2014).

Clinical signs of poisoning include salivation, weakness, mydriasis, miosis, nystagmus, blindness, dysphoria, agitation, hyperactivity, tremors and ataxia. Gastrointestinal, cardiovascular, respiratory and urogenital clinical signs are also described. Coma, seizures, hypothermia and respiratory arrest may occur (Khorzad *et al.*, 2012; Edwards *et al.*, 2014). There is no specific antidote, but experimental studies and case reports supported the use of intravenous lipid emulsion (ILE) in the management of intoxication from lipophilic drugs (Fernandez *et al.*, 2011). Treatment of baclofen toxicosis through ILE has been described in six dogs and one cat (Khorzad *et al.*, 2012; Bates *et al.*, 2013; Edwards *et al.*, 2014).

The present report describes the second case of baclofen toxicosis in a cat that was successfully treated with ILE at lower dose as an adjunct to supportive therapy.

History and clinical examination: A 1-year-old spayed female domestic shorthair weighing 3 kg was presented at the Small Animal Emergency Service because of severe hyperexcitability, disorientation and ataxia. The owner reported that the cat accidentally ingested a quarter of a 20 mg baclofen tablet. The cat vomited several times before presentation to the hospital.

On general physical examination, rectal temperature was 38.4°C and capillary refill time was <2 sec. Respiratory rate was 32 breaths/min and mucous membranes were pink and moist. The cat showed bradycardia (130 beats/min) with normal sinus rhythm. Pulse quality was normal and systolic blood pressure (Doppler method) was 120 mmHg.

Neurological exam revealed disoriented mentation and marked hyperexcitability. General proprioceptive ataxia was noticed at gait examination. No proprioceptive or postural reaction deficits were found. Menace response was absent bilaterally and bilateral mydriasis was observed. Pupillary light reflex was present. The remainder of the neurological examination was unremarkable. Blood samples were taken for routine laboratory evaluations. Complete blood count (CBC) did not show any abnormality. Biochemical profile was normal with the exception of increased alanine aminotransferase (ALT=520U/L; reference interval, 12-130U/L) and aspartate aminotransferase (AST=338U/L; reference interval, 0-48U/L) activities. Venous blood gas analysis revealed mild hypokalemia (K=3mmol/L; reference interval, 3.9-5.5mmol/L).

Diagnosis and treatment: On the basis of medical history and clinical signs, diagnosis of acute baclofen toxicosis was made. The cat was admitted to the Intensive Care Unit. An intravenous catheter was placed in the right cephalic vein and intravenously Ringer lactate solution at a rate of 5 ml/kg/h was supplemented with potassium chloride (28 mEq/L) for maintaining hydration, restoring normal potassium level and promoting drug elimination. Omeprazole (1 mg/kg, IV, q24h) and ondansetron (0.2 mg/kg, IV, q8h) were added for treatment of vomiting. Approximately, 2 hours following hospital admission, the cat was severely depressed. Mental state progressively worsened to coma. Bilateral miosis and bilaterally absent pupillary light reflex were noticed with hypothermia (rectal temperature, 36.7°C). The cat was tachypneic (40 breaths/min) with superficial breath. However, oxygen saturation measured by pulse oximetry was >95%. Bradycardia worsened (120 beats/min) but pulse quality and systolic blood pressure remained normal. The cat was warmed with an external heating device. Therapy with an intravenous emulsion of 20% soybean oil in water was started (Intralipid; Fresenius Kabi Italia). A bolus of 2 ml/kg in 15 minutes followed by constant rate infusion (CRI) of 0.05 ml/kg/min for 4 hours was administered. Within one hour of finishing the initial bolus and starting the lipid CRI, the cat's breathing patter underwent a change with the excursions becoming deeper and heart rate increased to 144 beats/min. The rectal temperature increased to 38.1°C. Patient mental state improved although it appeared still severely disoriented. Pupils were normal in size, pupillary light reflex and menace reaction were present bilaterally. The lipid CRI was continued for further 3 hours. During that time, the cat became appropriately responsive during handling. It started to stand and walk with mild ataxia. Respiratory and heart rate normalized. Upon discontinuation of the lipid emulsion, intravenously fluid therapy was continued with Ringer lactate solution at a rate of 5 ml/kg/hr. On day 2, the cat showed complete resolution of neurologic signs. Heart and respiratory rate were in the reference range. The cat developed hyperthermia (rectal temperature, 40°C). On day 3, rectal temperature decreased up to 39.5°C without drug administration. The cat began eating and drinking itself. On day 4, rectal temperature was normal. Intravenously fluid therapy was gradually decreased up to the interruption. On day 5, rectal temperature, heart and respiratory rate were within reference interval. Neurological exam revealed no abnormalities. The cat was discharged from the hospital. The owner reported that the cat was completely normal during a telephone follow-up conversation 5 days and one month after being discharged.

DISCUSSION

Little information is available about baclofen intoxication in cats. Five cats, of which only two survived, were reported in a retrospective study (Khorzad *et al.*, 2012). Recently, the use of ILE was described in a cat with acute baclofen intoxication (Edwards *et al.*, 2014). The ILE is a solution of medium and long chain triglycerides traditionally used to deliver essential fatty acids as part of parenteral nutrition. In the last decade, there has been increasing evidence supporting its use to attenuate or reverse clinical manifestations of lipophilic toxins in people and domestic animals (Fernandez *et al.*, 2011). In dogs, ILE was used for management of ivermectin, moxidectin, diltiazem, loperamide, ibuprofen and baclofen intoxications. In cats, ILE was described in lidocaine, permethrin and ivermectin toxicosis (Kidwell *et al.*, 2014; Long *et al.*, 2017; Robben and Dijkman, 2017). The exact mechanism of ILE remains incompletely elucidated. The lipid sink theory proposes that the administration of ILE creates a lipid partition within the plasma that sequesters lipophilic drugs, drawing them away from target tissues and eliminating them with endogenous fat particles. The ILE is also thought to increase the amount of free fatty acids available to the myocardium for energy production. Other theorized mechanisms include a positive inotropic effect secondary to increased calcium concentration within the cells, inhibition of sodium channels and cytoprotection (Fernandez *et al.*, 2011; Robben and Dijkman, 2017).

The cat of this case ingested about 1.6 mg/kg of baclofen. Currently, there is no established toxic dose in domestic animals. The ingested dose of baclofen is known in 3 cats: 1.7 mg/kg, 10 mg/kg and 14.7 mg/kg, respectively. The cat that received the higher dose died and the survival status of the cat receiving the lower dose is not known (Khorzad *et al.*, 2012). The cat ingested 10 mg/kg survived (Edwards *et al.*, 2014). In dogs, clinical signs are reported following to ingestion of doses from 0.7 mg/kg to 61 mg/kg. Death was reported at dose as low as 2.3 mg/kg. Given the wide range of described toxic doses and that 92% of baclofen poisonings result in the development of clinical signs, all ingestions of this drug should be considered clinically important (Khorzad *et al.*, 2012). Cats show ataxia, CNS depression, agitation, vomiting, diarrhoea, hypertension, bradycardia, vocalization, miosis, mydriasis, drowsiness and lethargy, tachypnea, respiratory arrest (Khorzad *et al.*, 2012; Edwards *et al.*, 2014). In the cat of this report clinical signs due to depression of the CNS were predominant. Lipid emulsion therapy started 2 hours after the admission to the hospital. The cat received a bolus of 2 ml/kg in 15 minutes following by a CRI of 0.05 ml/kg/min over 4 hours. The total amount of administered ILE was 42 ml. This dose is lower than that used in the previously reported cat with baclofen toxicosis (Edwards *et al.*, 2014). It was chosen to avoid fluid overload. In veterinary medicine, there is no established recommended dose for ILE in the treatment of lipophilic drug poisonings and it is often extrapolated from human data (Fernandez *et al.*, 2011). However, in all cases, including the present case, the lipid infusion was continued until a clinical response was noted. Cessation of ILE therapy should be undertaken with caution as recurrence of clinical signs has been reported (Edwards *et al.*, 2014).

In both people and companion animals, ILE is considered relatively safe. A single study evaluating toxic effects in a murine model found that the lethal dose 50 was 67.7±10.7 ml/kg, which is significantly higher than the doses advocated for use in drug toxicosis (Kaplan and Whelan, 2012). Persistent lipemia and suspected corneal

lipidosis following ILE therapy were described in one cat with permethrin toxicosis (Seitz and Burkitt-Creedon, 2016). The cat of this report tolerated ILE administration well. The fever origin and its relationship with ILE administration remained unknown. Neither phlebitis nor clinical or laboratory evidence of inflammation or infection was found. Fever was described as side effect in people treated with ILE as component of parenteral nutrition (Kaplan and Whelan, 2012).

Conclusions: This report supports the use of ILE as adjunctive therapy in the treatment of baclofen toxicosis in cats. In circumstances where clinical signs are difficult to control with conventional therapies the use of ILE, which is relatively inexpensive, safe and accessible, appears justified.

Authors contribution: PC, AI and GC took part in the care of the patient and contributed in the preparation of the manuscript. All authors critically revised the manuscript and approved the final version.

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