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Objective—To identify dogs and cats with baclofen toxicosis and characterize the patient population, clinical signs, and outcome.

Design—Retrospective case series.

Animals—140 dogs and 5 cats with baclofen toxicosis.

Procedures—An animal poison control center electronic database was reviewed from November 2004 through April 2010 to identify dogs and cats with baclofen toxicosis. Information on signalment, clinical signs, and amount of baclofen ingested was obtained. Clinical signs were categorized as CNS, gastrointestinal, general malaise, cardiovascular, respiratory, or urogenital. Follow-up communications were performed to determine overall outcome.

Results—Dogs had a median age of 0.67 years (range, 0.1 to 15 years) and cats of 1 year (range, 0.7 to 16 years). Of 145 patients, 133 (92%) developed clinical signs of baclofen toxicosis. A total of 259 signs fell within defined categories: CNS (121/259 [46.7%]), gastrointestinal (69/259 [26.6%]), general malaise (27/259 [10.4%]), cardiovascular (23/259 [8.9%]), respiratory (14/259 [5.4%]), and urogenital (5/259 [1.9%]). For 68 dogs with known survival status, survival rate was 83.8% (57/68); of these dogs, the amount of baclofen ingested was known for 53 (46 survivors and 7 nonsurvivors). Amount of baclofen ingested was significantly lower in survivor dogs (median, 4.2 mg/kg [1.91 mg/lb]; range, 0.61 to 61 mg/kg [0.28 to 27.7 mg/lb]), compared with nonsurvivor dogs (median, 14 mg/kg [6.4 mg/lb]; range, 2.3 to 62.3 mg/kg [1.04 to 23.77 mg/lb]). Of 5 cats, 2 survived, 1 died, and 2 had unknown outcomes.

Conclusions and Clinical Relevance—Clinical signs of baclofen toxicosis occurred in most patients, with the CNS being the system most commonly affected. (J Am Vet Med Assoc 2012;241:1059–1064)

Baclofen (γ-aminobutyric acid), a centrally acting skeletal muscle relaxant, is often used in people with multiple sclerosis, cerebral palsy, and spinal disorders (including spinal cord injury and other diseases) to prevent spasticity. The exact mechanism of action of baclofen is unknown but it is believed to act by depressing monosynaptic and polysynaptic afferent reflex activity in the spinal cord. Baclofen is a derivative of the inhibitory neurotransmitter GABA and inhibits substance P, thereby reducing myocardial epinephrine and norepinephrine. Baclofen also stimulates GABA receptors located on presynaptic nerve terminals that inhibit release of neurotransmitters such as glutamate, aspartate, and substance P. Further stimulation of GABA receptors results in hyperpolarization and increased inhibitory tone.

In human medicine, baclofen is often given orally or intracereally via a surgically placed pump. When given orally, baclofen is rapidly and completely absorbed from the gastrointestinal tract, reaches a peak plasma concentration within 2 to 3 hours, and has a plasma half-life of 2 to 6 hours. With intrathecal administration, baclofen is administered into the CSF, allowing for rapid effect. For both routes, baclofen is eliminated unchanged predominantly via the kidneys (approx 70% to 85%), whereas the remainder is metabolized by the liver to an inactive product, β-(p-chlorophenyl)-γ-hydroxybutyric acid. In humans, baclofen has a mean elimination half-life of 3 to 4 hours.

Clinical signs of baclofen overdose in humans include coma, flaccidity, respiratory depression, hypotension, bradycardia, and tachycardia. Clinical signs can develop rapidly or be delayed and may last for several days. In a retrospective study of 19 humans with baclofen overdose, doses > 200 mg were more likely to result in delirium, coma, and seizures and required longer hospitalization time. Even with therapeutic dosing, the most common adverse events reported in humans include sedation, drowsiness, dizziness, ataxia, and respiratory and cardiac depression.

In veterinary medicine, the use of baclofen in dogs is considered extralabel use. Baclofen has been used to...
reduce urethral resistance in the treatment of urinary retention (1 to 2 mg/kg [0.45 to 0.91 mg/lb], PO, q 8 h); however, it is infrequently used because of its narrow margin of safety in veterinary medicine. Additionally, it has also been shown to transiently inhibit lower esophageal sphincter relaxation in dogs and theoretically is of benefit in the treatment of gastroesophageal reflux disease.\(^6\) The use of baclofen is generally not recommended in cats.\(^12\)

Currently, there is no established toxic dose of baclofen in dogs or cats, although fatalities in dogs have been reported with ingestions as low as 8 to 16 mg/kg (3.6 to 7.3 mg/lb).\(^1\) Doses as low as 1.3 mg/kg (0.6 mg/lb) have caused clinical signs of vomiting, depression, and vocalization in dogs.\(^1\) The veterinary literature contains only a few documented cases of baclofen toxicosis in dogs. In 1 case report,\(^13\) a dog was evaluated 6 hours after ingestion of baclofen; the estimated ingestion was 4 to 8 mg/kg (1.8 to 3.6 mg/lb), and severe clinical signs were seen including lateral recumbency, stupor, ptosis, miotic pupils, and vocalization. This dog survived following 6 days of hospitalization and supportive care.\(^13\) In another case report, a dog ingesting approximately 21 to 52 mg/kg (9.5 to 23.6 mg/lb) of baclofen survived after the initiation of hemodialysis and hemoperfusion; this was the first reported case documenting toxicosis in a dog on the basis of measured serum baclofen concentrations.\(^14\) Finally, another dog was successfully treated with hemodialysis and mechanical ventilation after ingesting 20 mg/kg (9.1 mg/lb) of baclofen.\(^15\) Given the wide range of toxic doses in the previous case reports, all ingestions of baclofen should be considered clinically important until further studies are done that specifically describe the pharmacokinetics and metabolism of baclofen in dogs and cats. To the authors’ knowledge, no large veterinary studies evaluating baclofen toxicosis in dogs or cats exist. Therefore, the goals of the study reported here were to evaluate the patient population (including breed, sex, age, and body weight), clinical signs observed, medical treatments performed, and overall prognosis associated with baclofen toxicosis in small animal veterinary medicine.

**Materials and Methods**

**Criteria for case selection**—The electronic computer database of Pet Poison Helpline,\(^4\) an animal poison control center based in Minneapolis, was searched to identify dogs and cats with baclofen exposure from November 2004 through April 2010. Inclusion criteria included a witnessed or suspected ingestion of a baclofen product. Exclusion criteria included poor product identification, multiple drug (ie, polypharmacy) ingestions, and incomplete medical records. During this period, 168 cases were identified, of which 23 were excluded. A total of 145 cases (140 dogs and 5 cats) were included in the final analysis. In all 145 cases, the active ingredient ingested was considered to be baclofen on the basis of witnessed or suspected exposure to missing medication or chewed medication containers.

**Procedures**—The electronic medical records were reviewed, and signalment (including age, breed, sex, and body weight), historical data, clinical signs, amount of baclofen ingested, veterinarian evaluation (characterized as either inpatient or outpatient care), treatment, and outcome were recorded in a commercially available spreadsheet program.\(^5\) Clinical signs were grouped into associated organ systems to characterize the data: CNS (CNS depression, coma, ataxia, blindness, vocalization, tremors, seizures, dysphoria, agitation, miosis, and nystagmus); gastrointestinal (anorexia, vomiting, hypersalivation, diarrhea, and regurgitation); general malaise (drowsiness or lethargy and hypothermia); cardiovascular (tachycardia, bradycardia, hypotension, hypertension, pallor, and arrhythmias); respiratory (tachypnea, dyspnea, decreased respiratory rate, apnea, and pulmonary edema); and urogenital (urinary incontinence and urinary retention).

Follow-up with pet owners or hospital staff was performed by telephone interviews and facsimile correspondence at the time of the study design to obtain additional information, including development of clinical signs, medical treatment, and overall outcome. For animals that were not hospitalized or for whom veterinary medical treatment was not sought, follow-up information from the pet owner was obtained to verify outcome. For patients for whom veterinary attention was sought, follow-up information with both the pet owner and the veterinarian was obtained to verify outcome. Three attempts were made to contact each pet owner or veterinarian before the case was considered closed. Patients were considered survivors if they recovered. Patients were designated as nonsurvivors if they died or were euthanized while treated at a veterinary clinic or if they were reported on follow-up with the pet owner to have died at home.

**Statistical analysis**—For parametric data, the mean and SD were reported; for nonparametric data, median values and ranges were reported. A Wilcoxon-Mann-Whitney test was performed to determine significant differences between survivors and nonsurvivors in regard to age, body weight, amount of baclofen ingested, and number of clinical signs. All analyses were performed with a commercially available statistical software package.\(^6\) Values of P < 0.05 were considered significant.

**Results**

A total of 145 cases (140 dogs; 5 cats) were included in this study. Despite numerous attempts at follow-up, 74 cases were excluded from the survivability data because follow-up information was judged to be incomplete. Information on dogs and cats was separated for evaluation of survivability data. Information on dogs and cats was combined for the comparison of median amount of baclofen ingested between patients with clinical signs of toxicosis and clinically normal patients.

**Call initiation**—In 65 of 145 (44.8%) cases, the initial phone call to the animal poison control was made by the animal’s owner. The remaining calls (80/145 [55.2%]) were initiated by a veterinary professional (eg, veterinarian or veterinary technician). Calls originated from 39 states as well as Ontario and Quebec, Canada. No states were overrepresented.
Population distribution—Of 145 animals, 81 (55.9%) were male, 62 (42.7%) were female, and 2 (1.4%) did not have a sex recorded at the time of the call. The median age for dogs (n = 134; age unknown for 6 dogs) was 0.67 years (range, 0.1 to 15 years), and the median age for cats (5) was 1 year (range, 0.7 to 16 years). The median age of dogs and cats overall (n = 139) was 0.8 years (range, 0.1 to 16 years). The median body weight of dogs (n = 139; body weight unknown for 1 dog) was 6 kg (13.2 lb) with a range of 0.9 to 52.3 kg (1.98 to 115.06 lb). Body weights of 1.8 kg (3.96 lb) and 6.4 kg (14.08 lb) were known for 2 of 5 cats.

Thirty-four specific dog breeds, including mixed breeds, were represented. Mixed-breed dogs (29/140 [20.7%]), Labrador Retrievers (12/140 [8.6%]), and Chihuahuas (12/140 [8.6%]) comprised most of the breeds exposed. Other represented breeds included Yorkshire Terriers (n = 11/140 [7.9%]), Schnauzers (7/140 [5%]), Miniature Poodles (5/140 [3.6%]), and German Shepherd Dogs (5/140 [3.6%]). The remaining breeds had < 5 representatives. For cats, 1 domestic mixed-breed cat and 4 domestic shorthair cats were represented.

Survival status was known for 68 dogs (57 survivors and 11 nonsurvivors); information on 66 dogs (55 survivors and 11 nonsurvivors) included age and body weight. No significant (P = 0.97) difference was found in age between dogs that survived (median, 0.67 years; range, 0.15 to 13 years; n = 55) and dogs that did not survive (median, 0.75 years; range, 0.23 to 15 years; 11). Also, no significant (P = 0.87) difference was found in body weight between dogs that survived (median, 6.8 kg [14.96 lb]; range, 1.22 to 37.7 kg [2.68 to 82.94 lb]; n = 55) and dogs that did not survive (median, 8.64 kg [19 lb]; range, 1.36 to 52.3 kg [2.99 to 115.1 lb]; 11).

Of 68 dogs with known survival status, information on 53 dogs (46 survivors and 7 nonsurvivors) included the amount of baclofen ingested, which was significantly associated with survival outcome. The median amount of baclofen ingested was significantly (P = 0.036) lower for dogs that survived (median, 4.2 mg/kg [1.91 mg/lb]; range, 0.61 to 61 mg/kg [0.28 to 27.7 mg/lb]; n = 46), compared with that of dogs that did not survive (median, 14 mg/kg [6.68 mg/lb]; range, 2.3 to 52.3 mg/kg [1.04 to 23.77 mg/lb]; 7).

Of the 145 cases, the amount of baclofen ingested was known for 90 dogs and cats. A significant (P = 0.018) difference was found between the amount of baclofen ingested in dogs and cats that had clinical signs of baclofen toxicosis (median dose, 7.1 mg/kg [3.2 mg/lb]; range, 0.7 to 61 mg/kg [0.32 to 27.7 mg/lb]; n = 83) versus those that were clinically normal (median dose, 2.2 mg/kg [1 mg/lb]; range, 1 to 11 mg/kg [0.45 to 5 mg/lb]; 7). The lowest dose of baclofen ingested at which clinical signs developed was 0.7 mg/kg; this occurred in a 12-year-old dog with CNS depression, dyspnea, and hypothermia. The lowest dose at which death was reported was 2.3 mg/kg (1 mg/lb); this occurred in a 9-month-old dog that was laterally recumbent, was vomiting, and had seizures. This particular dog did not receive medical attention until several hours after ingestion.

Clinical signs—A total of 133 of 145 (92%) patients developed clinical signs of baclofen toxicosis. No clinical signs were reported for 12 of 145 (8.3%) cases (Table 1). For the 133 patients with clinical signs, 239 signs of toxicity fell within the defined organ system categories as follows: CNS (121/239 [46.7%]), gastrointestinal tract (69/259 [26.6%]), general malaise (27/259 [10.4%]), cardiovascular system (23/259 [8.9%]), respiratory system (14/259 [5.4%]), and urogenital system (5/259 [1.9%]).

For dogs, no significant (P = 0.88) difference was found in the observed number of clinical signs between survivors and nonsurvivors. The median number of clinical signs reported for survivors was 3 (range, 0 to 7), whereas for nonsurvivors, the median number of clinical signs observed was 2 (range, 1 to 5). In the 57 dogs that survived, the following clinical signs were reported on the basis of system categories: CNS (48/57 [84.2%]), gastrointestinal tract (37/57 [64.9%]), respiratory system (9/57 [15.8%]), cardiovascular system (9/57 [15.8%]), and generalized malaise (7/57 [12.3%]). In the 11 dogs that did not survive, 11 had CNS signs, 3 had gastrointestinal tract signs, 2 had cardiovascular system signs, and 1 had respiratory system signs.

A known amount of baclofen ingested was reported for only 2 of 5 cats (1.7 mg/kg [0.77 mg/lb] and 14.7 mg/kg [6.68 mg/lb]). Because of the limited number of affected cats, no correlation can be made between the amount of baclofen ingested and clinical signs. However, clinical signs observed in these 5 cats included ataxia (3/5), CNS depression (2/5), agitation (2/5), vomiting (2/5), hypertension (1/5), bradycardia (1/5), vocalization (1/5), miosis (1/5), drowsiness and lethargy (1/5), and diarrhea (1/5).

Treatment—Information about specific treatments received during hospitalization was not readily available from the records, nor could it be accurately ob-

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>No. (%) of affected animals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNS depression</strong></td>
<td>57 (42.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>48 (36.1)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>44 (33.1)</td>
</tr>
<tr>
<td>Vocalization</td>
<td>40 (30.1)</td>
</tr>
<tr>
<td>Coma</td>
<td>33 (24.8)</td>
</tr>
<tr>
<td>Drowsiness or lethargy</td>
<td>27 (20.3)</td>
</tr>
<tr>
<td>Hypersalivation</td>
<td>26 (19.8)</td>
</tr>
<tr>
<td>Agitation</td>
<td>20 (15.0)</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>10 (7.5)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>9 (6.8)</td>
</tr>
<tr>
<td>Tremors</td>
<td>9 (6.8)</td>
</tr>
<tr>
<td>Miosis</td>
<td>9 (6.8)</td>
</tr>
<tr>
<td>Seizures</td>
<td>8 (6.0)</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>6 (4.6)</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>6 (4.5)</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>5 (3.8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (3.8)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Hypernatremia</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Blindness</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

Table 1—Summary of specific clinical signs of baclofen toxicosis in dogs (n = 128) and cats (5) in descending order.
tained from the owners or hospital facility at the time of the follow-up call. As a result, specific treatments were not fully evaluated. Five treatment protocols incorporated ILE, an emerging form of treatment for intoxications due to fat-soluble agents. In each of these cases, clinicians reported a positive response to treatment evidenced by an increase patient awareness and activity very shortly after ILE. Of the 3 dogs treated by ILE for which outcome was known, 2 survived. Of 145 dogs and cats, 21 (14.5%) were treated with cyproheptadine, a serotonin antagonist, in the treatment regimen. Of the 11 cyproheptadine-treated dogs where outcome was known, 8 survived. Two animals required the use of positive pressure ventilation, and both survived. For the 39 cases where information regarding hospitalization and outcome was available, 34 (87.2%) animals were hospitalized, 3 (7.7%) were managed at home, and 2 (5.1%) were treated on an outpatient basis.

**Outcome**—The overall survival rate associated with baclofen toxicosis in dogs was 57 of 68 (83.8%). Eleven of 68 (16.2%) animals were nonsurvivors. Five of the nonsurvivors were euthanized because of the severity of their disease. Of the nonsurvivors, 2 died during hospitalization and 4 died at home. Of the 5 cats, 2 were known survivors, 1 died, and the remaining 2 had unknown outcomes, despite multiple attempts at follow-up. The known nonsurvivor ingested a baclofen dose of 14.7 mg/kg (6.68 mg/lb) and died 2 hours after exposure and within 20 minutes after evaluation at the veterinary hospital. Clinical signs in this cat included ataxia, tachypnea, and mydriasis. The 2 cats that were survivors were hospitalized, administered IV fluid therapy, and given a single dose of activated charcoal.

**Discussion**

The prevalent use of baclofen in human medicine poses an increased risk of inadvertent drug exposure in pets. This is of particular concern for pet owners with multiple sclerosis or spinal cord trauma and injuries, as they are the most likely population to have been prescribed this agent, making the drug prominent and available within their household.

The patient population in the present study was predominantly dogs, which compares with the overall incidence of calls seen at Pet Poison Helpline. Published reports on animal calls to Pet Poison Helpline over a period of 1 year are reported to be approximately 88% dog exposures, 10% cat exposures, and 2% other species. Although neither sex was overrepresented, the age of animals affected in the present study was notable. The range of ages for dogs was 0.1 to 15 years; however, median age was 0.67 years. The young median age may correlate to the more inquisitive nature of younger animals, in comparison with their adult or geriatric counterparts. Pet education advocating adequate crate and house proofing as part of preventative care is warranted at routine puppy and kitten visits.

Baclofen appears to have a narrow margin of safety in veterinary species, and clinical signs can develop quickly following ingestion. Wismer previously reported an onset of clinical signs ranging from 15 minutes to 7 hours from the initial time of ingestion. In the present study, the time from baclofen ingestion was not recorded, and therefore the onset of clinical signs could not be specifically evaluated. However, > 90% of veterinary patients developed clinical signs, with the CNS being the most predominant system affected. With baclofen toxicity, the severity of CNS signs can be substantial, as animals often are evaluated for vocalization, dysphoria, lateral recumbency, or coma. Clinically, dogs poisoned by baclofen may need to undergo positive pressure ventilation as a result of severe obtundation, respiratory depression, and respiratory arrest or hypventilation. This suggests the potency and serious implications of baclofen toxicosis, particularly in those animals that go untreated.

One of the limitations of this retrospective study was that severity scoring of clinical signs was not evaluated. That said, in the authors' experience, baclofen toxicosis typically includes more severe CNS signs, compared with other medications (eg, nonbenzodiazepine sleep aid medications and opioid toxicosis). As baclofen toxicosis resulted in clinical signs in 92% of patients, with almost 60% of these including CNS signs or generalized malaise, hospitalization is often necessary. In the present study, patients typically developed multiple clinical signs; 259 clinical signs were reported in 133 patients. For example, an animal that is comatose will be unlikely to have only 1 clinical sign in 1 body system. Instead, severely affected patients will often have respiratory compromise (eg, hypoventilation), cardiovascular compromise (eg, bradycardiac), and general malaise. Ideally, future studies on baclofen toxicosis may benefit from creating a severity scoring system that more objectively evaluates the patients’ clinical signs.

Chodorowski et al did not find a significant relationship in humans between the amount of baclofen ingested and the clinical outcome reported. However, in the present retrospective study, the amount ingested directly correlated with both outcome and the development of clinical signs. The median amount of baclofen ingested by survivors was 4.2 mg/kg (compared with 14 mg/kg in nonsurvivors), and there was a similar range in toxicosis (up to a maximum of 61 mg/kg in survivors, compared with 52.3 mg/kg in nonsurvivors). Although the amount of baclofen ingested was significantly associated with outcome in the present study, it should not be used solely as a predictor of outcome; rather, it may help guide the treating veterinarian as a prognostic marker. For example, although death occurred in a dog that ingested a dose of 2.3 mg/kg, a dog ingesting 61 mg/kg survived. However, it is important to note that the dog that died was not evaluated until several hours after ingestion. This emphasizes the importance of early treatment for the poisoned patient. One dog in the present study developed clinical signs consistent with toxicosis (CNS depression, dyspnea, and hyperthermia) at a dose of 0.7 mg/kg, demonstrating the narrow margin of safety of baclofen for veterinary patients.

Because of limitations of the study design and lack of complete follow-up for all patients, it is difficult to ascertain why some animals that ingested higher amounts of baclofen survived while others, ingesting lower amounts, did not. Potential reasons for this may include...
include time between exposure and hospitalization, status of patient at the time of ingestion (concurrent disease processes), and the clinician’s understanding and prognosis of the intoxication, which could influence time to onset of decontamination and medical care. In addition, nonsurvivors that had ingested a lower amount than survivors may have been euthanized because of their severe neurologic status or because of financial limitations. Given time and potentially more aggressive treatment options (eg, ILE, cyproheptadine, and positive pressure ventilation), these patients may have had a different outcome.

Treatment recommendations for baclofen toxicosis should be focused on rapid and aggressive decontamination, along with intensive and supportive treatment. For decontamination, emesis induction should be performed only with recent ingestion (typically < 20 to 30 minutes) in clinically normal patients. Emesis induction should not be performed in clinically affected patients because of the risk of potential aspiration of gastric contents. With massive ingestions, the use of sedation, intubation to protect the airway, and gastric lavage may be necessary; this should be followed with 1 dose of activated charcoal with a cathartic. Because baclofen does not undergo enterohepatic circulation, repeated doses of activated charcoal are not necessary and should not be administered.4,5

The use of IV fluid therapy is imperative in the baclofen-poisoned patient. Because these patients are often too obtunded to allow for safe oral intake of food or water, IV fluid therapy is necessary to prevent dehydration, treat hypotension, and aid in enhanced elimination of baclofen.4,5 Additional treatments should include supportive care such as cardiac and blood pressure monitoring. The use of pulse oximetry, end-tidal carbon dioxide monitoring, and blood gas analysis is necessary to evaluate the patient’s oxygenation and ventilation status because hypercapnia and secondary hypoxemia may result. Often, ventilatory support in the form of positive pressure ventilation may be necessary as the result of the severity of respiratory depression. Although only 2 (1.3%) dogs in the present study required the use of positive pressure ventilation, this may be the result of the lack of availability or resources in veterinary medicine.

General treatment for baclofen intoxication includes management of bradyarrhythmias (typically with atropine), heat support for hyperthermia, and oxygen therapy.4,5 Tremors, seizures, and dysphoria should be treated with diazepam at the lowest effective dose to reduce risk of further sedation. Refractory seizures may require administration of propofol or general anesthesia. Baclofen has been known to cause substantial agitation during drug withdrawal19,20; therefore, the use of acepromazine, diazepam, or midazolam may be necessary as an anxiolytic. Attempted reversal with the opioid antagonist, naloxone, can be considered but is often of little clinical benefit.21 In addition, the use of cyproheptadine hydrochloride, a serotonin antagonist, may be given orally or rectally as needed to reduce vocalization or disorientation.4,5 Although the exact mechanism of action of cyproheptadine as a treatment for baclofen toxicosis is unknown, studies22,23 have shown that both 5-HT and baclofen modulate the same potassium channels and have a functional relationship in the CNS. In humans with intrathecal baclofen withdrawal syndrome, the use of cyproheptadine has proven effective.24 Baclofen withdrawal syndrome is thought to be a form of serotoninergic syndrome caused by downregulation of GABA receptors, leading to excess of serotonin or an acute serotonin syndrome. A serotonin antagonist such as cyproheptadine can therefore be effective in baclofen withdrawal syndrome.24 Finally, hemodialysis and hemoperfusion may shorten the elimination half-life of baclofen and reduce hospitalization time,4,5,15 although access to these procedures is limited in veterinary medicine.

Although there is no specific antidote for baclofen toxicosis, ILE, a relatively new experimental treatment for fat-soluble drugs, should be considered.6,3 In human medicine, ILE has been used as an antidote for toxicosis associated with accidental IV administration of local anesthetics (eg, bupivacaine), verapamil, cyclic antidepressants, and propranolol.12 The first published case reports on ILE in humans appeared in 2006 and, as a result of its success, its use has steadily grown in popularity in human hospitals.26 In veterinary medicine, ILE has been recommended for fat-soluble toxicants such as macrocyclic lactones (eg, ivermectin, moxidectin, and milbemycin) and baclofen.16,17,18 In the present retrospective study, the number of cases that were treated by ILE as an antidote for baclofen intoxication was low (n = 5), likely because ILE as a treatment was not well recognized in veterinary medicine until recently. Regardless, every patient that was treated by ILE had a rapid and positive improvement in mentation.

The exact mechanism of action of ILE on fat-soluble drugs is currently unknown, but several hypotheses exist. It has been proposed to act by a lipid sink mechanism, as a fatty acid source for myocardial energy, or by directly increasing the cardiac myocyte calcium concentration. According to the lipid sink proposal, the creation of a lipid partition (lipid sink) within the intravascular space allows for preferential sequestration of lipophilic drugs into the newly formed compartment.4,5,17,27,28 Intravenous lipid emulsion administration may also modify energy sources to the heart. The heart uses fatty acids for myocardial ATP production, so ILE provides energy in the form of lipid to the myocytes.17,28 Finally, some toxicants may impair fatty acid transport into the cardiac mitochondria,27 so ILE may aid in restoring myocardial function by restoring intracellular calcium concentrations, thereby acting as a direct inotrope.22,23

The use of cyproheptadine and ILE resulted in lower survival rates (72.7% [8/11] treated dogs for which the outcome was known) and 66.7% [2/3] treated dogs for which the outcome was known, respectively), compared with the group mean (83.8%). These percentages should be interpreted judiciously, however, because the number of patients treated with cyproheptadine and ILE was very small, compared with the overall study population size. Statistical evaluation of outcome was not performed for these 2 treatment modalities because of lack of power. However, the lower survival rates may be a manifestation of the severity of clinical
signs. Clinically, patients with more severe signs may have been treated with cyproheptadine or ILE as part of more aggressive treatment modalities. Further studies to evaluate the benefit of each of these treatments are warranted.

There were few cats represented in the present study (n = 5); only 3 had complete follow-up, with 2 survivors and 1 nonsurvivor. To the best of the authors' knowledge, this is the first report of baclofen toxicity in cats. Unfortunately, because of the lack of statistical power (n = 5), little information could be obtained to provide strong evidence or conclusions. We suspect that when given appropriate and immediate medical treatment, cats would respond in a similar manner to dogs. Further studies involving a higher number of cases and thorough follow-up with cats need to be conducted.

Because of the limitations of the retrospective nature of the present study, uniform data collection from one case to another could not be performed, nor could the effect of treatment on outcome be evaluated. Nevertheless, given that 92% of baclofen poisonings result in the development of clinical signs, aggressive decontamination, treatment, and supportive care are warranted. Intravenous administration of lipid emulsion as an antidote for this fat-soluble drug should be considered as a novel treatment in severely affected dogs and cats. Future studies specifically evaluating the effects of individual treatments are needed.

References


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c. Microsoft Excel, Microsoft Corp, Redmond, Wash.