EQUINE

Oleander, a flowering evergreen shrub of the Apocynaceae (ie, dogbane) family, is commonly found in the southern and western United States, South America, and regions of Europe, Africa, and Asia. Yellow oleander (Thevetia peruviana) is commonly found in South Asia and South America, whereas the white-, pink-, and red-flowering varieties of oleander (Nerium oleander) are commonly found in areas of Africa and Europe near the Mediterranean Sea.1 Oleander has been traditionally used as an abortifacient, insecticide, molluscicide, rodenticide, and antibacterial agent and for the treatment of ringworm, heart failure, malaria, and indigestion.1–3 Results of other studies4–8 suggest oleander may be useful as a chemotherapeutic agent. However, in humans and other animals, oleander has toxic effects that are attributable to cardenolides, including the cardiac glycosides oleandrin and nerine. The toxic effects of these agents are cumulative, and all parts (fresh or dried) of the plant are toxic; amounts of cardenolides are higher in oleander seeds than they are in any other part of the plant.1,3,9–11 Among Nerium varieties, red- and pink-flowering plants may have higher amounts of cardenolides than white-flowering plants.1,3 Toxic effects of oleander may vary for different flowering varieties, quantities, and parts of a plant consumed and may be affected by health status and comorbidities of an animal.1

Cardiac glycosides of oleander likely cause damage via inactivation of Na+, K+-ATPases in plasma membranes of cardiac myocytes.1,12 Inhibition of Na+, K+-ATPases results in increased sodium concentrations intracellularly and potassium concentrations extracellularly. High intracellular sodium concentrations secondarily inhibit activity of sodium-calcium channels, resulting in an increased rate of influx of calcium ions

Oleander toxicosis in equids: 30 cases (1995–2010)

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Objective—To determine clinical, laboratory analysis, and necropsy findings for equids with oleander toxicosis and to identify factors associated with outcome.

Design—Retrospective case series.

Animals—30 equids.

Procedures—Medical records of equids with detectable concentrations of oleandrin in serum, plasma, urine, or gastrointestinal fluid samples and equids that had not received cardiac glycoside drugs but had detectable concentrations of digoxin in serum were identified via a medical records database search. Descriptive statistics were calculated for medical history, physical examination, laboratory analysis, and necropsy variables. Logistic regression analysis was used to identify physical examination and laboratory analysis factors significantly associated with outcome.

Results—3 of 30 (10.0%) equids died before or immediately after arrival at the hospital. Of the other 27 equids, 23 (85.2%) had gastrointestinal tract abnormalities, azotemia was detected for 19 (70.4%), and a cardiac arrhythmia was ausculted for 18 (66.7%). Mortality rate for all equids was 50.0%; mortality rate for hospitalized equids was 44.4%. The most common cause of death was cardiac dysfunction. Odds of survival to discharge from the hospital were lower for equids with cardiac arrhythmias versus those without arrhythmias and decreased with increasing Hct and serum glucose concentrations. Odds of survival increased with increasing serum chloride concentration and duration of hospitalization.

Conclusions and Clinical Relevance—Equids with oleander toxicosis frequently had simultaneous gastrointestinal tract, cardiac, and renal problems. Oleander intoxication should be a differential diagnosis for equids with colic in geographic areas where oleander is found, especially when azotemia or cardiac arrhythmias are detected concurrently. (J Am Vet Med Assoc 2013;242:540–549)

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<td>GI</td>
<td>Gastrointestinal</td>
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<td>HR</td>
<td>Heart rate</td>
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<td>RR</td>
<td>Respiratory rate</td>
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and release of intracellular calcium from the sarcoplasmic reticulum.\textsuperscript{3–9,12,13} Cardenolides may also inhibit efflux of calcium from cells, leading to further increases in calcium concentrations in cells.\textsuperscript{2} High intracellular concentrations of calcium in myocardial cells raise the resting membrane potential and cause an increased rate of spontaneous cell depolarization; such high intracellular calcium concentrations initially cause a positive inotropic effect, followed by development of abnormalities in electrical conductivity of the myocardium, arrhythmias, and loss of myocardial contractility.\textsuperscript{1,13} Glycosides may also directly alter ATPase-dependent transport processes in renal tubules.\textsuperscript{11} Saponins and triterpenoids in oleander may directly damage GI tract mucosa.\textsuperscript{9} Ischemic damage secondary to reduced cardiac output may cause lesions in any organ system, including kidneys and the GI tract.

Oleander toxicosis has been detected in humans and other animals, including sheep, goats, cattle, camels, monkeys, mice, and equids.\textsuperscript{3,9–11,13–17} Clinical signs of oleander toxicosis include cardiac arrhythmias (including brady- and tachyarrhythmias), GI tract signs, and general malaise. Renal and hepatic toxic effects of oleander are rarely detected in humans, but renal failure is commonly detected in animals of other species.\textsuperscript{1,13} Neurologic abnormalities can develop in humans and other animals after ingestion of oleander.\textsuperscript{3,10}

Other authors have investigated oleander toxicosis in cattle, sheep, goats, and camels.\textsuperscript{9,11,13,13} To the authors’ knowledge, oleander toxicosis in equids has been reported in only 2 case reports.\textsuperscript{10,14} The purpose of the study reported here was to determine clinical, laboratory analysis, and necropsy findings for equids with oleander toxicosis and to identify factors associated with survival of animals to discharge from the hospital. To the authors’ knowledge, no other studies have been conducted in which factors associated with survival of animals with oleander toxicosis were identified. The hypothesis was that GI tract, cardiac, and renal signs of oleander intoxication in equids would be similar to such signs in animals of other species and that detection of cardiac and renal signs would be negative prognostic indicators.

Materials and Methods

Case selection—The medical records of the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California–Davis were searched to identify equids examined from January 1, 1995, through July 15, 2010, that had detectable concentrations of oleandrin in serum, plasma, urine, or GI tract fluid samples, and equids examined during that time that had not received cardiac glycoside drugs but had detectable concentrations of digoxin in serum samples. Equids with positive results for digoxin were included because oleandrin may have cross-reactivity with antibodies in digoxin assays, even in assays with digoxin-selective monoclonal chemiluminescent antibodies, given the structural similarity between those molecules; an animal with oleandrin in serum may have positive results when tested via a digoxin assay.\textsuperscript{18} A diagnosis of oleander intoxication was made for diagnostic findings, and such animals were included in the study reported here. Oleandrin concentrations in various samples were quantified via a liquid chromatography–mass spectrometry method.\textsuperscript{19} Serum digoxin concentrations were determined with a paramagnetic particle chemiluminescent immunoassay.\textsuperscript{4}

Medical records review—Information obtained from medical records included age, sex, breed, medical history, date of referral to the hospital, clinical signs at the time of hospital admission, clinico-pathologic data, treatments administered, progression of clinical signs during hospitalization, outcome, duration of hospitalization, and necropsy findings. In addition, data regarding housing and changes in environment, caretakers’ perceived likelihood of oleander ingestion by animals, estimated duration of clinical signs, number of veterinary examinations of each animal for the problem prior to hospital referral, treatments administered before referral, and reason for referral were recorded. Clinico-pathologic data included results of CBCs, serum biochemical analyses, cytologic examination of peritoneal fluid obtained via abdominocentesis, and cardiac troponin I, oleandrin, and digoxin assays. Results of ultrasonography, radiography, and echocardiography were also obtained. Surgical reports were reviewed for animals that underwent ventral midline celiotomy. Long-term follow-up information for equids that survived to discharge from the hospital was obtained via telephone interviews of owners conducted from 3 months to 14 years after discharge of animals from the hospital.

Statistical analysis—Descriptive statistics were calculated for data regarding histories and results of physical examinations, diagnostic tests, and necropsies of equids. Range, mean, and SD values were determined for age; weight; duration of clinical signs; number of times equids were examined by referring veterinarians prior to hospital referral; rectal temperature, HR, and RR at the time of hospital admission; duration and cost of hospitalization; and results of CBCs and serum biochemical analyses. Logistic regression analysis was used to determine age, sex, breed, historical, physical examination, and clinico-pathologic variables significantly associated with survival of equids. Assumptions of linearity for log odds of survival were verified for all continuous variables.\textsuperscript{b}

Results

Via the medical records search, 172 equids were identified in which oleander intoxication was suspected. Animals were excluded from the study if a diagnosis of oleander intoxication could not be confirmed via detection of oleandrin in serum, plasma, urine, or GI tract fluid samples or via detection of digoxin in serum samples of animals that had not received cardiac glycoside drugs. Thirty equids were included in the study. Of the 30 equids, 7 (23.3%) were Arabians; 6 (20.0%) were Quarter Horses; 5 (16.7%) were ponies, American Miniature Horses, or miniature donkeys; 3 (10.0%) were American Paint Horses; 2 (6.7%) were warmbloods; and 1 (3.3%) each were Morgan, Icelandic, Standardbred, Tennessee Walker, Friesian, Lipizzan, and mixed breeds. Thirteen (43.3%) equids were females, 11 (36.7%) were geldings, and 6 (20.0%) were sexually intact males. Ages ranged from 0.25 to
14 years (mean ± SD, 6.5 ± 5.1 years); age was not recorded for 1 adult equid. Five (16.7%) equids were < 1 year old, 9 (30.0%) equids were 1 to 5 years old, 6 (20.0%) equids were 6 to 10 years old, and 9 (30.0%) equids were > 10 years old. Age and sex distributions of equids in the present study were representative of the population of equids evaluated at the teaching hospital during the study period. Breed distributions were not representative of the hospitalized population of equids because Arabians and pony and miniature breeds were overrepresented in this study. Weights were determined for 23 of the 30 equids. Weights ranged from 68 to 570 kg (149.6 to 1,254.0 lb; mean ± SD weight, 346.1 ± 146.5 kg [761.4 ± 322.3 lb]). Of the 23 equids for which weights were determined, 9 (39.1%) were < 300 kg (660 lb), 11 (47.8%) were 300 to 500 kg (660 to 1,100 lb), and 3 (13.0%) were > 500 kg (< 1,100 lb).

Most (26/30 [86.7%]) equids were from facilities where no other animals had signs of oleander intoxication. Four of the 30 (13.3%) equids were from facilities where other equids had signs of oleander intoxication on the basis of histories provided by caretakers; however, causes of clinical signs in those other animals were not determined.

Equids included in this study frequently had recent changes in environment or housing. Seven of the 30 (23.3%) equids had recently been moved to a different facility or turnout area. Three (10%) equids had recently escaped from their stall or pasture, 3 (10%) lived in an area where landscaping maintenance of oleander plants had recently been performed, and 1 (3.3%) had recently been moved to an area near oleander plants. Owners or caretakers for 20 of the 30 (66.7%) equids were aware that there was oleander on the property, the owner or caretaker for 1 (3.3%) equid did not believe there was oleander on the property, and owner or caretaker knowledge of oleander on the property was not recorded for 9 (30%) equids. Owners or caretakers for 14 (46.7%) equids believed it was impossible that their animal had ingested oleander, ingestion was known to have occurred for 2 (6.7%) equids, owners or caretakers were uncertain of the possibility of oleander ingestion for 12 (40.0%) equids, and owner or caretaker knowledge of oleander ingestion was not recorded for 2 (6.7%) equids. Equids were referred to the hospital during all seasons. Ten (33.3%) equids were referred in the winter (December through February), 8 (26.7%) in the fall (September through November), 7 (23.3%) in the spring (March through May), and 5 (16.7%) in the summer (June through August). Twelve (40.0%) equids were referred to the hospital from 1995 through 2000, 6 (20.0%) were referred from 2001 through 2005, and 12 (40.0%) were referred from 2006 through 2010.

Reasons for referral of equids to the hospital included colic (12/30 [40%]), lethargy or anorexia (6/30 [20%]), diarrhea (4/30 [13.3%]), tachycardia (3/30 [10%]), witnessed ingestion of oleander (2/30 [6.7%]), azotemia (1/30 [3.3%]), fever (1/30 [3.3%]), and ataxia (1/30 [3.3%]). Thus, most (22/30 [73.3%]) equids of this study were referred for GI tract-associated complaints. The estimated duration of clinical signs prior to referral ranged from 0 (ie, referral immediately after clinical signs were detected) to 120 hours (mean ± SD, 43.2 ± 34.9 hours). Prior to hospital referral, 4 (13.3%) equids had clinical signs for < 12 hours, 8 (26.7%) equids had clinical signs for ≥ 12 to < 24 hours, 8 (26.7%) equids had clinical signs for ≥ 24 to < 48 hours, 6 (20.0%) equids had clinical signs for ≥ 48 to < 72 hours, and 4 (13.3%) equids had clinical signs for ≥ 72 hours. Most (25/30 [83.3%]) equids were evaluated by a veterinarian prior to referral. The number of times veterinarians examined animals prior to referral ranged from 0 to 4 (mean ± SD, 1.3). Sixteen (53.3%) equids were examined by a veterinarian 1 time prior to referral, 6 (20.0%) equids were examined 2 times prior to referral, 2 (6.7%) equids were examined 3 times before referral, and 1 (3.3%) equid was examined 4 times prior to referral. Three (10.0%) equids were not examined by a referring veterinarian prior to referral. Information regarding veterinary examinations of animals prior to referral was not recorded in medical records for 2 (6.7%) equids. Treatments administered to equids prior to referral included the following: NSAID (19/30 [63.3%]); bismuth subsalicylate, mineral oil, magnesium sulfate, or electrolyte solutions via nasogastric tube (14/30 [46.7%]); antimicrobial drugs (4/30 [13.3%]); activated charcoal administered orally (3/30 [10%]); fluids administered IV (3/30 [10%]); antiparasitic drugs (1/30 [3.3%]); and drugs intended to prevent spasm of smooth muscles of the GI tract (1/30 [3.3%]).

Of the 30 equids referred to the hospital in this study, 3 (10.0%) were dead at the time of arrival to the hospital or died immediately after arrival despite resuscitative treatments. Therefore, 27 equids were admitted to the hospital. Twenty-three (85.2%) of these animals had GI tract signs (determined on the basis of clinical signs, results of nasogastric intubation, amount and consistency of feces, and results of abdominal ultrasonography and radiography). Gastrointestinal tract signs included colic (4/27 [14.8%]), diarrhea or loose consistency of feces (6/27 [22.2%]), gastric reflux (6/27 [22.2%]), signs of GI tract hypermotility (1/27 [3.7%]), abdominal distention (2/27 [7.4%]), signs of ileus or GI tract hypomotility (19/27 [70.4%]), anorexia (1/27 [3.7%]), and detection of small intestinal mural thickening via ultrasonography (2/27 [7.4%]). Of the 27 equids that were admitted to the hospital, 16 (59.3%) had signs of decreased tissue perfusion, including a weak peripheral pulse strength and a capillary refill time > 2.5 seconds. Eighteen of those 27 (66.7%) equids had mucous membranes that were described in the medical records as hyperemic, injected, or toxic. Eighteen of 27 (66.7%) equids had cardiac arrhythmias that were detected via auscultation. Electrocardiography was performed for 21 (77.8%) animals, 13 (61.9%) of which had an arrhythmia; therefore, at least 48.1% of equids admitted to the hospital had an arrhythmia that was confirmed via ECG. All arrhythmias were of ventricular origin and included ventricular premature contractions (2/13) and ventricular tachycardia (11/13). Some equids with ventricular arrhythmias also had other arrhythmias, including third-degree atrioventricular block (1/13), bundle branch block (2/13), and ventricular fibrillation (2/13). Of the 27 equids admitted to the hospital, 6 (22.2%) had a cardiac murmurs,
1 (3.7%) had muffled heart sounds, and 1 (3.7%) had jugular pulses. Other abnormalities detected during initial evaluations included icterus (2/27 [7.4%]) and nasal discharge (4/27 [14.8%]). One (3.7%) equid each had a cough, edema of forelimb and thoracic region soft tissues, pleural transudate, forelimb lameness, increased strength of digital pulses, enlarged thyroid gland, profuse sweating, and neurologic abnormalities including obtundation and ataxia without a meningeal response.

Rectal temperatures of the 27 equids admitted to the hospital at the time of admission ranged from 36.9°C (101°F) to 39.4°C (103°F); mean ± SD, 38.0°C ± 0.7°C (100.7°F ± 1.3°F). Of those 27 equids, 9 (33.3%) had a rectal temperature ≥38.3°C (101.0°F); 4 [44.4%] of these animals had a rectal temperature >38.9°C (102°F) and 18 (66.7%) had a rectal temperature <38.3°C (101°F).

Heart rates of the 27 equids at the time of hospital admission ranged from 24 to 160 beats/min (mean ± SD, 92.7 ± 10.8 beats/min). Eight (29.6%) had an RR of ≤ 20 breaths/min, 6 (22.2%) had an RR from 21 to 30 breaths/min, 6 (22.2%) had an RR from 31 to 40 breaths/min, and 6 (22.2%) had an RR > 40 breaths/min.

Results of CBCs and serum biochemical analyses indicated various clinicopathologic abnormalities in equids (Tables 1 and 2). Of the 24 equids for which serum creatinine concentrations were available, 19 (79.2%) were azotemic; therefore, at least 70.4% of the 27 horses admitted to the hospital were azotemic. Other commonly detected clinicopathologic abnormalities included an elevated serum glucose concentration (21/24 [87.5%] in horses for which results were available; 77.8% of the 27 horses admitted to the hospital) or Hct (16/27 [59.3%]) higher than the reference range. Other diagnostic tests included cytologic examination of peritoneal fluid samples obtained via abdominocentesis, ultrasonography, radiography, urinalysis, and de-
termination of serum cardiac troponin I concentrations. Peritoneal fluid samples were obtained via abdominocentesis for 18 of 30 (60.0%) equids referred to the hospital. Of those 18 peritoneal fluid samples, 8 (44.4%) were classified as transudate, 7 (38.9%) were classified as modified transudate, and 3 (16.7%) were classified as exudate. Total protein in these peritoneal fluid samples ranged from 0.8 to 5.5 g/dL (mean ± SD, 2.9 ± 1.5 g/dL; reference range, < 2.5 g/dL). Total nucleated cell count in these peritoneal fluid samples ranged from 480 to 26,000 cells/µL (mean ± SD, 4,849 ± 6,019 cells/µL; reference range, < 5,000 cells/µL). Serum cardiac troponin I concentrations were determined for 7 equids. Serum cardiac troponin I concentrations ranged from 0 to 30.63 ng/mL (reference range, 0.01 to 0.07 ng/mL); values for 5 of those animals were higher than the reference range, and values for 2 were within the reference range. No relationship was detected between a serum cardiac troponin I concentration higher than the reference range and detection of cardiac arrhythmias in the equids of this study. Ultrasonography, radiography, and urinalysis were not performed for a high enough number of equids of this study for determination of conclusions regarding results of those tests.

Most commonly, equids of this study had azotemia with GI tract and cardiac abnormalities (16/30 [53.3%]). Smaller percentages of equids had GI tract and cardiac signs only (3/30 [10.0%]), GI tract and renal signs only (2/30 [6.7%]), or cardiac and renal signs only (1/30 [3.3%]).

Complications that developed in equids after admission to the hospital included increased amount of peritoneal fluid (9/27 [33.3%]), acute renal failure (5/27 [18.5%]), colic requiring surgical treatment (5/27 [18.5%]), pleural and pericardial effusion (5/27 [18.5%]), pneumonia (4/27 [14.8%]), gastritis (4/27 [14.8%]), gastric reflux (4/27 [14.8%]), cellulitis (1/27 [3.7%]), pulmonary edema (1/27 [3.7%]), pleural effusion (1/27 [3.7%]), and pericardial effusion (1/27 [3.7%]). One (3.7%) animal each had selenium deficiency or enterocolitis caused by Clostridium difficile, Clostridium perfringens, or Salmonella typhimurium.

Treatments administered to equids during hospitalization included IV administration of crystalloid fluids (27/27 [100.0%]), colloidal fluids (ie, blood, plasma, or hetastarch; 11/27 [40.7%]), hypertonic saline (7.2% NaCl) solution (5/27 [18.5%]), parenteral nutrition (4/27 [14.8%]), solutions containing sodium bicarbonate (3/27 [11.1%]), and solutions containing dimethyl sulfoxide (2/27 [7.4%]). Antiarrhythmic drugs were also administered, including lidocaine (14/27 [51.9%]), magnesium sulfate (2/27 [7.4%]), procainamide (1/27 [3.7%]), and phenytoin (1/27 [3.7%]). Anti-inflammatory drugs were administered including flunixin meglumine (17/27 [63.0%]) and dexamethasone (2/27 [7.4%]). Antimicrobial drugs were administered to 13 (48.1%) equids and included penicillin G procaine, penicillin G potassium, gentamicin, ceftiofur, metronidazole, and vancomycin. Treatments administered via nasogastric tube included activated charcoal (10/27 [37.0%]), di-tri-octahedral smectite (2/27 [7.4%]), and mineral oil (4/27 [14.8%]). Other medications were administered to 10 (37.0%) equids for the treatment of GI tract problems, including omeprazole, succarylactate, misoprostol, and ranitidine. Additional treatments included the following: ventral midline celiotomy (5/27 [18.5%]); vitamins B (5/27 [18.5%]) and E (2/27 [7.4%]); drugs intended to increase GI tract motility (ie, prokinetics) including cisapride, erythromycin, metoclopramide, and neostigmine (4/27 [14.8%]); diuretics including furosemide (4/27 [14.8%]) and mannitol (1/27 [3.7%]); dopamine (3/27 [11.1%]); application of ice to distal aspects of limbs (3/27 [11.1%]); polyvinyl B (2/27 [7.4%]); catheterization of the urinary bladder (2/27 [7.4%]); placement of a thoracic cavity drain (1/27 [3.7%]); nasal administration of oxygen (1/27 [3.7%]); aminoacaproic acid (1/27 [3.7%]); low–molecular weight heparin (1/27 [3.7%]); and antiparasitic drugs (1/27 [3.7%]).

Of the 5 equids that underwent ventral midline celiotomy, 2 survived to discharge from the hospital. One of those animals had a large colon torsion, and the other had entrapment of the small intestine in a rent of the mesentery of the proximal portion of the small intestine. Of the 3 equids that underwent ventral midline celiotomy and did not survive to hospital discharge, 1 died during anesthetic induction because of cardiac arrest, 1 died during anesthetic recovery after surgery (no GI tract abnormalities were found in this animal during surgery), and 1 was euthanized during anesthetic recovery because of an inability to stand attributable to hind limb dysfunction (this animal had cecal and small intestinal distention and bruising of the jejunum that were detected during surgery).

For the 30 equids referred to the hospital, duration of hospitalization ranged from 0 to 16 days (mean ± SD, 4.3 ± 4.6 days). Of those 30 equids, 9 (30.0%) were hospitalized for < 12 hours (including the 3 animals that died before or immediately after arrival at the hospital), 4 (13.3%) were hospitalized for 12 to 24 hours, 7 (23.3%) were hospitalized for 24 hours to 5 days, and 10 (33.3%) were hospitalized for > 5 days. Of the 10 equids hospitalized for > 5 days, 7 were hospitalized for 5 to 10 days and 3 were hospitalized for > 10 days. The costs of diagnostic tests, treatments, and hospitalization ranged from $0 to $11,003.70 (mean ± SD, $3,238.40 ± $3,013.90).

Of 27 equids in this study that were hospitalized, 15 (55.6%) survived to discharge from the hospital. Therefore, the mortality rate for the 27 equids admitted to the hospital was 44.4%, and the mortality rate for all 30 equids was 50.0%. None of the equids were euthanized for financial reasons; all animals that did not survive died or were euthanized because of medical conditions. Five of the 15 equids that died in this study died of cardiovascular failure; 1 horse each had the following clinical signs prior to death: ventricular fibrillation, ventricular tachycardia refractory to lidocaine treatment with subsequent cardiac arrest, cardiac arrest before antiarrhythmic treatment could be administered, cardiovascular collapse (HR at the
time of collapse, 150 beats/min), and cardiac arrest after anesthetic induction. Three animals died before or immediately after arrival at the hospital. One equid died during anesthetic recovery. Six animals were euthanized. One equid each was euthanized for the following medical reasons: inability to stand after surgery, poor response to treatment of acute renal failure, poor response to treatment of ventricular tachycardia with pericardial effusion and reduced cardiac contractility, progressively worsening neurologic signs, poor response to treatment of acute renal failure with ventricular tachycardia and seizures, and neurologic signs with uncontrollable signs of pain.

A necropsy was performed for each of the 15 equids that died. Cardiac lesions identified during necropsies included the following: myocardial necrosis (12/15); epicardial, myocardial, or endocardial hemorrhage (11/15); myocardial thrombosis (3/15); and left ventricular dilation (1/15). All 15 of these animals had myocardial necrosis or some type of cardiac hemorrhage, and 9 of 15 had both of these cardiac abnormalities. Six of the 15 equids that died had effusion in a body cavity, including pleural (2/15), peritoneal (3/15), and pericardial effusion (5/15). Other abnormalities commonly found during necropsies included the following: hepatocellular necrosis and hepatitis (6/15); GI tract hemorrhage and edema (6/15); hemorrhage of other abdominal organs including liver, pancreas, or adrenal glands (6/15); pulmonary congestion (6/15); enteritis or enterocolitis (8/15); and renal abnormalities including necrosis, infarction, tubular mineralization, or congestion (8/15). Other abnormalities found less frequently included gastric inflammation or ulceration (4/15); hepatic capsular fibrosis (3/15); biliary stasis or hyperplasia (3/15); adrenal gland necrosis (4/15), and splenic hyperplasia and hemosiderosis (3/15).

A diagnosis of oleander toxicosis was most often made for equids of the present study via assay of serum, plasma, urine, or GI tract fluid samples obtained while animals were alive (although results for some animals were not available until after they had died). A diagnosis of oleander toxicosis was made for 17 of 30 (56.7%) equids in this study only on the basis of assay results from samples obtained after the animals had died. A diagnosis was made for 4 (13.3%) equids on the basis of assay results from various samples obtained before and after the animals had died. Twenty-seven (90.0%) equids had positive results for oleandrin in serum, plasma, urine, or GI tract fluid samples; 2 (7.4%) of these animals also had positive results for digoxin.
in serum samples. Three of the 30 (10.0%) animals had negative results for oleandrin in various samples and had positive results for digoxin in serum samples (these animals had not received cardiac glycoside drugs). Correlation analysis for amounts of oleandrin and digoxin in samples could not be performed because results of some oleandrin assays indicated a range of values rather than 1 value, and digoxin concentrations were infrequently measured for animals in the study.

Factors that were determined to be positive prognostic indicators for survival to discharge from the hospital included the absence of cardiac arrhythmias, decreased Hct and serum glucose and log-transformed creatinine concentrations, and increased serum chloride concentration and hospital duration. Detection of cardiac arrhythmias (via auscultation or ECG) was associated with decreased odds of survival (OR, 0.062; \( P = 0.009; 95\% \ CI, 0.00 \text{ to } 0.53 \)). An increased Hct value was associated with decreased odds of survival (OR, 0.94 [for each 1% increase in Hct]; \( P = 0.033; 95\% \ CI, 0.87 \text{ to } 1.0 \)). An increased serum glucose concentration was associated with decreased odds of survival (OR, 0.72 [for every 25 mg/dL increase in serum glucose concentration]; \( P = 0.011; 95\% \ CI, 0.97 \text{ to } 1.0 \)). An increased serum chloride concentration was associated with increased odds of survival (OR, 1.2 [for each 1 mmol/L increase in serum chloride concentration]; \( P = 0.012; 95\% \ CI, 1.0 \text{ to } 1.4 \)). Longer duration of hospitalization was associated with increased odds of survival (OR, 3.20 [for each additional day of hospitalization]; \( P < 0.001; 95\% \ CI, 1.5 \text{ to } 11 \)). A significant inverse relationship was identified between log-transformed serum creatinine concentration values and survival of equids (\( P = 0.038 \)); this finding indicated that for each 1 mg/dL increase in the log-transformed serum creatinine concentration value, the OR for survival of equids decreased by a value of 0.33 (OR, 0.65; 95% CI, –0.38 to 1.0). Serum chloride and glucose concentrations, Hct values, and hospital duration for equids that survived to discharge from the hospital and those that did not survive were summarized (Figures 1–4). No other variables (signalment, historical data, or other physical examination or clinicopathologic findings) were significantly associated with survival of equids.

Follow-up information was obtained from owners of 11 of the 15 equids that survived to discharge from the hospital. Of these 11 animals, only 1 had long-term complications potentially attributable to oleander intoxication. The owner of this equid (which had abnormalities in cardiac function during hospitalization) presumed that the animal had persistently reduced cardiac function; therefore, that animal was only used for light riding exercise. This presumed decrease in cardiac function was not confirmed when the animal was rechecked 6 months later.
via follow-up echocardiography or detection of clinical signs of reduced cardiac function (eg, decreased level of athletic performance or exercise intolerance). The other 10 equids reportedly did not have long-term complications attributable to oleander intoxication. Two of the 11 equids for which follow-up information was obtained had died or had been euthanized for reasons unrelated to oleander intoxication by the time follow-up information was obtained.

Discussion

Results of the present study supported the hypothesis that clinical findings for equids with oleander toxicity were similar to those for animals of other species with that problem. Most commonly, equids with oleander intoxication had azotemia with GI tract and cardiac abnormalities. Smaller percentages of equids of this study had GI tract and cardiac signs only, GI tract and renal signs only, or cardiac and renal signs only. Most (22/30 [73.3%]) equids of this study were referred to the hospital for GI tract signs (ie colic, anorexia, or diarrhea). Therefore, oleander intoxication should be considered as a differential diagnosis for equids with colic or other GI tract problems in geographic areas where oleander is commonly found, especially when animals concurrently have azotemia or cardiac arrhythmia.

The overrepresentation of Arabians, ponies, and miniature breeds in this study may not be clinically important because there is no medical reason that such equids would be more susceptible to oleander toxicosis versus other breeds. Equids of small breeds, such as ponies and miniature breeds, may be more susceptible to oleander intoxication than equids of larger breeds because smaller amounts of oleander would cause toxic effects in a small animal versus a large animal. However, no significant association was detected between body weight and survival for equids of this study.

Survival of equids in this study was not significantly associated with signalment variables, season, duration of clinical signs prior to referral, or number of times animals were evaluated by a veterinarian prior to referral. Although owners or caretakers of most (66.7%) equids knew that there were oleander plants on their property, almost half (46.7%) of the owners or caretakers did not believe their animal could have ingested oleander. This finding suggested that caretakers may not have believed that the presence of oleander plants on the property was relevant to the medical histories of animals; therefore, it may be important for veterinarians to explicitly question caretakers regarding potential toxic plant exposures of animals. Medical history findings such as recent changes in housing or ownership, performance of landscape maintenance, or escape of animals from housing may prompt veterinarians to include exposure to toxic substances in a differential diagnosis list.

Survival of equids in this study was positively associated with a long duration of hospitalization and was negatively associated with a high Hct, high serum glucose concentration, high log-transformed serum creatinine concentration, low serum chloride concentration, and detection of cardiac arrhythmias. The serum biochemical analysis abnormalities that were associated with nonsurvival of equids may have been attributable to severe disease. Horses with GI tract disease that have a high Hct and hyperglycemia have reduced odds of survival. Hypochloremia is often caused by loss of chloride via the GI tract or kidneys and is associated with a poor prognosis for horses with persistent azotemia. Uncompensated loss of chloride in horses with renal or GI tract disease may indicate severe disease; such horses may have decreased odds of survival.

Azotemia was not significantly associated with nonsurvival of equids in this study; therefore, the hypothesis that equids with signs of renal disease would have a worse prognosis than equids without such signs was not supported. However, high log-transformed serum creatinine concentration values were significantly associated with nonsurvival of equids. High non–log-transformed serum creatinine concentrations may have been significantly associated with nonsurvival of equids if more animals had been included, which would have increased the statistical power of the study. A circulating creatinine concentration > 2.0 mg/dL at the time of hospital admission is a negative prognostic indicator for horses with acute diarrhea. Horses with primary GI tract disease and azotemia that persist for > 72 hours are 3 times as likely to die as horses with primary GI tract disease that do not have persistent azotemia. These findings may be clinically relevant for equids with oleander intoxication because such animals frequently have GI tract abnormalities, are hypovolemic, and have reduced renal perfusion.

The finding of the present study that cardiac arrhythmias were significantly associated with nonsurvival supported the hypothesis that equids with cardiac abnormalities would have a worse prognosis than equids without such signs; this finding is clinically important because cardiac arrhythmias can be readily diagnosed via physical examination and ECG. Arrhythmias of equids in this study were of ventricular origin, many arrhythmias worsened during hospitalization, and all equids that did not survive had cardiac lesions; these findings supported another finding of this study that equids with arrhythmias had a poor outcome. These results suggested that cardiac monitoring should be performed for animals with oleander intoxication. Testing for circulating cardiac troponin I concentrations may be indicated for animals in which oleander intoxication is suspected because an increase in circulating cardiac troponin I concentration may precede development of ventricular arrhythmias. Results of this study may indicate circulating cardiac troponin I concentrations peak shortly after systemic administration of endotoxin and precede development of ventricular arrhythmias in horses. Although antiarrhythmic medications, most commonly lidocaine, were administered to many equids of the present study, such treatment was not always successful. Further research may be warranted regarding antiarrhythmic and cardioprotective treatments for equids.

The finding of the present study that a long duration of hospitalization was associated with increased odds of survival may be surprising; however, patients that survive typically have a longer duration of hospi-
talization versus those that do not survive. In addition, long-term outcomes for patients that survived were good; only 1 equid had long-term negative effects attributed to oleander intoxication, and those effects were not confirmed via cardiac evaluations. No other equids that survived in this study had long-term complications attributable to oleander intoxication.

Although the time between ingestion of oleander and development of clinical signs or initiation of treatments could not be determined for equids of this study; the finding that animals with a long duration of hospitalization had increased odds of survival suggested that treatment may reduce the severity of clinical signs and improve outcomes. Despite treatment, a large amount of oleander may cause rapid development of severe, fatal disease, as has been determined for sheep. Authors of a report concluded that ingestion of large amounts of oleander may reduce morbidity and mortality rates of animals because ingestion of such amounts causes vomiting. However, because equids cannot vomit, it is likely that ingestion of large amounts of oleander would result in severe disease in such animals. Ingestion of an amount of oleander weighing as little as 0.003% of body weight (as few as 10 to 20 oleander leaves) may be lethal to horses. This suggests that equids can easily ingest lethal amounts of oleander. Treatment of animals with oleander intoxication may not alter the course of disease unless such treatment is started immediately after ingestion of the plants. However, equids of this study that were admitted to the hospital had a lower mortality rate than that for all equids (treated and untreated), suggesting that treatment in the hospital was beneficial for equids with oleander intoxication. The 3 equids that died before or immediately after arrival at the hospital may have had better outcomes if they had been hospitalized earlier after ingestion of oleander.

The mean ± SD cost of hospitalization and treatment for equids with oleander intoxication in the present study ($3,238.40 ± $3,013.90) was higher than the mean ± SD cost of hospitalization and treatment for equids with colic treated medically in this same hospital from 2005 to 2011 ($1,811.10 ± $637.37). However, the cost for equids with oleander intoxication was similar to that for equids with renal failure ($3,541.93 ± $1,986.50) and was less than that for equids with colic treated via 1 surgical procedure ($6,951.12 ± $2,227.65) in this same hospital during the same time period.

Limitations of the present study included those attributable to a retrospective study design (eg, incomplete medical records and differences among animals regarding diagnostic tests conducted and treatment received). Other limitations of this study included an inability to determine the time between ingestion of oleander and development of clinical signs and initiation of treatment, an inability to determine the amount of oleander ingested, an inability to determine a value (rather than a range of values) for oleandrin concentrations in all samples assayed, and an inability to definitively distinguish equids that may have ingested oleander from those that may have ingested other digitalis-containing plants (eg, foxglove), particularly in equids for which a diagnosis was determined via detection of digoxin alone. Additionally, the number, type, and time of collection (after oleander ingestion) of samples assayed for detection of oleandrin or digoxin varied among equids. With increasing time after ingestion of a toxin, positive results for detection of the toxin may be less likely for assays of gastric fluid samples and may be more likely for assays of fecal and urine samples because those are the typical routes of toxin excretion. Equids with a diagnosis of oleander intoxication determined via positive results for digoxin alone may have had positive results for oleandrin if urine samples or other GI tract fluid samples had been assayed.

Detection of oleandrin in samples obtained from equids in a clinical setting may be difficult, even when multiple samples are analyzed. Therefore, oleander intoxication may not have been diagnosed for some affected equids evaluated at the hospital during the study period and such equids may have been excluded from this study, decreasing the statistical power. Despite this difficulty in determining a diagnosis of oleander intoxication, a diagnosis was determined for most (17/30 [56.7%]) equids of this study via testing of samples obtained while animals were alive (although results were not available for some of these animals until after they had died). Therefore, collection of samples for oleandrin testing while equids are alive may be clinically valuable for animals with clinical signs consistent with cardenolide intoxication.

Statistical analyses were not conducted regarding treatments of equids for oleander intoxication in this study; therefore, no conclusions were determined regarding such treatments. However, early treatment of systemic abnormalities and oral administration of activated charcoal are recommended to reduce the risk of development of clinical signs attributable to oleander intoxication in animals. Determination of a diagnosis of oleander intoxication on the basis of clinical signs may be necessary because results of assays for detection of toxins may not be immediately available. Animals with recent changes in housing or environment may be at higher risk for oleander intoxication versus animals without such changes, and such information in a medical history may increase the suspicion that animals have been exposed to environmental toxins. Equids that ingest oleander may develop renal dysfunction, fatal cardiac arrhythmias, and colic; such animals should be monitored closely, and treatments should be selected on the basis of clinical signs. The mortality rate for equids with oleander intoxication in this study was high (50.0%). The mortality rate of such animals may be reduced with rapid initiation of treatment after ingestion of oleander.

References
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