Infusion of a lipid emulsion to treat lidocaine intoxication in a cat

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Case Description—A 5-year-old castrated male domestic shorthair cat was examined because of presumptive lidocaine intoxication. Thirty minutes earlier, the cat had received an SC injection of approximately 140 mg of lidocaine hydrochloride (20 mg/kg [9.1 mg/lb]) to facilitate closure of a wound on the left pelvic limb.

Clinical Findings—Initial physical examination revealed severe lethargy and respiratory distress; erratic, poor-quality pulses with severe hypotension; and pulmonary edema.

Treatment and Outcome—Initial supportive treatment included administration of oxygen and IV administration of lactated Ringer’s solution. Additional treatment with a 20% lipid emulsion (1.5 mL/kg [0.68 mL/lb], IV) delivered over a 30-minute period resulted in dramatic improvement in cardiovascular and behavioral variables. No adverse effects from lipid emulsion administration were detected on routine hematologic evaluation, thoracic radiography, or computed tomography.

Clinical Relevance—IV administration of a lipid emulsion was used in the treatment of lidocaine intoxication in a cat. Rapid infusion of a lipid emulsion may be a therapeutic option for veterinary patients with toxicosis attributable to local anesthetics or other lipid-soluble drugs. (J Am Vet Med Assoc 2010;237:1455–1458)

A 5-year-old 6.8-kg (15.0-lb) castrated male domestic shorthair cat was examined at the Small Animal Emergency Service of the University of Illinois Veterinary Teaching Hospital because of severe lethargy and respiratory distress. Thirty minutes before admission, the cat had received an SC injection of approximately 140 mg of lidocaine hydrochloride (20 mg/kg [9.1 mg/lb]) to aid debridement and repair of a 5-cm circumferential wound on the lateral aspect of the proximal portion of the left pelvic limb.

Physical examination revealed that the cat was severely lethargic, unresponsive to stimuli, and unable to support itself in sternal recumbency. Rectal temperature was 38.3°C (101.0°F). The cat had an irregular pulse rate that varied from 60 to 200 beats/min; a rapid, gasping, open-mouth breathing pattern; dark red mucous membranes; and a prolonged capillary refill time of >3 seconds. Pulse quality was poor. Thoracic auscultation revealed an irregular heart rhythm consistent with the pulse findings and bilateral crackles throughout all lung fields. An attempt was made to measure systolic blood pressure via Doppler oscillometry, but it was unsuccessful. Venous blood samples were collected for a CBC, serum biochemical analysis, and venous blood gas analysis. An attempt was made to obtain an arterial sample for blood gas analysis, but it was unsuccessful.

Results of the CBC revealed leukopenia (3.87 × 10^3 cells/µL; reference range, 5.50 × 10^3 to 19.50 × 10^3 cells/µL) and lymphopenia (0.66 × 10^3 cells/µL; reference range, 1.70 × 10^3 to 7.00 × 10^3 cells/µL). Results of the serum biochemical analysis revealed hypokalemia (3.54 mmol/L; reference range, 3.7 to 4.91 mmol/L), hypocalcemia (1.10 mmol/L; reference range, 1.17 to 1.37 mmol/L), hypernatremia (152.2 mmol/L; reference range, 144 to 152 mmol/L), and hyperchloremia (121.4 mmol/L; reference range, 110.04 to 117.96 mmol/L). Venous blood gas analysis revealed a mild decrease in bicarbonate concentration (16.6 mmol/L; reference range, 17.08 to 24.64 mmol/L); however, pH, partial pressure of oxygen (venous), partial pressure of carbon dioxide (venous), and lactate concentration were all within the respective reference ranges. On the basis of the medical history and clinical signs, a presumptive diagnosis of acute intoxication attributable to a local anesthetic was made.

The cat was admitted to the intensive care unit for treatment. Supportive treatment (administration of oxygen via a facemask) was initiated. Attempts were made to place catheters in a jugular and cephalic vein, but ultimately they were unsuccessful. Thirty minutes after admission (15 minutes after instituting oxygen administration), the cat was less lethargic and able to remain in sternal recumbency without support but remained unable to support its head. Pulse quality had improved. A catheter was placed in a medial saphenous vein. Systolic blood pressure was measured (190 mm Hg). The cat was placed in an oxygen cage (fraction of inspired oxygen, 40%), and lactated Ringer’s solution was administered at a rate of 80 mL/kg/d (36.4 mg/lb/d).

At that time, the cat received an IV infusion of a 20% lipid emulsion* for specific treatment of lidocaine toxicosis. A dose (3 mL/kg [1.4 mL/lb]) delivered over a

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provide systemic analgesia, and to reduce the minimum alveolar concentration of inhalant anesthetics needed for anesthesia.\(^1\)\(^-\)\(^6\) Mepivacaine and bupivacaine are other local anesthetics that have been used in veterinary medicine. Both have a longer duration of action than does lidocaine, with the effects of mepivacaine lasting 90 to 180 minutes and the effects of bupivacaine lasting 240 to 480 minutes.\(^7\)

Similar to other local anesthetics, toxic effects of lidocaine are related to excessive plasma and tissue concentrations. Some of the more serious toxic effects result from effects on the CNS and the cardiovascular system. Clinically, these can be evident as lethargy, unconsciousness, coma, convulsions, seizures, hypotension, bradycardia, and cardiovascular collapse and can result in death.\(^2\) Several of these signs were observed in the cat described here. At admission, the cat was lethargic, and severe hypotension was evident as an inability to obtain an initial blood pressure measurement and difficulty in inserting a catheter in a vein.

The dosages of local anesthetics that cause CNS toxicity are less than the dosages that cause signs of cardiovascular toxicity.\(^3\) The reported plasma concentration of lidocaine in humans at which signs of CNS toxicity are apparent is 5 to 10 µg/mL, whereas plasma concentrations > 25 µg/mL are associated with cardiovascular toxicity.\(^2\) Lidocaine intoxication of the CNS often manifests initially as twitching and weakness of skeletal muscles and progresses to drowsiness and then seizures. In severe cases, CNS depression and coma can follow seizures. There is evidence that the plasma concentration at which CNS toxicity develops may be more a function of the rate of administration and subsequent increase in the plasma concentration, rather than a function of the total amount of drug administered.\(^4\)

Cardiovascular effects of toxic dosages of lidocaine may be evident as refractory hypotension from direct vasodilatory effects on vascular smooth muscle and reduced cardiac output from myocardial depression.\(^2\) Electrocardiographic findings from local anesthetic–induced cardiovascular toxicity include a prolonged PR interval and widening of the QRS complex.\(^2\)

Lidocaine and other local anesthetics generate methemoglobin, which typically comprises < 1% of the total blood hemoglobin content, from oxidation of hemoglobin, thereby potentially reducing the ability of RBCs to carry oxygen. Heinz bodies, which can result in RBC lysis, can also form as a result of oxidative damage to RBCs from toxic concentrations of local anesthetics.\(^7\)

In domestic cats, lidocaine is commonly used to provide local analgesia and anesthesia for routine procedures, such as dental extractions, onychectomy, wound debridment, and epidural anesthesia.\(^7\) Although relatively free of adverse effects when proper dosages are used, excessive or IV administration of lidocaine can result in toxic effects similar to those seen in human patients. These toxic effects can develop as the dosage of lidocaine approaches 6 mg/kg (2.7 mg/lb) in cats. Seizure activity can be elicited in cats via IV administration of lidocaine at a dosage of 11.7 ± 4.6 mg/kg (5.3 ± 2.1 mg/lb).\(^8\) Therefore, it is recommended that the dosage of lidocaine used for local anesthesia in cats should not exceed 3 to 4 µg/kg (1.4 to 1.8 mg/lb).\(^9\) The cat described here received an approximate
dosage of 20 mg/kg. Lidocaine infusions for analgesia or reduction in the minimum alveolar concentration of inhalant anesthetics are not recommended in cats. It is postulated that cats are more susceptible to the toxic effects of amide local anesthetics (such as lidocaine), compared with the susceptibility of other species, because of a reduced ability for glucuronide metabolism of drugs in the liver.

Treatment of intoxication attributable to a local anesthetic has traditionally been limited to palliative care. This includes administration of benzodiazepine drugs to control seizures, fluid administration and dopamine infusions to correct hypotension and hypovolemia, anticholinergic drugs for bradycardia, oxygen insufflation, N-acetylcysteine to treat dyspnea and prevent reperfusion injury, and methylene blue or vitamin C to treat methemoglobinemia. If cardiac arrest occurs, prolonged cardiopulmonary resuscitation may be necessary, particularly for animals with intoxication attributable to long-acting local anesthetics.

Lipid emulsions have been used successfully for the treatment of humans with acute intoxication attributable to local anesthetics. Prompting the Association of Anaesthetists of Great Britain to develop and adopt guidelines that lipid emulsions be immediately available for all patients given potentially cardiotoxic doses of local anesthetic drugs. Lipid emulsions are most commonly used for IV administration to provide nutrients (ie, parenteral nutrition) as well as serving as a delivery vehicle for hydrophobic drugs, such as propofol. The lipid component of these emulsions forms chylomicrons, which aids in their ability to be rapidly and widely distributed.

The exact mechanism of action for lipid emulsions in the treatment of intoxication attributable to local anesthetics is unknown. However, 3 theories have been postulated as to why lipid infusions appear to be clinically beneficial. First, a new pharmacokinetic equilibrium within an expanded plasma lipid base is achieved, which reduces the toxic effects by reducing the free drug concentration. Therapeutically, because of a high binding capacity of these emulsions, lipids are thought to exert an effect on local anesthetics by physically binding and trapping circulating local anesthetic molecules, thus rendering them inactive. It is probable that the high lipid solubility of local anesthetics and the high binding capacity of the lipid emulsions explain their clinical efficacy. Second, because fatty acids can increase calcium concentrations in cardiomyocytes, exogenously delivered lipids may cause an increase in inotropy that overcomes the depressive effects of the intoxication. Third, local anesthetics inhibit carnitine acyltransferase, which is necessary to transport fatty acids across myocardial mitochondrial membranes for oxidative phosphorylation. Bolus administration of a lipid emulsion may overcome the decreased fatty acid transport via mass action or an unknown mechanism. Studies in laboratory animals have confirmed the efficacy of lipid emulsions for countering the cardiovascular effects of toxic doses of local anesthetics.

In addition to treatment of intoxication induced by local anesthetics, lipid infusions have been used as a treatment for various intoxications in humans and domestic animals, including intoxication attributable to cyclic antidepressants, verapamil, β-adrenoceptor blockers, and clonidine.

A lipid emulsion has been used to treat toxoid toxicosis in a puppy. Treatment with a lipid emulsion is not without potential complications. These emulsions can promote bacterial growth, which requires that aseptic procedures be used during administration to prevent contamination and possible sepsis. Intravenous administration of a lipid emulsion may cause immunosuppression through immune-cell dysfunction. Other potential effects include phlebitis, thrombosis, hypertriglyceridemia, and hepatic lipodosis. The dosage of a 20% lipid infusion has varied in human clinical case reports. The dosage used in the cat described here was extrapolated from a single human case report in which the authors reported success with a dosage of 3 mL/kg. In the cat of our case report, dramatic clinical response was achieved with a dosage of 1.5 mL/kg delivered over a 30-minute period, and at least in this cat, administration of an additional 1.5 mL/kg dose was not necessary. After resolution of the condition in the cat reported here, a review of the use of lipid emulsion as a treatment for lidocaine intoxication in humans was published. The authors of that report made a recommendation for administration of a 20% lipid emulsion at a dosage of 1.5 mL/kg at infusion rates of 0.25 to 0.5 mL/kg/min (0.11 to 0.23 mL/lb/min), which could be repeated up to 3 times. On the basis of the findings in the cat described here, this recommendation may also be applicable to veterinary patients.

It is important to mention that although lidocaine was not detected in the second plasma sample obtained from the cat described here, this may not have been a result of the use of the lipid emulsion. The half-life of lidocaine in cats is approximately 1.7 hours, and a lack of lidocaine in the second sample was most likely the result of typical elimination of the drug.

The present case report confirmed the IV administration of a lipid emulsion for treatment of local anesthetic–induced toxicosis in a veterinary patient. The authors recognize the limitations of this report in that it represents only a single cat and that findings were based on subjective assessment of the cat. Further investigation into the use of lipid emulsions for the treatment of toxicosis attributable to local anesthetics is warranted. In this cat, no adverse effects from the lipid infusion were detected. Additionally, rapid infusion of a lipid emulsion may be a treatment option for patients with toxicosis attributable to other lipid-soluble drugs.

References


a. Liposyn II, Hospira Inc, Lake Forest, Ill.