

Focus on Hope

Newsletter for The Hope Center for Advanced Veterinary Medicine

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Diabetic Ketoacidosis

By Angie Gasser, DVM, DACVIM

Diabetic ketoacidosis (DKA) is a complication of unregulated diabetes mellitus (DM) that manifests as marked hyperglycemia, metabolic acidosis, hyperketonemia, electrolyte deficits, and dehydration. The pathophysiology of DKA begins with an insufficient quantity or peripheral activity of insulin, along with the release of glucagon and stress hormones. An increase in lipolysis and free fatty acid oxidation occurs, which leads to ketogenesis. Increased ketone body formation, along with hypoperfusion from dehydration, can lead to significant systemic acidosis. Hyperglycemia and hyperketonemia induce osmotic diuresis at the level of the kidneys. This leads to loss of free water, sodium, potassium, calcium, magnesium, and impaired renal absorption of phosphorous.



Dr. Angie Gasser, DACVIM

Most dogs and cats that present in DKA crisis are middle-aged. Often DKA occurs at the time of initial diagnosis of DM. DKA animals most often present ill, with anorexia, vomiting, lethargy, and dehydration. There may also be a characteristic “fruity” breath from the ketoacidosis. Mild DKA patients (minimally acidemic) that are not ill do not necessarily need to be hospitalized, but need to start insulin therapy and be closely monitored at home.

Fasting hyperglycemia with glucosuria, ketonuria, and metabolic acidosis confirm the diagnosis of DKA. Suspicion of DKA in the face of a small bladder or negative urine ketones should be further evaluated with a serum ketone check. This is performed by combining a drop of serum from the patient with a drop of hydrogen peroxide, and then testing for ketones on the dipstick. Diagnostic testing should include a CBC, chemistry panel, urinalysis, urine culture/sensitivity, blood gas analysis, and imaging (radiographs, abdominal ultrasound) to evaluate for concurrent illness. The majority of patients that present with DKA do have concurrent illness such as pancreatitis, hepatobiliary disease, renal disease, infection (especially urinary tract), heart failure, and insulin antagonistic disorders such as Cushing’s disease and diestrus.

Prior to initiation of treatment, it should be confirmed that the owner is committed to the management of a diabetic pet. Prognosis for a DKA patient is guarded, with about 30% mortality. An ill DKA patient needs intensive care and monitoring (often at least 3-5 days), as this is a life-threatening emergency and takes time for response to medical management.

Total body depletion of potassium is common, even with normal potassium values at presentation. Potassium replacement should be given in the fluids as long as the serum potassium is not above 5 mEq/L (if so then look for a cause such as urethral obstruction, acute renal failure, Addison’s disease, etc). The rate of replacement should not exceed 0.5 mEq/kg/hr. Serum potassium should be monitored closely during hospitalization, especially as insulin therapy is started.

Phosphorous is often normal at presentation, but there is also a risk of total body depletion. Risk of hemolytic anemia and neuromuscular signs occur when the phosphorous is less than 1.5 mg/dL. Phosphorous supplementation should be administered in the fluids (K phos is best with 0.9% NaCl or other calcium-free solutions) and monitored closely during hospitalization.

Magnesium is often low from chronic loss and poor intake. Supplementation (dilute in 0.9% NaCl or D5W) should be given if serum magnesium is less than 1.2 mg/dL or if hypokalemia is

refractory to treatment. Magnesium should be monitored periodically during hospitalization.

Metabolic acidosis can be profound in DKA patients, both from the ketoacidosis and lactic acidosis. Treatment with IV fluids should be initiated to correct the dehydration, as well as with insulin to reverse the ketogenesis. Bicarbonate therapy is rarely needed, and should only be used for life-threatening acidosis (pH < 7.0 or persistent pH < 7.2 despite correction of dehydration). Only one third of the calculated bicarbonate deficit should be given, slowly over two hours, and then the blood gas rechecked.

Insulin treatment should be started once the hypovolemia is corrected and the patient has been rehydrated for 2-8 hours. In cases of severe hypokalemia, insulin therapy should be delayed. A continuous rate infusion (CRI) or intra-muscular (IM) protocol of short-acting, regular insulin should be used at the doctor’s discretion. The blood glucose should be lowered slowly and maintained in the 200-300 mg/dL range.

Insulin should be given regularly unless BG < 100. Dextrose therapy should be used to allow more continuous insulin therapy to assist in reversal of ketogenesis. Electrolytes, PCV, blood gas analysis, hydration, and urine ketones should be monitored most intensively at presentation, then less frequently once response is seen. Nutritional support should be initiated, as needed, once the patient is stable, especially in cats.

Antibiotics, antiemetics, and gastro-protectants should be used as clinically indicated.

The patient should be switched to long-acting insulin once eating, hydrated, and not vomiting. The ketonuria may not always be resolved. Currently the best available starting long-acting insulin for a dog is Humulin-N® (NPH). The best starting long-acting insulin for a cat is Lantus® (Glargine) or PZI (BCP PZI® or ProZinc®). Long-acting insulin therapy is usually started at every 12 hours after meals for both dogs and cats. Some cats can be transient diabetics (Type II), often secondary to concurrent pancreatitis or obesity, and Glargine and dietary management have been shown to aid in the reversal of DM in many cases.

Diet is very important in assistance of diabetic control and a meal every 12 hours prior to insulin is ideal. Dogs should eat a moderate carbohydrate, high fiber diet (protein and fat depend on other disease states), such as Hill’s w/d®, Purina OM®, or Royal Canin Diabetic HF®. A senior or light commercial diet with the addition of fiber supplement could also be used. Approximately 60-75% of cats will be managed more effectively on a low carbohydrate, high protein diet such as Hill’s m/d® or Purina DM®. There are also a number of commercial “all natural” high protein diets for cats available. If there is concurrent hepatic or renal insufficiency, then a lower protein diet may be recommended over a diabetic diet. The remaining percentage of cats will do better on a moderate carbohydrate, high fiber diet like dogs, or their diabetic control will be dietary independent. DM monitoring should include clinical signs and Ketodiastix urine monitoring at home, body weight checks, and BG curves or fructosamine levels on a routine basis. The insulin dose should never be changed unless instructed by a veterinarian. Changing insulin dose based on a “spot check” blood glucose may be less than ideal and can lead to sub optimal insulin dosing. Remember, it takes the body about one week to adjust to a new insulin dose and type, so patience is the key!

Lipid Therapy

By Beth Venit, DVM

The ASPCA Animal Poison Control center has added a new treatment to their arsenal. Intravenous lipid therapy is the newest treatment to be added in their fight against toxicities, and new applications are being discovered as more research is performed. ASPCA may recommend this drug for toxicities from local anesthetics (bupivacaine, lidocaine), calcium channel blockers, Moxidectin, Baclofen, Bromethalin, and Permethrin.

The most commonly used drug for IV lipid therapy is Intralipid, which is the base for drugs such as Propofol, and is used in TPN solutions. It is a 20% lipid solution comprised of soybean oil emulsion, egg phospholipids, and glycerol. It can be obtained from the same companies that supply IV fluids and has a total shelf life of 2 years.

The primary investigator for IV lipid therapy is Dr. Guy Weinberg, a professor of Anesthesiology at the University of Illinois College of Medicine at Chicago. He reported an incident of severe ventricular arrhythmia in a human patient that was most consistent with a bupivacaine toxicity from a local block, but the dose was appropriate. This patient had carnitine deficiency, which was then postulated to lower the threshold for bupivacaine-induced cardiotoxicity. Local anesthetics inhibit the mitochondria enzyme carnitine-acylcarnitine translocase (CAT) and prevent ATP production from fatty acids. This can cause severe systemic toxicity and lead to cardiovascular and neurologic effects: bradycardia, hypotension, ventricular fibrillation, tremors, seizures, respiratory arrest and death. Dr. Weinberg postulated that adding more lipids in a "normal" patient could override the CAT inhibition.

Additional studies confirmed that supplying more fatty acids resolved the toxicity. This led to the theory that IV lipid therapy increases the overall fatty acid pool, which then overrides LA inhibition of the carnitine system. This explains the disproportionate cardiotoxicity relative to neurotoxicity. Cardiac cells prefer lipid energy, neurons prefer carbohydrates. This theory was dubbed the "lipid flux" theory.

A 2010 study in JAVMA presented the case of a 5-year old, 6.8kg MN DSH that received a subcutaneous injection of 140 mg lidocaine (20.6 mg/kg) for debridement and repair of a wound. The toxic dose for cats is 6mg/kg. The cat presented to the ER unresponsive and with dyspnea, bilateral crackles, lethargy, irregular pulses (60-200 bpm), dark red mucous membranes, and poor pulse quality. Initial treatment included oxygen supplementation and IV fluids. The patient was able to lie in sternal recumbency but still not able to lift his head. He then received IV lipid: 1.5mL/kg over 30 min. 15 min post-infusion, the cat was aware of his surroundings and started to groom. The next day, the cat was weaned out of oxygen. No significant methemoglobinemia was detected, no Heinz body formation.

Later studies then suggested that IV lipid may actually work by providing a "lipid sink," a medium within the bloodstream to which lipophilic drugs bind. This essentially removes the toxins from the bloodstream and hastens metabolism and excretion. This discovery creates the possibility that IV lipid therapy may be effective against other lipophilic drugs, such as calcium channel blockers, baclofen, macrocyclic lactones, and moxidectin

Calcium channel blockers act on voltage-gated transmembrane channels in smooth muscle. With this, we can see hypotension, brady- or tachycardia, seizures, and pulmonary edema. A 2007 blinded randomized

placebo-controlled study used 14 male mixed breed dogs. Verapamil given as a CRI (6mg/kg/hr) until the MAP was reduced by 50%. The dose was then titrated to maintain this MAP for 30 minutes. Verapamil CRI was reduced to 2mg/kg/hr for an additional 90 minutes. The dogs were then all treated with atropine, calcium chloride, and 0.9% NaCl. The dogs were then either given 7mL/kg 20% intravenous lipid emulsion or 7mL/kg saline over 30 minutes. Survival rates in the intravenous lipid emulsion group were 100% compared to 14% in the control group.

Baclofen is an antispasmodic that is also used in the treatment for alcohol and cocaine abuse and is an agonist for GABA receptors. It can cause vomiting, weakness, respiratory depression, seizures, and comas. Serious toxicities may require mechanical ventilation for days. An informal case report demonstrates resolution of a serious toxicity after a couple of doses with IV lipid.

Macrocyclic lactones include moxidectin and ivermectin. They bind ion channels in non-mammalian peripheral nerves and usually have a wide safety margin in mammals due to the blood brain barrier. However, as we know, we can still see toxicities in collies and collie-derived breeds or even in non-collies breed with large overdoses, usually through ingestion of the equine formulation or via feces of treated animals. Clinical signs include depression, weakness, recumbency, mydriasis, blindness, ataxia, and coma. The treatment traditionally has been supportive, yet some serious cases require mechanical ventilation. Using standard therapy, recovery can take days to weeks. A report in JVECCS in 2009 detailed a moxidectin toxicity in a 16-week old Jack Russel terrier puppy. The puppy experienced severe neurologic and cardiovascular clinical signs, and by the time treatment was initiated, the puppy was comatose and was placed on a ventilator. Symptomatic therapy was employed and 2 doses of IV lipid therapy were given. The puppy improved over 13 hours and was able to be discharged 2 days after admission.

Permethrin acts on insect nervous system by interfering with sodium channels to disrupt nerve function. Toxicity leads to muscle spasms, paralysis, and death. It is extremely toxic to cats and causes hyperexcitability, depression, vomiting, ataxia, hyperesthesia, muscle fasciculations, generalized tremors, seizures, hyperthermia, and death. Exposure can result from label abuse or even from a cat playing with a recently-treated dog. Signs can start up to 48-72 hours post-exposure and can persist for 2-3 days. The traditional treatment is symptomatic: methocarbamol and diazepam or propofol CRI to control seizures. IV lipid therapy has also been successfully used against this drug, but no formal paper exists at the time of this article.

As of now, no veterinary protocols have been approved for the administration of IV lipid therapy, and we must use the protocols established for humans: 1.5ml/kg 20% lipid bolus, followed by 0.25ml/kg/min infusion until circulation is restored. Do not exceed 10mL/kg for 30 minutes. Rebolus may be necessary if circulatory stability is not attained, but check for lipemia before rebolusing. If lipemic, wait for plasma to clear before rebolus. Lipemia suggests that the lipid therapy is still in circulation; adding more lipid would therefore not be of any benefit. The tonicity of 20% lipid emulsion is 600-900 mOsm/l (TPN = 1000-3000 mOsm/l), allowing for administration through a peripheral catheter, but a central line is preferred. Use aseptic technique when placing catheters.

More research is clearly needed in this new area of veterinary medicine, but expect to find that ASPCA Animal Poison Control will be recommending this drug more frequently as new uses are found.

More information on Dr. Weinberg and his research can be found at: www.lipidrescue.org



Dr. Beth Venit



Dr. Guy Weinberg
Lipid Therapy Investigator

Hospital Security

In the United States, theft from animal hospitals continues to be a growing problem. The combination of potent medications as well as historically lax security measures compared to human hospital or pharmacy facilities provides an opening for criminals looking for an easy target. After-hours hospitals are not the only facilities that are vulnerable. Recent news articles at VeterinaryPracticeNews.com and DVM360.com discuss veterinary robberies perpetrated with handguns in broad daylight as criminals search for money and drugs. At The Hope Center, we had a recent incident with a former employee who possessed intimate knowledge of the facility and our security measures that resulted in a drug theft. Charges have been filed and the person has been arrested, but we hope by sharing our experience that other veterinary hospitals may benefit and avoid becoming a target.

During an overnight shift, a former Hope Center employee entered the hospital under the guise of having her sick pet treated. As the pet was being examined, the person visited with former coworkers and friends. After she excused herself to go speak with an employee in the lab area she began exhibiting odd behavior and the doctor became suspicious about her intentions. The pet was treated and the former employee left, but given that she had been left unaccompanied for a period of time the doctor requested that video footage be reviewed immediately. The video confirmed that the individual had taken items from a storage cabinet where our propofol was kept. Shortly thereafter the individual was found in our parking lot after injecting an unknown quantity of propofol. Paramedics and Police were called to treat and arrest the individual.

The Hope Center has extensive security protocols in place, including magnetic self-locking doors, entry fobs and numerous cameras inside and outside the building. Our scheduled drugs are separated into working stock and back stock and are double locked with restricted employee access as per standard industry requirements. Prior to the above described incident we designed security systems to protect against outside threats. After the incident we realized that former employees, acquaintances, and family members can easily bypass some of our standard security measures and if the staff is not vigilant while visitors are in the facility then potentially disastrous unintended consequences can result. Visitors are now accompanied at all times while in the building (other than in the client waiting areas) and cannot be left alone at any time. We also determined that while propofol and Tramadol are not controlled drugs that they, too, would be locked up and handled in the same manner as our other scheduled drugs. Both have been shown to be a priority for drug-seeking criminals.

Further we invited security experts to walk through the building and examine our strengths and weaknesses. The experts were able to identify some key improvements to our security including repositioning or replacement of night-vision cameras; improved lighting in certain areas; the addition of motion sensor lighting; and panic buttons throughout the hospital and on mobile lanyards for staff to wear while outside walking dogs in the evening hours. Plans are underway to install biometric locks requiring thumbprint identification which will also allow for dual credentialed entryways with a 4-digit access code.

The Hope Center had a system in place which we felt was above average and adequately secured us from outside threats, but we were still exposed to threats from individuals who had earned our trust and sought to exploit it. Once we recognized those dangers, we moved quickly to educate our staff and review our technology and policies. If you'd like to learn more about the steps we've taken to secure our facility, please contact us at 703-281-5121.

Coming Up...

News and Announcements

New Intern Class

We welcome Drs. Erin Baxter and Michelle Larsen as our 2011-2012 veterinary intern class. They will rotate through each department in The Hope Center over the next 12 months. The intern program at The Hope Center has been highly successful with over half of our alumni moving on to residencies and internships in specialty fields.

From our 2010-2011 intern class, Dr. Lesia Denysyk has been accepted into an Oncology Residency and Dr. Courtney Mason will be joining The Hope Center as an emergency clinician.

Dr. Slade Leaving Internal Medicine

Dr. Dennis Slade will be leaving The Hope Center in August to be closer to family in New York. Dr. Slade has been with the hospital since 2009 and been a great asset to our team. We wish him and his family the best of luck.

We are pleased to welcome Dr. Amy Cordner to the Internal Medicine department. Dr. Cordner is a board-certified internist and will begin seeing patients this Fall.

Upcoming Events

September

[Fall Specialist Symposium](#)

The Hope Center welcomes the local veterinary community to join us for our 2011 Fall Specialist Symposium on September 25th. The event will be worth 4 hours of RACE approved Continuing Education credit.

[National Capital Cat Show](#)

The East Coast's Premier CFA Cat Show, where up to 450 cats will compete in Championship, Premiership, Kittens and Household Pet classes.

October

[Fairfax Pets On Wheels](#)

16th Annual Paws for a Cause 3K Walk - On October 2, 2011 at 12:00 noon, bring your friends, family and pets for this wonderful 3K walk through the shady streets of Fairfax.

[HART Homecoming](#)

Walk for the Animals - Sunday, October 2nd will be a wonderful opportunity for animal lovers to gather and help raise awareness for a great cause. Enjoy a great afternoon at Bull Run Regional Park with contests, delicious food, vendors, and lots of adorable critters.

In Upcoming Issues...

- Bartonella
- Vasopressors
- Cardiac Biomarkers

Have an article idea or request? Email your idea to Contact@HopeCenter.com