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HOW I TREAT ELECTROLYTE DISTURBANCES IN DIABETIC KETOACIDOSIS

Nishi Dhupa, BVM, DACVIM, DACVECC
College of Veterinary Medicine
Cornell University, Ithaca, NY

INTRODUCTION
Diabetic ketoacidosis (DKA) results from an absolute or relative insulin deficiency in conjunction with glucagon and stress hormone excess. It is crucial to identify underlying disease factors contributing to stress in these patients. Stress factors include changes in environment, dehydration and concomitant disease. Commonly associated diseases include renal disease, urinary tract and other infection, and pancreatitis; in cats, hepatic lipidosis is also commonly seen. DKA is characterized by hyperglycemia, dehydration, ketonemia, metabolic acidosis and multiple electrolyte abnormalities. Treatment must be intensive and directed towards the correction of fluid, electrolyte and acid-base abnormalities as well as the correction of abnormal carbohydrate metabolism. The treatment itself (particularly the correction of acid-base imbalance with sodium bicarbonate therapy and the use of insulin therapy) may exacerbate the electrolyte abnormalities, and careful monitoring and aggressive treatment of these abnormalities is critical. Without treatment, DKA is fatal and it should be considered a medical emergency. The mortality rate for DKA is 25-30 %, even with aggressive treatment.

CLINICAL SIGNS
Clinical signs seen in dogs and cats with ketoacidosis include polyuria, polydipsia, weight loss, anorexia, vomiting, diarrhea, lethargy, weakness, dehydration, obtundation and hyper- or hypoventilation. These clinical signs may develop in various combinations and are usually severe in the ketoacidotic animal. Moderate to severe potassium, phosphorous and magnesium abnormalities will contribute to lethargy, polyuria, anorexia, skeletal muscle weakness, obtundation, ventilatory abnormalities, and in the case of phosphorous – red cell hemolysis and anemia.

FLUID, ACID-BASE AND ELECTROLYTE ABNORMALITIES
Hyperglycemia causes an osmotic diuresis, predisposing to dehydration. Excessive fluid loss can lead to severe hypovolemia, with associated hypotension, compromised tissue perfusion, and lactic acidosis. Ketonemia further compounds the metabolic acidosis. DKA patients also suffer total body depletion of sodium, potassium and phosphorous due to anorexia, vomiting and osmotic diuresis. Magnesium is also lost into the urine and severe hypomagnesemia may be associated with a refractory hypokalemia. The electrolyte abnormalities may be severe and life-threatening and without insulin therapy to reverse the ketoacidotic state, will lead to death.

TREATMENT
This is aimed at a) fluid resuscitation of the hypovolemic and hypotensive patient, b) reversal of the ketoacidotic state, with insulin being the mainstay of therapy, and c) correction of electrolyte abnormalities. The use of insulin is essential, but may result in further exacerbation of the hypokalemic and hypophosphatemic state as insulin facilitates the translocation of these electrolytes into the intracellular space. Animals with mild or moderate electrolyte disturbances on first evaluation may well have dramatic reductions in serum levels of those electrolytes within a few hours of initiating insulin therapy.

A) Fluid Resuscitation
The fluid of choice is an isotonic solution such as 0.9% sodium chloride, lactated Ringer’s solution or Plasmalyte-A. ‘Shock’ doses (20-40 ml/kg) of fluids may be required in cases of severe hypovolemic shock or acidosis. In more stable patients, fluid requirements should be calculated to restore hydration over 10-12 hours.

B) Reversal of Metabolic Acidosis
1) Sodium bicarbonate therapy: Metabolic acidosis may correct following intravenous fluid and insulin therapy via oxidation of ketone bodies and excretion of hydrogen ions in the urine. In cases of severe acidosis (pH < 7.1; TCO2 < 10 mEq or mmol/l) judicious administration of sodium bicarbonate is recommended in order to improve cardiac contractility and peripheral vascular tone. The estimated dose of NaHCO3 = 0.3 x BW kg x (18-serum HCO3). One quarter of the deficit is administered intravenously over 20 minutes; the remainder is administered in intravenous fluids over 4-6 hours. Side effects of sodium bicarbonate therapy include decreased serum potassium concentrations and hyperosmolality.

2) Insulin therapy. Regular, crystalline insulin is the insulin of choice in DKA. It may be administered intravenously or intramuscularly.
   i) Intravenous insulin
   If given intravenously, insulin is diluted in isotonic saline solution and administered as a constant rate infusion (CRI) at a dose of 2 U/kg/24hr for dogs and 1.1 U/kg/24hr for cats. If the total daily dose of insulin is placed in 240 mls of saline, is can be infused at a rate of 10 ml/hr. When provided intravenously, insulin acts rapidly to lower the blood glucose level and frequent monitoring is recommended. Intravenous insulin infusion can exacerbate hypokalemia and hypophosphatemia, so close attention must be paid to serum values of these electrolytes, and aggressive supplementation is usually required.

   ii) Intramuscular insulin
   Alternatively, regular insulin may be administered by the intramuscular route. It is used hourly at a dose of 0.1-0.2 U/kg until blood glucose concentration decreases to less than 300 mg/dl (165 mmol/l). At that point, insulin frequency can be reduced to every 6 hours and it may be administered intramuscularly or subcutaneously (if the patient is well hydrated). Blood glucose monitoring should be hourly initially, but may be measured every 2-4 hours once the frequency of insulin administration decreases. Intramuscular injection of rapid acting insulin can also exacerbate electrolyte abnormalities, necessitating aggressive supplementation of potassium and phosphorous.
iii) Supplementation with dextrose

It is important to note that the metabolism of ketones requires insulin. If the blood glucose level drops into the normal range, but ketonemia persists, insulin therapy must be continued. This necessitates the supplementation of intravenous fluids with dextrose, in order to prevent the onset of hypoglycemia. The continued supplementation of dextrose provides a carbohydrate substrate that enhances the metabolism of ketones.

B. Correction of Electrolyte Abnormalities

1. Potassium: Serum potassium levels may decline precipitously following fluid and insulin therapy. Clinical signs include marked skeletal muscle weakness (as evidenced by poor neck muscle tone), paralytic ileus, respiratory paralysis and cardiac arrhythmias. Supplementation of intravenous fluids with Potassium Chloride (KCl) is essential.

2. Phosphorus: Hypophosphatemia may develop following insulin therapy due to intracellular shifting of phosphorus. Hypophosphatemia causes skeletal muscle weakness, hemolytic anemia and respiratory failure, due to decreased 2,3DPG and ATP levels in active tissue and red blood cells. If phosphorus levels decrease below 1.8 mg/dl (0.58 mmol/l) or CPK levels are high (>1500), phosphate replacement is indicated. Potassium phosphate may be dosed as an intravenous constant rate infusion of 0.01-0.03 mmol/kg/hr, for 12-24 hours. Serum phosphorus concentration must be monitored closely during therapy. Over-supplementation may cause hypocalcemia.

3. Magnesium: Hypomagnesemia (< 1.8 mg/dl or 0.7 mmol/l) has been associated with the development of refractory hypokalemia. In these cases, magnesium supplementation can be provided intravenously, using magnesium sulfate at a dose of 1-2 mEq/kg/day (or 0.5-1 mmol/kg/day). Once potassium levels have normalized, the magnesium infusion rate is lowered to 0.3-0.5 mEq/kg/day (or 0.15-0.25 mmol/kg/day) for a further 2-5 days. Too rapid cessation of magnesium therapy can result in a recurrence of hypokalemia and hypomagnesemia.

References available from author upon request.

### Insulin CRI - Therapy Adjustments

<table>
<thead>
<tr>
<th>If glucose is:</th>
<th>Fluids +/- dextrose</th>
<th>Insulin CRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 250 mg/dl (137.5 mmol/l)</td>
<td>Isotonic fluid</td>
<td>10 ml/hr</td>
</tr>
<tr>
<td>150-250 mg/dl (82.5-137.5 mmol/l)</td>
<td>IV fluid + 2.5 % dextrose</td>
<td>10 ml/hr</td>
</tr>
<tr>
<td>100-150 mg/dl (55-82.5 mmol/l)</td>
<td>IV fluid + 5% dextrose</td>
<td>5 ml/hr</td>
</tr>
<tr>
<td>&lt; 100 mg/dl (55 mmol/l)</td>
<td>IV fluid + 5% dextrose</td>
<td>Stop CRI</td>
</tr>
</tbody>
</table>

### Potassium replacement*

<table>
<thead>
<tr>
<th>Serum K (mEq or mmol/l)</th>
<th>KCl /L fluids (mEq or mmol/l)</th>
<th>Max. rate (ml/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.6-5.0</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>3.1-3.5</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>2.6-3.0</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>2.1-2.5</td>
<td>60</td>
<td>8</td>
</tr>
<tr>
<td>&lt; 2.0</td>
<td>80</td>
<td>6</td>
</tr>
</tbody>
</table>

*Rate of supplementation should not exceed 0.5 mEq or mmol/kg/hr