How do I treat diabetic ketoacidosis?

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Diabetic ketoacidosis (DKA) may be the cause for first presentation of a patient or may occur at any time during the treatment of diabetes mellitus. In some dogs and cats DKA may be a recurrent disorder, either because of repetitive management faults or due to the presence of a chronic concurrent disease. Clinical signs of DKA include anorexia, lethargy, weakness, vomiting, abdominal pain, dehydration and possibly stupor or coma. The typical signs of diabetes (pu/pd, polyphagia) are often no longer present at the time of presentation. Diagnosis of DKA requires a high index of suspicion, in particular in patients in which diabetes has not been noticed previously. The diagnosis is established in the presence of hyperglycemia, moderate to severe concentrations of ketones in urine or blood and anion-gap acidosis. β-hydroxybutyrate is the most abundant ketone body in patients with DKA. However, it is not detected by the commonly used urine test strips, and therefore ketonuria may be underestimated and the diagnosis of DKA may even be missed. Recently, a hand-held meter (Precision Xceed, Abbott Laboratories) has been validated for use in dogs and cats which is easy to use and allows detection of β-hydroxybutyrate in serum.[1,2]

Many animals have concurrent disease such as pancreatitis, hepatic lipidosis syndrome (cats), urinary tract infection, hypercortisolism, neoplasia or renal failure, and therefore a variety of additional laboratory abnormalities may be found.
DKA is one of the most complex metabolic emergencies and its treatment is highly demanding. It usually requires hospitalisation of the patient in a 24-hour facility in which frequent reevaluations of physical and laboratory variables and adjustment of therapy is feasible.[3] The major life-threatening abnormalities are dehydration (due to osmotic diureses, anorexia, vomiting), hyperosmolarity (due to hyperglycemia and water loss) and metabolic acidosis (due to increased ketogenesis). The fundamental principles of treatment are: fluid therapy, electrolyte supplementation, insulin administration and treatment of concurrent diseases.

<u>Fluid therapy</u>

IV fluid therapy should be initiated immediately. 0.9% NaCl is considered the initial fluid of choice because most patients are hyponatremic on presentation. The amount of fluid is calculated based on the degree of dehydration + maintenance + ongoing losses:

Dehydration deficit (ml) = % dehydration x body weight in kg x 10;
Maintenance = 60 ml/kg/24 h (for cats and for dogs between 10 – 20 kg, the volume is higher in smaller, less in bigger dogs);
Ongoing losses = estimated loss due to vomiting, diarrhoe, osmotic diureses (at least 2.5 – 5% of kg body weight).
The total amount is given over 12 – 24 hours. Reassessment should be done often, in particular during the early phases of therapy. It is important to remember, that the calculation of fluid deficits are estimates and that requirements may be higher, in particular in cases with severe osmotic diuresis. 0.9% saline is a non-buffered solution which may contribute to metabolic acidosis. We therefore consider to switch to a buffered crystalloid solution (such as Plasma- Lyte) as soon as serum phosphorus level is constant and phosphate supplemenation no longer needed (see later).

Potassium supplementation

The potassium deficit can be severe, although serum potassium concentration may be normal or even elevated. The initial dose depends on the pretreatment potassium concentration. Intravenous potassium administration should not exceed 0.5 mmol/kg/h to avoid cardiac arrhythmias.

serum potassium mmol/l	mmol/l KCl added per liter of 0.9% NaCl	maximum rate ml/kg/h
3.6 – 5.0	20	24
3.1 – 3.5	30	16
2.6 – 3.0	40	11
2.1 – 2.5	60	8
< 2.0	80	6

The serum potassium concentration should be reevaluated 2 hours after initiating therapy and then every 4 – 6 hours thereafter.

Phosphate supplementation

Similar to potassium, the organism is phosphate deficient, regardless of the serum phophorus concentration. We usually supplement phosphate by adding half of the calculated dose of potassium supplementation as potassium phosphate and the other half as potassium chloride. We do not mix potassium phosphate with calcium containing fluids, such as Ringers solution and Plasma-Lyte.

Bicarbonate supplementation

The metabolic acidosis typically resolves with fluid therapy and insulin administration. The use of sodium bicarbonate is controversial in human and veterinary medicine. Sodium bicarbonate therapy in DKA may have detrimental effects: e.g. worsening of hypokalemia, decrease of oxygen release at the tissue level, paradoxic central nervous system acidosis.[4] We do not recommend to use sodium bicarbonate in patients with DKA.

Insulin therapy

Insulin therapy is essential in the treatment of DKA, because without insulin ketonemia does not resolve and ketogenesis continues. However, an additional effect of insulin is a shift of potassium into cells, which may lead to life-threatening hypokalemia in potassium depleted individuals. Therefore, insulin therapy should be postponed until potassium (and phophorus) have been supplemented and serum levels are stable. We routinely wait for 4 – 6 hours until insulin therapy is started. Short-acting insulins (regular insulins or insulin analogues) are the insulins of choice for DKA. In our hospital we use NovoRapid (insulin aspartat), a human insulin analog. Two protocols are known: intermittent, intramuscular technique and continuous rate infusion.

Intermittent, intramuscular technique

Short acting insulin is given i.m. at a dose of 0.05 – 0.1 U/kg every hour and blood glucose concentration is measured prior to each application. The desired decrease of blood glucose concentration is 3 – 4 mmol/l per hour until a blood glucose concentration between 12 and 15 mmol/l is reached. If the blood glucose concentration decreases to less than 12 mmol/l, glucose is added to the intravenous fluid solution to make a 5% glucose solution (e.g. 100 ml 50% glucose to 1000 ml 0.9% NaCl). Short acting insulin is then given every 4 – 6 hours at a dose of 0.1 – 0.3 U/kg s.c.

Continuous rate infusion

This protocol involves administration of short-acting insulin diluted in 0.9% NaCl using an intravenous infusion pump in a separate line. An insulin solution is made by adding a dose of 2.2 U/kg short-acting insulin for dogs and 1.1 U/kg for cats to 250 ml 0.9% NaCl. Glucose is added to the insulin solution as soon as blood glucose falls below 15 mmol/l.[5]

blood glucose concentration mmol/l	i.v. fluid solution	infusion rate ml/h
> 15	0.9% NaCl	10

12 - 15	0.9% NaCl + glucose 5% final glucose concentration	7
8 - 12	0.9% NaCl + glucose 5% final glucose concentration	5
5 - 8	0.9% NaCl + glucose 5% final glucose concentration	5
< 5	stop insulin infusion	

Independent of the protocol, treatment with longer acting insulin is initiated when the patient has been stabilized and has begun to eat.
In Zurich duration of hospitalisation is between 2 days and 2 weeks (mean 7 days).
Prognosis is largely dependent on the intensity of treatment and monitoring and on concurrent diseases. Mortality ranges between 20 – 30%.

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