Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State in Cats

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KEYWORDS

• Feline • Diabetes mellitus • Ketoacidosis • Hyperosmolar state

KEY POINTS

- Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state are life-threatening presentations of diabetes mellitus.
- Treatment requires careful attention to restoring fluid volume, electrolyte deficits, and acid-base deficits.
- Rapid-acting insulin is used to reverse ketoacidosis and should be administered until blood or urine ketone concentrations have normalized.
- Insulin treatment itself can cause hypokalemia and hypophosphatemia; potassium and phosphate should be supplemented and their levels monitored frequently.
- Hyperosmolar hyperglycemic state is a rare form of complicated diabetes mellitus with a high mortality rate.

INTRODUCTION

Diabetes mellitus is defined as persistent hyperglycemia and is the result of insulin deficiency. Classically, high blood glucose concentrations lead to glucosuria, polyuria, polydipsia, and hyperphagia.[1] Insulin deficiency also results in ketosis, the result of breakdown of triglycerides.[2] Ketosis refers to the presence of triglyceride breakdown products such as β-hydroxybutyrate, acetoacetate, and acetone (the so-called ketone bodies). Insulin deficiency reduces intracellular glucose concentrations to a level that is insufficient for normal metabolism, resulting in some tissues using increased circulating ketones instead of glucose as their main energy source. However, these ketone bodies also lead to diabetic complications. Ketone bodies stimulate the chemoreceptor trigger zone in the medulla oblongata, leading to anorexia and vomiting. Ketosis also contributes to the osmotic diuresis that is present in clinical diabetes mellitus. These clinical signs all contribute to a propensity to dehydration, volume depletion, hypokalemia (and total body potassium deficits), and acidosis that characterizes DKA. Correcting these abnormalities is required to help the patient to survive in the

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Vet Clin Small Anim 43 (2013) 367–379
http://dx.doi.org/10.1016/j.cvsm.2013.01.004 **vetsmall.theclinics.com**
0195-5616/13/$ – see front matter

short term. Controlling ketoacidosis and the associated fluid and electrolyte abnormalities are the key components of stabilizing ketoacidotic diabetic cats and take precedence over controlling blood glucose concentrations on the first day of treatment.

The prognosis for recovery from DKA varies, and reported survival rates from tertiary referral hospitals range from 69% to 84%,[3,4] and up to 96% to 100% in hospitals accepting a mix of referral and primary accession patients.[5,6] Higher survival rates are reported in uncomplicated DKA cases. Cats with severe DKA can readily develop renal failure because severe dehydration coupled with sodium loss results in renal hypoperfusion. Dehydration and electrolyte derangements can also cause hyperviscosity, thromboembolism and severe metabolic acidosis. All these conditions can (and do) cause death in cats with severe DKA. However, cats with DKA that survive to discharge are as likely to achieve remission as diabetic cats without DKA.[7]

Hyperosmolar hyperglycemic state is another life-threatening presentation of diabetes mellitus. Like DKA, the hyperosmolar hyperglycemic state presents with depression, dehydration, hypovolemia, and hypokalemia.[8] Hyperosmolar hyperglycemic state was formerly called nonketotic hyperosmolar diabetes mellitus, but it has been recognized that up to one-third of humans with hyperosmolar hyperglycemia have some degree of ketonemia or acidosis, and hyperosmolar hyperglycemic state is now recognized as being on a continuous spectrum with DKA.

It is important to recognize the time course for development of ketosis and acidosis. Once insulin concentrations are suppressed to fasting levels (despite the presence of hyperglycemia) ketonemia and ketoacidosis can occur within approximately 12 and 16 days, respectively, if uncomplicated by precipitating conditions. Ketoacidosis can occur as early as 4 days after ketonemia is first detected.[9] Approximately 1 week before ketonuria is detectable on dipsticks, fasting visible lipemia is detectable, indicating breakdown of lipids. Once hyperglycemia occurs, the effect of glucose toxicity continues a cycle of suppression of insulin secretion and ever-increasing glucose concentrations. Even in cats with normal residual beta cell mass, marked suppression of insulin secretion occurs on average 4 days after blood glucose concentrations reach 30 mmol/L (540 mg/dL). This highlights the importance of instituting insulin therapy early in newly diagnosed diabetic cats to prevent the development of ketoacidosis. Risk factors for developing DKA include undiagnosed diabetes mellitus, inadequate insulin dose or dosing frequency, missed insulin doses, and intercurrent illnesses such as sepsis or acute necrotizing pancreatitis.

Both DKA and hyperosmolar hyperglycemic patients are more likely than well diabetic patients to have concurrent diseases, including acute pancreatitis, urinary tract infection, pneumonia, chronic kidney disease, neoplasia,[8] and acromegaly.[10] These concurrent diseases can contribute their own clinical signs in affected diabetic cats, altering both the prognosis and the treatment strategies required to manage complicated cases of diabetes. Identifying these diseases early is an important component of addressing the needs of diabetic cats with complications, but the treatment of these diseases is outside the scope of this article.

CLINICAL SIGNS, DIAGNOSIS, AND ASSESSMENT

DKA is suspected in diabetic cats if the cat is unwell (anorexic or inappetant, quiet or depressed), collapsed, moribund, or comatose. Diagnosis requires measurement of the levels of blood or urine ketones and confirmation of acidosis and hyperglycemia. Blood ketone levels can be measured using a portable meter similar to blood glucose meters (eg, Abbott Precision Xtra[11] or Precision Xceed,[12] Abbott GmbH, Wiesbaden,