Proceedings of the 36th World Small Animal Veterinary Congress
WSAVA
Oct. 14 - 17, 2011
Jeju, Korea

Next Congress:

Reprinted in IVIS with the permission of WSAVA
http://www.ivis.org
ENDOCRINE EMERGENCIES

Johan P. Schoeman, BVSc, MMedVet(Med), PhD, DSAM, DECIM-CA
Department of Companion Animal Clinical Studies
Faculty of Veterinary Science, University of Pretoria
Onderstepoort, South Africa

Abstract
This paper will discuss the diagnosis and management of the most important endocrine diseases that can present as an emergency. Differential diagnoses for the presentation will also be addressed. The pathophysiology of these conditions as well as their clinical signs is beyond the scope of this paper. Endocrine diseases discussed in this paper are hypoadrenocorticism, diabetic ketoacidosis, hypoglycaemia and hypo- and hypercalcaemia.

CANINE HYPOADRENOCORTICISM (ADDISON’S DISEASE)
This is an uncommon endocrinopathy typically occurring in middle-aged female dogs. Acute adrenocortical insufficiency is a medical emergency requiring immediate therapy. The most common signs in these dogs include weakness and collapse, vomiting, diarrhea and abdominal pain. The immediate findings of hyperkalaemia and hyponatraemia (Na/K < 23:1) strongly suggests hypoadrenocorticism, however the confirmation still requires an ACTH stimulation test.

Differential diagnosis for Hyperkalaemia:
- Urinary tract disease (acute renal failure, obstructive urinary tract disease, urinary tract rupture)
- Gastrointestinal tract (GIT) disease (severe enteritis, severe enteroparasitism, perforated ulcer, gastric dilation-volvulus (GDV).
- Massive soft tissue trauma (as in crush injury)
- Rapid tumour lysis following sudden tumour necrosis, due to chemotherapy.

Differential diagnosis for Hyponatraemia
- Diseases causing the loss of Na+-rich fluids (vomiting, diarrhea, osmotic diuresis with Diabetes Mellitus) or diseases causing the retention of Na+ poor fluids (congestive heart failure). Lipaemia causes an artifactual hyponatraemia.

Treatment of the Addisonian crisis
Emergency treatment for Addison’s should be started immediately and continued until the diagnosis is confirmed or ruled out. Aims of therapy will include: Correction of fluid imbalances; Correction of electrolyte...
abnormalities and provision of a source of glucocorticoid. Hypotension, vascular collapse and shock are usually the cause of death; so rapid correction is required. High dose (shock rates) normal saline (no potassium) is the dose and fluid of choice. Hypoglycaemia should be corrected if present. The glucocorticoids of choice is usually dexamethasone (0.5 – 1 mg/kg IV). This glucocorticoid does not interfere with the measurement of endogenous cortisol and thus an ACTH stimulation test can be performed concurrently with the initial emergency treatment. Methylprednisilone sodium succinate [Solu-Medrol®] (4 – 20 mg/kg IV q 6-8 hrly) may also be used, but then the ACTH stimulation test should be completed before this treatment.

**Glucose treatment:** Should NaCl alone be ineffective in reducing potassium levels, the addition of IV glucose treatment would be the next step. 1 – 2 ml of a 50% dextrose solution given as a bolus IV will have an insulin secretogogue effect that encourages the inward movement of potassium into cells, thus reducing the blood concentration. Crystalline insulin will further assist this mechanism.

**Mineralocorticoid treatment:** This is an essential part of treatment in the long term and may prove essential in the crisis situation as well. Desoxycorticosterone palvitate (DOCP) is available in some countries in the world as an IM injection form of aldosterone. Fludrocortisone acetate (Florinef®) is the tablet form of aldosterone that is used in chronic management, but is of little use in a crisis situation. Hydrocortisone [Solu Cortef®] is available in an IV form for man and has sufficient mineralocorticoid action to be useful in the crisis (it is however expensive). Dose: 1.25 mg/kg IV followed 6 hourly by 0.5 – 1 mg/kg until the patient is stable.

**Bicarbonate treatment** has two important beneficial effects, namely it replaces sodium and it corrects the metabolic acidosis associated with Addison’s and in doing this, assists in driving excess potassium back into cells. The dose is calculated based on knowing the base deficit (from blood gas measurement) or from knowing the blood bicarbonate concentration from a total venous CO2. The amount of bicarbonate to be given (mEq) = (body weight) x (0.4) x (base deficit). 25% of this dose is infused over the first 6 hours and the situation re-evaluated.

**Calcium treatment:** This appears to pharmacologically antagonize the cardiotoxic effects of hyperkalaemia. It is only very rarely used. Dose: 0.5 – 1 ml/kg of a 10% Ca gluconate given slowly IV with ECG monitoring.

Most dogs make a rapid improvement within hours of instituting treatment. If there is no improvement over the first few hours, the diagnosis should be reconsidered (with the other differentials receiving renewed attention). Fluid treatment should be continued for 24 hours and after this small quantities of food and water should be offered. After 24 hours, if vomiting does not occur, maintenance therapy should be initiated.

**Canine and Feline Diabetic Ketoacidosis (DKA)**

Establishing the diagnosis is usually no challenge. It is very important that an aggressive diagnostic work up is instituted to detect all the abnormalities present as well as to identify underlying precipitating causes that will need specific management.

The goals of treatment are to:

Provide insulin to shut off the synthesis of ketones and lower blood glucose; correct water and electrolyte imbalances; correct the acidosis; identify precipitating factors and treat them specifically; Provide a CHO substrate once insulin therapy becomes effective.

There are very helpful “recipes” and flow diagrams that should be used when treating these cases. In short the fluid of choice should provide water, potassium, phosphorous and dextrose, as and when needed, according to the blood glucose levels as insulin therapy becomes effective (Fluids used usually include resuscitative crystalloids with either KCl or KPO4 or both added to the drip). Correction of acid base balance may be achieved simply through improving perfusion, encouraging diuresis and shutting down ketogenesis. However,
sometimes bicarbonate treatment may be needed.

**Insulin therapy**

Actrapidâ (the short acting, potent crystalline insulin) is the insulin of choice. The easiest method of administration is using the intermittent intramuscular regimen:

An initial dose of 0.2 IU /kg is given IM. This is followed by 0.1 IU /kg every hour. Blood glucose is monitored every 30 – 60 mins and should not fall faster than 5.5 mmol/l /hour. The dose should be decreased if it falls faster than this and slightly increased if it is not falling faster than 2.5 mmol/l/hour. The goal is to get blood glucose down to around 16 mmol/l over a 6 – 10 hour time period (more rapid drops are associated with possible brain oedema). The moment blood glucose levels reach 16 mmol/l, hourly insulin can be changed to every 6 hours @ 0.5 IU/kg and an IV dextrose solution should be initiated to keep blood glucose between 8 and 16 mmol/ l until the patient is eating and bright, at which time a long term management program can be phased in.

**Hypoglycaemia (and Insulinoma)**

**Differential diagnosis for hypoglycaemia**

Endocrine causes: Excess insulin (endogenous through beta cell neoplasia (insulinoma) or by mistaken injection; Cortisol deficiency and Hypopituitarism.

Congenital hepatic vascular shunts; Acquired hepatic vascular shunting; Hepatic cirrhosis – end stage chronic hepatic fibrosis; Severe hepatic necrosis as may happen with toxins (e.g. aflatoxicosis) or infectious agents (e.g. viral hepatitis)

Massive tumour consumption of glucose (paraneoplastic hypoglycaemia)

Puppy hypoglycaemia; Toy and miniature breed hypoglycaemia; Sepsis; Acute babesiosis; Uraemia; Severe malnutrition; Severe polycythaemia

Artifact (Blood left to stand in a non-fluorinated tube (gray top) for too long – glucose will be consumed by the red cells).

**Insulin:Glucose ratio**

At the time of hypoglycaemia (which may need to be induced by a fast), a blood sample should be collected for insulin determination. Human insulin assays are valid in the dog. Low blood glucose should be associated with low insulin levels. Thus normal or high insulin levels in the face of hypoglycaemia, would confirm the diagnosis. In the past amended glucose: insulin ratios were used. These are no longer favoured as a means of diagnosis.

**Treatment**

Surgical removal of the tumour offers the chance to cure the dog. It may well be the best means of confirming a diagnosis as well. Even non-resectable tumours should be debulked as this will reduce the amount of insulin secreted and make medical management much easier, prolonging quality of life.

Medical treatment should follow the following order:

Diet: Feed small amounts of food frequently (4-6 times daily). Avoid simple sugars. This provides a constant source of glucose from the gut.

Glucocorticoid therapy: steroids induce a state of relative insulin resistance and encourage gluconeogenesis.

Diazoxide therapy: This drug inhibits the secretion of insulin and stimulates hepatic glyconeogenesis and glycogenolysis, thereby raising the blood glucose concentrations and is the drug of choice for long-term
management. **Dose:** 5-30 mg/kg twice daily. Start at the lower end of the dose range.

Injectable somatostatin will inhibit insulin secretion and has been used in a few cases but is prohibitively expensive and impractical at this stage.

**Medical therapy for the acute hypoglycaemic crisis:**

1-2 ml of 50% dextrose given IV will be life saving. If the IV route cannot be established this may be sprayed onto the animal’s oral mucous membranes and this will also work. Owners at home can use sugar water or syrup by this route as well. Such IV bolussing can be dangerous in insulinomas. This will cause a strong insulin release and profound hypoglycaemia – and a hypo-hyper cycle will be set up, which can be very difficult to break. Severe neuroglycopaenia with seizures can cause cerebral oedema and or necrosis. Specific treatment for cerebral swelling may need to be instituted in these cases.

**Hypocalcaemia**

**Differential diagnosis for hypocalcaemia**

The following list includes the more important causes of hypoCa2+. There are several more not included, but these would be regarded as very rare or of no clinical significance:

Eclampsia; Chronic renal failure; Hypoalbuminaemia; Acute pancreatitis; Acute renal failure; Hypoparathyroidism; Intestinal malabsorption syndromes; Phosphate-containing enemas; Massive blood transfusions with citrated blood

**Diagnostic evaluation**

Any dog showing neuromuscular type signs or signs of episodic weakness should have a Ca2+ level determined. Ca2+ is 50% serum protein bound and as such total Ca2+ levels should be corrected for albumin concentration. Ionized Ca2+ is a far better reflection of body Ca2+ levels and is now more routinely offered by most laboratories.

**Treatment:**

The tetanic phase requires emergency IV Ca2+ treatment. Slow IV (place a catheter) **Ca gluconate** (CaCl is very tissue irritating) @ 1 – 1.5 ml /kg of a 10% solution. Carefully monitor the patient. Although ECG monitoring is recommended, it is my experience that this is often difficult because of the severe muscle tremors present. Response is rapid, and within minutes the dog should calm. The end point of treatment is when the dog begins to lick its lips (due to salivation) or vomits. The final dose required is unpredictable – the dose given above is a guideline. Hyperthermia may require cooling to slow respiration (heatstroke is a possible danger).

Once the crisis has been managed, a longer-term approach to control is needed. A subcutaneous injection of Ca gluconate (never CaCl!!) diluted 50:50 with normal saline, can be given (the dose is between half and the full i/v dose given).

**Vitamin D treatment:**

PTH does not exist in a form suitable for long-term replacement therapy, so Vit D is used as the replacement hormone for long-term maintenance. This replacement treatment is usually permanent in dogs or cats with primary hypoparathyroidism. In cats that have post thyroidectomy hypoparathyroidism, Vit D treatment can
usually be slowly withdrawn as the remaining parathyroid tissue assumes full function. Because renal function is normal, the inactive and cheap form of Vit D (Vit D2) may be used (Ergocalciferol). The doses used are relative high (4000 – 6000 U/kg) because of the relatively low biological activity. Effect of this treatment is usually seen between 5 and 14 days after initiation of treatment. Patient should be hospitalized until Ca2+ levels are normal and stable. Treatment induced hypercalcaemia caused by this drug is not easily treated as fat depots (this is a fat soluble vitamin) have a long half life and weeks of hyperCa2+ may be caused by an overdose.

**Vit D3** (dihydrotachysterol) is far more metabolically active and raises Ca2+ levels within 1 – 7 days and its effects are also much shorter lived, making dose establishment much easier. It is much more potent and lower doses are required (0.03 mg/kg/day divided bid for 2 days, then 0.02 mg/kg/day for 2 days, then 0.01 mg/kg/day). The disadvantage of this drug is its expense.

**1,25-dihydroxyvitamen D** (Calcitriol) may also be used. It is more potent, faster acting (effects appear and disappear within a day or so) and requires even lower doses. (dose around 0.06 mg/kg/day). Disadvantages include expense and the capsule size, which cannot be easily broken down to sizes suitable for dogs and cats.

**Hypocalcaemia**

**Differential diagnosis for hypercalcaemia:**
Malignancy (especially lymphoma, apocrine gland adenocarcinoma); Renal failure; Hyperparathyroidism; Addison’s disease; Hypervitaminosis D (Vit D analog rat poison ingestion); Lipaemia

**Treatment of hypercalcaemia**
Primary hyperparathyroidism is rarely a hypercalcaemic emergency. The decision to treat hypercalcaemia will depend on the severity of clinical signs and not strictly on the absolute Ca level – there is no specific Ca concentration above which treatment must be initiated. Symptomatic treatment is indicated when a patient is dehydrated, azotaemic, shows ECG arrhythmia, severe neurologic dysfunction or weakness.

**Fluids treatment**
Saline diuresis is helpful in helping to promote calciuresis.

**Pharmacologic diuresis – Furosemide**
IV bolus furosemide treatment will further enhance calciuresis (5 mg/kg IV followed by a 5mg/kg/hr CRI)

**Glucocorticoids**
If at all possible this treatment should be delayed until a definite diagnosis has been made

**Other treatments**
Various other modalities include: phosphate infusions, calcitonin and various calcium chelators. Surgical removal of the affected parathyroid glands remains the treatment of choice for primary hyper PTH.

**Further reading:**
2. Feldman and Nelson’s Canine and feline endocrinology and reproduction 2004, 3rd edition, Elsevier science, USA