FECAVA BASIC PRACTICES
IN ENDOCRINOLOGY

Canine Hypoadrenocorticism: **Treatment**

Treatment:

ACUTE TREATMENT

- An acute adrenal crisis is an emergency and requires intensive care management.
- The intensity of treatment depends on the severity of clinical signs; initial stabilization and treatment can best be managed on an inpatient basis.
- The initial goals of treatment of adrenal crisis are to correct hypovolemia, hypotension, hyponatremia, hyperkalemia (and associated arrhythmias), hypoglycemia, and acidosis.

1. INTRAVENOUS FLUID THERAPY:
    - The degree of dehydration should be assessed from the history and clinical examination.
    - Most dogs with acute severe hypoadrenocorticism will be severely hypovolemic. Initial fluid infusion should be up to 90 mL/kg of crystalloid solution given as 20 to 30 mL/kg boluses (over approximately 20 minutes) until the animal is hemodynamically stable.
    - Traditionally, 0.9% saline was the recommended crystalloid solution; however, a disadvantage is the potential concern of increasing the sodium concentration too rapidly, which can result in central pontine myelinolysis. This is more likely to occur when the initial sodium concentration is <120 mEq/L. Sodium concentration should not increase by more than 10 to 12 mEq/L/day. Because of the potential disadvantage of 0.9% saline, some clinicians prefer using a buffer isotonic crystalloid solution containing low concentrations of potassium (4 to 5 mEq/L; e.g., lactated Ringer's solution or Normosol-R.)
    - If hypoglycemia is present, 50% dextrose solution should be added to the IV fluids to produce 5% dextrose solution.

2. TREATMENT OF HYPERKALEMIA:
    - The potassium concentration should be monitored every 6 hours in severe cases (>7 mEq/L) and every 24 hours in other cases.
    - Although most cases respond to fluid therapy alone, severe hyperkalemia (>7 mEq/L and/or bradycardia or other ECG abnormalities) may require additional treatment:
        - **a.** Slow administration of 10% calcium gluconate (0.5 mL/kg) does not decrease the potassium concentration but temporarily counteracts the impairment of myocardial excitability induced by hyperkalemia.
        - **b.** Intravenous administration of dextrose (1 to 2 g/unit of insulin) and regular insulin (0.2 U/kg) decreases the hyperkalemia by driving potassium intracellularly.
        - **c.** Correction of metabolic acidosis will also promote intracellular movement of potassium.
    - The ECG or point-of-care potassium assays can be used to monitor response during the treatment of hyperkalemia.

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3. GLUCOCORTICOID/MINERALOCORTICOID TREATMENT

- Ideally, glucocorticoid supplementation should be postponed until the ACTH stimulation test is completed.
- If immediate glucocorticoid supplementation is considered necessary before the ACTH stimulation test because the animal is hemodynamically unstable, dexamethasone (0.1-2 mg/kg IV) should be the drug of choice because dexamethasone does not have cross-reactivity with most cortisol assays. In these cases, the ACTH stimulation test should still be performed within 24-48 hours to prevent dexamethasone from interfering with the results of the ACTH stimulation test through suppression of the hypothalamus-pituitary-adrenal axis.
- The most common authors' choice is the administration of hydrocortisone at a dose of 0.625 mg/kg/h (CRI);[1] another option is prednisolone sodium succinate (2 mg/kg IV initially, and then 0.5 mg/kg IV q12h). Both these products have glucocorticoid and mineralocorticoid properties and should be administered only after the ACTH stimulation test is completed.

4. OTHER TREATMENTS

- During an adrenal crisis, supportive therapy, including gastro protectants and anti-emetics, is commonly necessary.

LONG-TERM TREATMENT

- Once the patient is stabilized, glucocorticoid and mineralocorticoid replacement therapy is required in most cases for the remainder of the animal's life.
- Patients with secondary hypoadrenocorticism require only glucocorticoid supplementation, adjusted based on clinical signs.

1. GLUCOCORTICOID THERAPY

- In the long term, the most commonly used glucocorticoid is prednisolone. If cortisone acetate tablets are available this is a very good alternative, as prednisolone is a rather potent glucocorticoid.
- In the first week after the diagnosis, relatively high dosages of prednisolone should be used, e.g., 1 mg/kg/day PO.
- The dose should then be gradually tapered over several weeks until the lowest dose that will control the clinical signs (e.g., vomiting, diarrhea, lethargy) and does not cause side effects (e.g., polyuria polydipsia, muscle wasting).
- In the long term, most dogs require a prednisolone dose of 0.1 to 0.2 mg/kg/day PO.
- Some dogs, particularly large breeds, require less than 0.1 mg/kg/day.

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2. MINERALOCORTICOID THERAPY

- Patients with mineralocorticoid deficiency should be treated with mineralocorticoids, such as DOCP or fludrocortisone.
- DOCP is administered SC approximately every 28 days initially.
- The label starting dose of DOCP is 2.2 mg/kg, but the authors and most endocrinologists routinely begin at 1.5 mg/kg with the owner's consent to use an off-label dose.[2]
- Alternatively, an oral mineralocorticoid replacement can be used (fludrocortisone acetate 5-10 µg/kg PO q12h as a starting dose).
- Fludrocortisone also has glucocorticoid activity and the maintenance dose of prednisolone for dogs receiving fludrocortisone may be lower than for dogs that are receiving DOCP.
- In some dogs, the glucocorticoid activity of fludrocortisone may be sufficient, and prednisolone may be discontinued.

3. MONITORING RESPONSE TO THERAPY

- Monitoring the success of treatment is best obtained by concentrating on the clinical picture and the Na and K concentrations.
- The dose of glucocorticoids should be adjusted based on the clinical signs: the dose is decreased if PU/PD, polyphagia, dermatological changes, and muscle wasting are present but increased if vomiting, diarrhea, or lethargy are detected.
- There is no value in measuring circulating cortisol concentration.
- Measure Na and K concentrations 10 and approximately 28 days (before the next injection) following the first administration of DOCP to determine whether the dose (at 10 days) and the dosing interval (at 28 days) are appropriate.
- Adjust the DOCP dose at day 28-30 in 10-20% steps to achieve electrolytes within their reference intervals at day 10 and day 28-30.
  - Monitoring electrolytes at day 10 enables assessment of the peak effect of the dose.
  - Monitoring electrolytes at day 28 enables assessment of the duration of the dose.
- Electrolytes should be within their reference intervals before administering a repeat DOCP dose.
  - If potassium is below and/or sodium is above their reference intervals at day 28:
    - Do not inject DOCP, even at a lower dose.
    - Repeat electrolyte testing every 5-7 days until they are within their reference intervals. Then re-inject DOCP at a lower dose and recheck at day 10 and day 28 post-injection.
  - If potassium is above and/or sodium is below their reference intervals at day 28 DOCP must be injected:
    - The dose should be increased and/or the dose interval shortened.
  - In cases of lack of expected efficacy, before increasing the Zycortal dose, consider whether the dog was adequately hydrated at injection, the product was adequately re-suspended, and whether the injection was successfully administered.

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- Once the dose has been determined, a stable dog will have electrolytes within their respective reference intervals at days 10 and 28 during at least two consecutive treatment cycles using that same dose. Thereafter dogs should be reassessed every 4-6 months at the time of injection.
- Most dogs require DOCP administration every 28-30 days. In uncommon cases, patients need injections as often as every 3 weeks. It is not recommended to administer DOCP at intervals longer than 30-35 days, even if electrolytes remain normal. In this case, the authors prefer to adjust the dose instead of extending the dosing interval.
- The majority of dogs with hypoadrenocorticism will be well controlled on a maintenance DOCP dose of 1 to 1.5 mg/kg injection every month.
- When using fludrocortisone, dose adjustments should be made in steps of 0.05-0.1 mg based on clinical signs and electrolyte concentrations. Following the initiation of therapy, the electrolytes should be checked weekly until they stabilize in the normal range; thereafter, electrolytes should be checked after 3 months and then every 6 months.
- In most dogs, the final fludrocortisone dosage needed is 10-20 µg/kg/day PO.[3]

COMPLICATIONS

- The development of clinical signs from glucocorticoid excess (e.g., polyuria, polydipsia, dermatologic changes, loss of muscle mass) are common and usually resolved by decreasing the dose of prednisolone. Fludrocortisone and DOCP (especially when used at high dosages) can also cause polyuria and polydipsia.

PROGNOSIS

- Hypoadrenocorticism is a readily treatable disease with an excellent prognosis, provided that that treatment is performed for life.
- In the uncommon cases of primary hypoadrenocorticism caused by granulomatous or neoplastic/metastatic disease and secondary hypoadrenocorticism caused by a pituitary mass, the prognosis is guarded.

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