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CANINE HYPOADRENOCORTICISM: LITERATURE REVIEW

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INTRODUCTION

The endocrine system is one of those responsible for producing hormones which, via the hematogenous route, reach and act on target cells, regulating metabolism and cellular functions, allied to the autonomic nervous system and one of its means of control is through negative feedback.[1] Hypoadrenocorticism (HA) is an endocrinopathy with a primary (classic or atypical) or secondary etiology and is considered rare in dogs, although it is highly relevant in clinical routine. It affects the adrenal gland and is characterized by a significant reduction in glucocorticoids and/or mineralocorticoids. Due to its lack of specificity in terms of clinical manifestations, untreated patients can develop the acute form of the disease (Addison's Disease/Addisonian Crisis), with a high risk of death. [2]

MATERIAL

Studies published between 2007 and 2023 were used, available in Google Scholar, PubMed, PubVet, Scielo and Institutional Repositories databases.

LITERATURE REVIEW

It is estimated that 1 in every 2,000 dogs treated in veterinary hospitals has hypoadrenocorticism. Despite its low occurrence, the incidence is higher in females between 1 and 14 years old (with a prevalence in castraded and middle-aged animals), and the possibility of other simultaneous endocrine disorders should not be ruled out. Some breeds, such as the Great Dane, Portuguese Water Dog, Rottweiler, Standard Poodle, West Highland White Terrier and Wheaton Terrier, are more predisposed.[3]

Hypoadrenocorticism is classified according to its etiology into primary and secondary. Primary hypoadrenocorticism can also be subdivided into classic or atypical.[10]

Classic primary hypoadrenocorticism is the most common type, where there is a deficiency in the secretion of glucocorticoids (cortisol) and mineralocorticoids (aldosterone) as a result of the destruction or atrophy of the three layers of the adrenal cortex (fasciculated, reticular and glomerular zones) due to immune-mediated causes, reticular and glomerular) due to immune-mediated causes, fungal diseases, amyloidosis, neoplasms or iatrogenic causes involving adrenalectomy, abrupt suspension of chronic use of exogenous glucocorticoids or drugs that inhibit cortisol synthesis, such as trilostane.[3, 4]

On the other hand, atypical primary hypoadrenocorticism accounts for only 10% of primary cases[6], showing only glucocorticoid deficiency, due to the preservation of the glomerular zone which produces mineralocorticoids, an important factor when assessing electrolytes.

The secondary origin is the least frequent of all cases of hypoadrenocorticism, where there is a decrease in the secretion of adrenocorticotrophic hormone (ACTH), responsible for stimulating the fasciculated and reticulated zones of the adrenals to produce glucocorticoids, generating as a consequence atrophy and a deficit in cortisol secretion.[7] In these conditions, mineralocorticoid secretion remains unchanged, since the glomerular layer is controlled by the renin-angiotensin system. The causes of a decrease in ACTH are usually abnormalities in the hypothalamus or pituitary gland, such as neoplasms, inflammatory or traumatic processes.[3]

The clinical manifestations tend to be nonspecific and occur intermittently, and may not be noticed by the guardians or easily confused with gastrointestinal, infectious or renal diseases, requiring investigation for differential diagnosis. Initial signs related to hypoadrenocorticism can include lethargy, depression, apathy, selective appetite, anorexia, intermit-

tent emesis, weight loss, diarrhea, abdominal pain, muscle weakness and tremors.[10]

If nonspecific supportive treatment is used, such as fluid therapy, symptoms tend to be initially responsive, but relapse occurs within days or weeks. The period of exacerbation of the disease occurs in stressful situations, such as changes in routine, which can lead to an Addisonian crisis and progression of the disease, with electrolyte alterations (low sodium:potassium ratio), dehydration, cardiovascular disorders (decreased cardiac contractility, hypovolemia, hypotension), polyuria/polydipsia, hyperlactatemia, hypothermia, azotemia, hypoglycemia, shock, metabolic acidosis and coma. [8, 3, 4]

To establish the diagnosis, it is necessary to associate the clinical history with a detailed anamnesis, a complete physical examination, as well as hematological, biochemical and imaging tests.[10]

Laboratory findings	Arregenerative/regenerative normocytic normochromic anemia; Lymphocytosis; Eosinophilia; Prerenal azotemia; Compensatory urinary density or isostenuria; Hypoglycemia; Hypoalbuminemia; Increased ALT, AST, FA;
Electrolyte disorders	Hyperphosphatemia; Hyponatremia; Hyperkalemia; Hypercalcemia; Hypochloremia; Metabolic acidosis; Reduction in the Na:K ratio (below 27:1);
X-ray	Microcardia; Narrowing of the caudal vena cava; Hypoperfusion of the lung fields;
Ultrasound	Reduction in the size of the adrenal glands (adrenocortical atrophy);
Electrocardiogram (ECG)	Arrhythmias due to hyperkalemia; T wave amplitude increase and P wave decrease; QT shortening and PR increase; 2nd degree BAV; Atrial fibrillation;

Table 1: Possible findings in complementary tests for primary AH (Vargas, 2015; BORIN-CRIVELLENTI, 2015).

Even when clinical manifestations and laboratory results are compatible with hypoadrenocorticism, it is necessary to carry out specific hormonal tests, with the ACTH stimulation test being the gold standard, which consists of measuring basal cortisol and cortisol after administration of ACTH, with a result of less than 2ug/dL being confirmed positive for hypoadrenocorticism. Since ACTH stimulates the secretion of glucocorticoids by the adrenals, in a healthy animal it will increase the production of cortisol, whereas in an AH patient there will be no such increase. [3, 5, 7]

It is of clinical relevance to point out that glucocorticoid supplementation is not contraindicated before or during the stimulation test, as long as the drug chosen is dexamethasone, as it is a type of synthetic corticoid that does not present a false negative with the methods that measure cortisol, while prednisolone and hydrocortisone interfere with the result.[3] It should also be borne in mind that chronic use of glucocorticoids can lead to false positives.[3]

Although the ACTH stimulation test is a sensitive diagnostic method, it does not differentiate between the forms of hypoadrenocorticism (primary or secondary). However, it is possible to analyze the occurrence of electrolyte alterations, which occur more frequently in primary hypoadrenocorticism, in addition to measuring serum ACTH, where primary hypoadrenocorticism will be elevated due to the absence of negative feedback from cortisol to the pituitary gland, while secondary hypoadrenocorticism will have reduced ACTH concentrations.[4]

Treatment consists of correcting clinical manifestations, especially during an Addisonian crisis, where there is a risk of shock. Intravascular volume and tissue perfusion should be re-established with fluid therapy with isotonic saline solution 0.9% NaCl, treatment of any arrhythmias, correction

of electrolyte imbalances and possible complications such as metabolic acidosis, hypoglycemia, as well as a glucocorticoid deficit, always assessing the presence of possible associated comorbidities.[10]

For glucocorticoid supplementation in Addisonian crisis, the drug of choice, according to VARGAS (2015), is dexamethasone, at a dose of 0.25mg/kg, every 12 to 24 hours in patients with mild hyponatremia and at a dose of 2mg/kg, every 12 to 24 hours for moderate to severe hyponatremia, Because it is fast-acting and can be administered intravenously, it does not interfere with specific hormone tests, as well as helping to maintain blood pressure and blood volume and preventing myelinolysis. Alternative options include methylprednisolone sodium succinate and hydrocortisone succinate. After 3 to 5 days, glucocorticoid replacement should be reduced and a maintenance dose of prednisolone (0.2mg/kg/day) established.[3]

For mineralocorticoid supplementation, there is the option of oral fludrocortisone, at a dose of 0.01-0.02mg/kg every 24 hours. During an Addisonian crisis or when secondary AH is diagnosed, mineralocorticoid supplementation is not necessary, as the deficit is caused by glucocorticoids.[3]

FINAL CONSIDERATIONS

The conclusion is that, although little reported, hypoadrenocorticism is highly relevant in small animal medicine. If an assertive diagnosis is made, ruling out possible differential diseases, since there are non-specific and intermittent symptoms, and a possible Addisonian crisis is controlled, as well as the owners being aware of the need for supplementation and periodic check-ups, the prognosis for patients with hypoadrenocorticism is good, with no reduction in life expectancy.

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