METHODOLOGIES FOR DEALING WITH CONCURRENT DM AND HAC ISSUES

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Gerard Mclauchlan, Ian Ramsey discuss approaches to spotting and treating these problems, with regard to small animals

BOTH diabetes mellitus (DM) and hyperadrenocorticism (HAC) are well-documented in the veterinary literature and are the two most common endocrinopathies of middleaged to elderly dogs (Nelson, 2010; Melian et al, 2010).

However, only a few retrospective reports describe the diagnosis and management of canine patients suffering from the diseases concurrently (Peterson et al, 1981; Blaxter and Gruffydd– Jones, 1990; McLauchlan et al, 2010). Recommendations regarding treating the concurrent diseases are limited by a lack of data.

Complicated diagnosis

Dogs with concurrent DM and HAC are challenging for any clinician to diagnose or treat. In most cases, controlling the HAC will be unlikely to result in complete resolution of the DM. However, reducing circulating cortisol levels may improve the patient's response to insulin.

This will reduce the chance of an animal developing complications. The diagnosis of concurrent DM and HAC is complicated by the fact that both endocrinopathies cause similar clinical signs and abnormalities in serum biochemistry (Nelson, 1981; Melian et al, 2010). Although most published reports document that the diabetes is the first condition diagnosed, it is likely that HAC may be the

primary problem in at least some of the cases (Peterson et al, 1981).

The owners of animals with either disease will commonly report polyuria/polydipsia (PU/ PD), polyphagia, lethargy, coat changes and muscle weakness (Nelson, 2010; Peterson, 1981). The presence of PU/PD was not a consistent finding in one older publication examining dogs with concurrent DM/HAC (Blaxter and Gruffydd-Jones, 1990), although this was contradicted in a more recently published paper (McLauchlan et al, 2010). Common biochemical abnormalities include increases in alkaline phosphatase, alanine aminotransferase, cholesterol and glucose concentrations. Glycosuria occurs once the renal threshold for glucose (about 10mmol/L) has been exceeded (Nelson, 2010).

DM is more commonly identified as the primary disorder, probably because it is more often clinically suspected and more easily/reliably diagnosed (based on appropriate clinical signs, fasting hyperglycaemia and glucosuria).

Most animals with DM will only be investigated for HAC if the diabetes is poorly responsive (resistant) to insulin therapy or the clinical signs continue, despite apparently well-controlled DM. Confirming the diagnosis of HAC after identifying DM may be difficult, as chronic metabolic stress placed on an animal with poorly controlled DM may result in a false positive of any of the tests that assess the adrenal axis. It is important, therefore, to attempt stabilisation of the DM before attempting to confirm concurrent HAC.

Stabilisation

Diabetic dogs suspected of having HAC should undergo a blood glucose curve to assess if they are insulin-resistant (defined here as an insulin dose in excess of 1.5 IU per dose; Nelson, 2010). If animals appear to not be responding to insulin therapy, then this should be serially increased until response is documented.

The degree of stabilisation does not need to be perfect, simply such that the patient is no longer losing weight, is not ketonuric and has reasonable activity levels. Thirst and appetite may not be normal, but hopefully will be reduced by this stage. Not all diabetic dogs with HAC are insulin-resistant and, in some cases, treatment is confined to insulin therapy alone. Knowing the animal has HAC, however, is useful prognostically and for subsequent treatment, even if there is no current plan to treat the HAC.

In the authors’ opinion, the test of choice for confirming the presence of HAC in an animal with concurrent DM would be an adrenocorticotropic hormone (ACTH) stimulation test, due to its increased specificity over the low-dose dexamethasone suppression tests (LDDST) or urine corticoid: creatinine ratio (UCCR). The chronic metabolic stress of diabetes mellitus is more likely to affect the LDDST and UCCR, thus increasing the possibility of false positive results with these tests over the ACTH stimulation test. Previous reports found mitotane was associated with a rapid

reduction in insulin requirement within three weeks and therefore recommended that insulin therapy was prospectively reduced when starting treatment for HAC (Peterson et al, 1981).

Trilostane trials

A more recent publication documenting concurrent HAC/DM in eight dogs showed that trilostane therapy was not consistently associated with a reduction in insulin requirements (McLauchlan et al, 2010). While the number in this series was small and there was variability in the management of the cases (in relation to frequency of insulin/ trilostane administration), it is possible that reductions in insulin at the start of trilostane may not be required in all cases.

Prospective trials are, therefore, required before further recommendations can be given regarding the use of trilostane in diabetics. However, based on the duration of action of the drugs, in the interim it would seem logical to administer trilostane and insulin at the same frequency (either once a day or, preferably, twice daily; Ramsey, 2010).

Cases receiving trilostane and insulin should be monitored at the very minimum by examining owners' records, urine testing and ACTH stimulation tests. Blood glucose curves and spot checks may provide useful information as well, but do not overrule the owner and clinical impressions of glycaemic control. Initially, tests should be performed every two weeks and then gradually increased to not less than every three months. Serum fructosamine has been found not to reduce consistently in cases with HAC and DM, despite increasing insulin therapy and trilostane treatment (McLauchlan et al, 2010). Whether fructosamine is the appropriate tool to assess glycaemic control in dogs with concurrent DM/HAC remains to be confirmed.

References

- Blaxter A C and Gruffydd-Jones T J (1990). Concurrent diabetes mellitus and hyperadrenocorticism in the dog: diagnosis and management of eight cases, *Journal of Small Animal Practice* **31**: 117-122.
- McLauchlan G, Knottenbelt C, Augusto M, Helm J, McGrotty Y and Ramsey I (2010). Retrospective evaluation of the effect of trilostane on insulin requirement and fructosamine concentrations in eight diabetic dogs with hyperadrenocorticism, J*ournal of Small Animal Practice* **51**: 642-648.
- Melian C, Perez-Alenza M D, Melian C and Peterson M E (2010). Hyperadrenocorticism in dogs. In Ettinger S J and Feldman E C (eds), *Textbook of Veterinary Medicine* (7th edn), W B Saunders, Philadelphia: 1,816-1,840.
- Nelson R W (2010). Canine diabetes mellitus. In Ettinger S J and Feldman E C (eds), *Textbook of Veterinary Medicine*(7th edn), W B Saunders, Philadelphia: 1,782-1,795.
- Peterson M E, Nesbitt G H and Schaer M (1981). Diagnosis and management of concurrent diabetes mellitus and hyperadrenocorticism in 30 dogs, *Journal of American Veterinary Medical Association* **1**: 66-69.

- Ramsey I (2010). Trilostane in dogs, V*eterinary Clinics of North America* **40**: 269-283.