The Hope Line

Winter 2020

Monitoring Trilostane Therapy

Canine hyperadrenocorticism (HAC) is a common endocrinopathy that can be managed with trilostane. Treatment should be initiated when clinical signs are present and should not be given based solely on labwork changes (e.g., treatment should not be initiated when an elevated ALP is present with no clinical signs). Typical starting doses are 1-2mg/kg once to twice daily.

1. Resolution of clinical signs

Classic clinical signs of HAC include polyuria, polydipsia, polyphagia, and panting and are typically what prompts investigation for, and treatment of, HAC. However, less subtle clinical signs that can also affect quality of life include muscle wasting and weakness, lethargy, and recurrent infection. Ideally, quantification of these symptoms at the start of treatment is helpful to determine efficacy of treatment with trilostane. This can be accomplished using quality of life questionnaires or ensuring that owners are questioned about thirst, urination, and appetite at every recheck. Typically, resolution of thirst and urination occur earlier in the course of treatment (within 1-3 weeks) while dermatologic changes can take longer (months). I have found that polyphagia and panting do not always resolve with treatment. Cortisol testing should always be interpreted in light of clinical signs.

2. Signs of oversuppression of cortisol

Clinical signs of oversuppression of cortisol (Addisonian crisis) include lack of appetite, GI signs (vomiting, nausea, diarrhea), lethargy, and collapse. Discontinuation of trilostane therapy is recommended if these symptoms occur and an ACTH stimulation test should be performed. A minimum database is also recommended to evaluate for electrolyte abnormalities associated with an Addisonian crisis (elevated potassium and decreased sodium). In addition, hypoglycemia and anemia can be seen. Dexamethasone or prednisone and supportive care (fluid therapy, anti-emetics) should also be administered. Occasionally, supplementation with mineralocorticoid is required. Trilostane therapy at a lower dose may be resumed once symptoms resolve and recovery of the adrenocortical axis is documented with an ACTH stimulation test or baseline cortisol. In some patients, cortisol production can be suppressed long-term (months to years).

Adrenal necrosis has been documented as a rare complication of trilostane therapy and requires emergency stabilization and prolonged glucocorticoid and mineralocorticoid supplementation.

3. Cortisol levels

Traditionally, an ACTH stimulation is run 14 days after initiation of trilostane therapy. Cortrosyn is administered at 5ug/kg. The test should be performed 4 -6 hours after the morning pill. Ideally, glucose and electrolytes should also be evaluated to monitor for oversuppression. Ideal post-stimulation cortisol is between 1.45 and 9.1.

Recommended action at the 14 day evaluation

Post ACTH serum cortisol (ug/dL)	Action
<1.45	Stop treatment for 7 days. Re-start at a decreased dose, recheck stim in 10-14 days at the lower dose
1.45-5.4	Continue on same dose
5.4-9.1	EITHER: Continue on current dose if clinical signs are well-controlled OR: Increase dose if clinical signs of HAC still evident
>9.1	Consider increasing the dose dependent on clinical signs

Trilostane Monitoring Tips Continued...

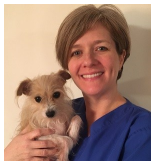
Post-trilostane baseline cortisol may also be considered to monitor therapy. A single blood sample is taken for a baseline cortisol assay. A timed post-trilostane baseline cortisol may reliably exclude the possibility of oversuppression of cortisol in dogs on SID therapy if >1.3 at 4-6 hours post-trilostane or >1.0 at 2-3 hours post-trilostane.

A timed post-trilostane baseline cortisol has limited to moderate ability to discriminate between dogs with optimal or inadequate control; >2.9 at 4-6 hours post-trilostane indicates inadequate suppression (SID dosing) and >4.4 at 2-3 hours post-trilostane indicates inadequate suppression (SID dosing). A value <2.3 at 3 hours post-trilostane indicates optimal control in a clinically well controlled dog (SID or BID dosing); a value <1.0 should raise concern for oversuppression as stated above. **All values should be interpreted in light of clinical signs. If the dog is ill, a full ACTH stimulation test should be performed (along with glucose and electrolytes). Dogs with concurrent illness or stress should have a full ACTH stimulation test performed.**

Long-term monitoring in clinically well-controlled dogs includes a physical exam, ACTH stimulation test, and chemistry panel every 3-4 months and 10-14 days after any dosing changes.

4. Pituitary macroadenoma syndrome

This syndrome occurs in pituitary dependent HAC when the pituitary tumor grows to a size that applies pressure to surrounding structures in the brain. Most common clinical signs are lethargy, mental dullness, loss of interest in normal activities, restlessness, decreased appetite, and disorientation. Symptoms may be dismissed by owners as changes related to aging. Diagnosis depends on advanced imaging (MRI or CT scan) to identify pituitary macroadenoma. Treatment is typically radiation therapy.



With close monitoring, trilostane can be an effective treatment for management of canine HAC.

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