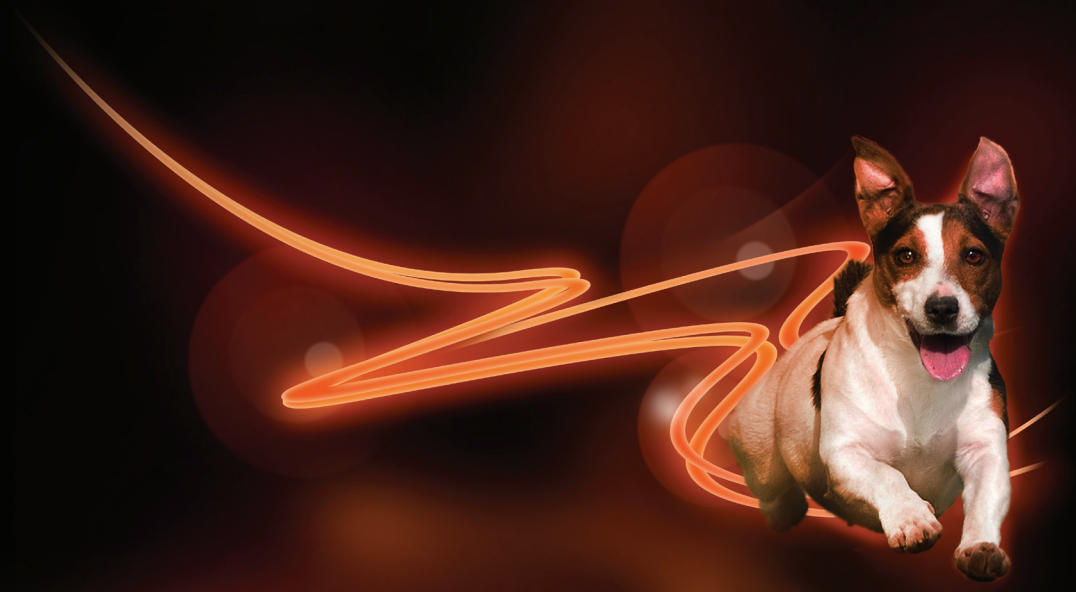
Summary of Macfarlane et al (2016) Pre-trilostane and three-hour post-trilostane cortisol to monitor trilostane therapy in dogs. Vet Rec 179: 597-605



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In a study of 93 well dogs with hyperadrenocorticism, the Pre-Vetoryl Cortisol, the 3-hour post Vetoryl cortisol and the post-ACTH cortisol were analysed and compared to the results of the categorisation of clinical control, as determined by the results of the owner questionnaire.

The results showed that although not perfect, both the Pre-Vetoryl Cortisol and the 3-hour post-Vetoryl cortisol were better at predicting clinical control, compared to the post-ACTH stimulation cortisol. When under controlled dogs were compared to controlled dogs both the sensitivity and specificity of the Pre-Vetoryl Cortisol was better than either the 3-hour post Vetoryl or the post-ACTH stimulation cortisol at differentiating between the two groups.

In the study there were eight results from dogs which had a post-ACTH stimulation cortisol result of ≤40 nmol/l, yet all dogs were well with no clinical signs at home of hypoadrenocorticism. It could be argued that these dogs should have their Vetoryl stopped or the dose reduced.

Follow-up of these eight dogs showed that none developed signs of hypoadrenocorticism, despite 50% having had no dose alteration. The other 50% had their Vetoryl dose reduced as the primary clinician was concerned about the possibility of hypoadrenocorticism, however there were no suggestive signs before or after the reduction.

These findings agree with another recent study[2] which showed that there is a small subset of dogs that are clinically well but have a low post-ACTH stimulation cortisol (test started 3-6 hours after the Vetoryl was given). This study demonstrated that repeating the ACTH stimulation test 9-12 hours after Vetoryl allowed for continued therapy without dose alteration if the post-ACTH simulation cortisol at this second point was above 55 nmol/l. No dogs in the follow-up period (>88 days) developed signs consistent with hypoadrenocorticism. As it is known that the cortisol 12 hours after Vetoryl is not significantly different from cortisol 24 hours after Vetoryl[3], this study is similar to the hypothesis of the Macfarlane et al 2016 paper[1]. If the Pre-Vetoryl Cortisol is ≥40 nmol/l and the patient is well, then a dose reduction may not be required (even if the post-ACTH stimulation cortisol contradicts this).

In the study, there were six test results that had a low Pre-Vetoryl Cortisol result (≤40 nmol/l). In all six cases, the dogs were clinically well according to the results of the owner questionnaire. In four of these dogs only the pre-Vetoryl result was low i.e. the post-ACTH stimulation performed later in the day was ≥40 nmol/l). In one of these dogs, the dose was not altered and the dog developed subsequent signs which were possibly consistent with hypoadrenocorticism (vomiting, diarrhoea and a low Na:K ratio) three months later. In another dog, the dose was reduced despite the owner reporting the dog was well. After the dose reduction the owner reported the dog had become much more interactive and had a brighter demeanour. Although not a definitive diagnosis, in both cases a low Pre-Vetoryl Cortisol was perhaps a more sensitive indicator that the dogs were being over-suppressed, than the post-ACTH stimulation cortisol.

The 3-hour post-Vetoryl cortisol was low in a large number of dogs in the study (31/110), which is similar to findings in other recent studies[4,5]. This means that it had very low specificity at highlighting dogs at risk of over-suppression.

Conclusions

- There are challenges in achieving stability of hyperadrenocorticism whilst maintaining safety. Monitoring of patient's condition should move towards a more comprehensive approach, placing more emphasis on at-home monitoring by the owner and not relying exclusively on laboratory measurements
- Whilst it could be seen as desirable to rely solely on owner observations, an objective tool is also required to ensure that treatment remains safe for those dogs whose owners' observational skills are inadequate or for those dogs who are developing sub clinical hypoadrenocorticism that could progress to an overt, life threatening disease. In addition, taking a good history takes time and this is not a luxury that veterinarians always have
- Traditionally the post-ACTH stimulation cortisol has been used as the primary laboratory tool to guide dose adjustments and to detect those dogs at risk of iatrogenic hypoadrenocorticism. There is now consistent evidence that the correlation between the post-ACTH stimulation cortisol and clinical control is poor. There is also evidence that supports the continued use of Vetoryl in a sub-set of dogs that are clinically well but have a low post-ACTH stimulation cortisol which had previously thought of as having sub-clinical hypoadrenocorticism and being at risk of overt clinical signs
- The Pre-Vetoryl Cortisol, although not perfect, is a promising new tool which has been shown to have better correlation with clinical control reported by owners. In addition, there are some instances when this result may be better than the post-ACTH stimulation cortisol at detecting iatrogenic hypoadrenocorticism. This test is easier, less expensive and has no side effects, offering a more practical solution for busy practice life
- Further studies into the use of the Pre-Vetoryl Cortisol (perhaps with haptoglobin) are ongoing to develop the optimal monitoring tools for both veterinarians and owners of dogs treated with Vetoryl

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VETORYL: Vetoryl contains Trilostane UK: POM-V IE: POM

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