PAPER

OPEN ACCESS

Pre-trilostane and three-hour post-trilostane cortisol to monitor trilostane therapy in dogs

L. Macfarlane, T. Parkin, I. Ramsey

Veterinary Record (2016) 179, 597
cite as doi: 10.1136/vr.103744

L. Macfarlane, North Downs Specialist Referrals, Surrey, UK
T. Parkin, Weipers Centre Equine Hospital, University of Glasgow, Glasgow, UK
I. Ramsey, Small Animal Hospital, University of Glasgow, Glasgow, UK

E-mail for correspondence: Lmacfarlane@ndsr.co.uk

This is a summary of a paper that is published in full at veterinaryrecord.bvapublications.com

Published Online First November 1, 2016

Context

The adrenocorticotrophic hormone (ACTH) stimulation test has been widely used and recommended as a monitoring tool for dogs receiving trilostane; however, it has never been validated for this purpose. As trilostane is relatively short acting, there could be variations in the results depending on the time since the last dose of trilostane and results may not reflect clinical control. Additionally, tetracosactide (synthetic ACTH) can be expensive in some countries and has had limited availability throughout much of Europe. Therefore, an effective monitoring tool for dogs receiving trilostane that does not require tetracosactide would be of considerable benefit.

This study aimed to compare one-hour post-ACTH stimulation cortisol concentration (post-ACTH), three-hour post-trilostane cortisol (also known as the baseline cortisol) and a novel monitoring method measuring cortisol concentration before trilostane was administered (pre-trilostane cortisol) with the scores provided from an owner-based questionnaire and with categories of clinical control based on those scores.

Main conclusion

Pre-trilostane and three-hour post-trilostane cortisol concentrations were better than the post-ACTH cortisol concentrations at discriminating between dogs with excellent control of their hyperadrenocorticism (HAC) and those that were undercontrolled. Of the two results, the pre-trilostane cortisol (using a cut-off of 138 nmol/l) was slightly better than the three-hour post-trilostane cortisol and had the added benefit of being more useful at suggesting possible oversuppression when it was less than 40 nmol/l. However, no cortisol result correlated well enough with the clinical score to be used as a stand-alone monitoring test.

Approach

A questionnaire for owners was developed to assess the clinical control of dogs with HAC receiving trilostane. The scores from this questionnaire were grouped into three categories of control based on the responses from a panel of veterinary surgeons. Two of these categories (poor control and reasonable control) were subsequently combined into one referred to as 'undercontrolled', while the third 'excellent control' was kept separate.

Owners were asked to complete this questionnaire at the time of presentation. At the same time a blood sample was taken before trilostane administration (pre-trilostane). The trilostane dose was then administered, along with the dog's normal meal provided by the owner. Three hours after the trilostane had been given, ACTH stimulation was performed by taking a blood sample (three-hour post-trilostane) and then administering 5 µg/kg of tetracosactide intravenously. A third blood sample was taken one hour after tetracosactide was administered (post-ACTH).

Results

In total, 110 tests from 67 individual dogs were included in this study. Seventeen of the tests from 11 dogs were assessed, from the owners' questionnaires, to have been from unwell dogs at the time of sampling and were removed from statistical analysis. None of the tests on unwell dogs had a pre-trilostane or post-ACTH cortisol concentration less than 40 nmol/l (thereby excluding iatrogenic hypocortisolism).

All three cortisol results from the remaining tests were significantly correlated to the total owner score, although the degree of correlation was not particularly strong. All three cortisol results were significantly lower in the dogs with excellent control compared to those that were undercontrolled. ROC curve analysis of pre-trilostane, three-hour post-trilostane and post-ACTH cortisol concentrations showed areas under the curves of 0.73, 0.73 and 0.64, respectively, suggesting that the first two measures were superior to the post-ACTH cortisol concentration. The three-hour post-trilostane cortisol was frequently less than 40 nmol/l, without any other evidence of oversuppression, suggesting that this measure was unsuitable as a monitoring method. Using a pre-trilostane cortisol of ≤138.0 nmol/l to distinguish those dogs that had excellent control from those that were undercontrolled gave a sensitivity of 55.4 per cent and a specificity of 86.5 per cent, whereas using post-ACTH stimulation cortisol of ≤130.0 nmol/l to distinguish those dogs that had excellent control from undercontrolled gave a sensitivity of 41.1 per cent and a specificity of 70.3 per cent.

In this study two dogs with pre-trilostane cortisol less than 40 nmol/l and post-ACTH stimulation cortisol greater than 40 nmol/l were identified. One dog responded positively to trilostane withdrawal and a further case had signs consistent with hypoadrenocorticism three months later.

Using univariate analysis, it was demonstrated that there were a number of factors that were significantly associated with the three cortisol results and the owners' scores. When these factors were carried forward to multivariable models, several remained significant but their effects were minor with the exception that pre-trilostane cortisol was 92.85 nmol/l higher in tests performed on entire female dogs when compared to the rest of the population. However, the small number of tests on such dogs (n=6) might account for this observation. Importantly, there was no effect of twice daily dosing or disease type on any of the cortisol results in the multivariable or univariate models, respectively. However, the number of confirmed adrenal dependent hyperadrenocorticism cases was too small to include in multivariable models.

Interpretation and significance of findings

The aim of trilostane therapy should be to satisfactorily control clinical signs, without resulting in iatrogenic hypocortisolism. This study questions the existing recommendations that post-ACTH stimulation cortisol should be used to both ensure adequate control and avoid oversuppression. Pre-trilostane cortisol was the objective measurement that had the most potential to balance safety with effective therapy. Further studies are needed with greater emphasis on the observations of owners and clinicians.