

Prednisolone therapy for atopic dermatitis is less effective in dogs with lower pretreatment serum 25-hydroxyvitamin D concentrations

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Conflict of Interest

No conflicts of interest have been declared.

Abstract

Serum 25-hydroxyvitamin D [25(OH)D] concentrations were measured in 20 dogs with atopic dermatitis prior to treatment with a standard therapeutic dosage of prednisolone (0.93–1.06 mg/kg) every other day for 5 weeks after 7 days of treatment with the same dosage once daily. The severity of their physical signs was scored before and 6 weeks after prednisolone treatment by the canine atopic dermatitis extent and severity index version 3 (CADESI-03) and the Edinburgh Pruritus Scale (EPS). The 20 dogs with atopic dermatitis that were treated with prednisolone did not have significantly lower serum concentrations of 25(OH)D than a group of 36 healthy dogs, and the physical severity of the atopic dermatitis was not correlated to pretreatment serum 25(OH)D concentrations. However, dogs which had a marked improvement of their physical signs, defined by a post-treatment EPS score of 0 and/or an 85% reduction in CADESI-03 score, had significantly higher pretreatment serum 25(OH)D concentrations than dogs with a suboptimal response ($P = 0.003$ and $P = 0.03$, respectively). Serum 25(OH)D concentrations were also measured in a previously published cohort of atopic dogs that were treated with ciclosporin. This cohort of dogs was recruited in a similar time frame to the prednisolone-treated dogs, and all samples were handled in the same way. In contrast to the prednisolone-treated dogs, there was no significant difference in 25(OH)D concentrations in dogs

that responded optimally to ciclosporin compared with suboptimal responders. Additional studies are required to establish whether vitamin D has a synergistic therapeutic effect with prednisolone in dogs with atopic dermatitis.

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Introduction

Canine atopic dermatitis (AD) is defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens.¹ The pathogenesis of canine AD and the factor(s) which predispose individual dogs to the development of disease have been the subject of considerable study, but much remains to be evaluated.^{2,3}

Currently, medications with good evidence⁴ of efficacy in canine AD include topical⁵ and systemic glucocorticoids⁶ and calcineurin inhibitors, such as oral ciclosporin⁷ (CsA) and topical tacrolimus.⁸ Allergen-specific immunotherapy may also be helpful in reducing the recurrence of physical signs upon subsequent exposure to environmental allergens to which the patient is hypersensitive.⁹ Although most cases of AD can be successfully managed, it remains difficult to predict which individual dogs will respond to therapy prior to commencement of treatment.

Traditionally, it has been considered that the main physiological function of vitamin D, in conjunction with parathyroid hormone and calcitonin, is to closely regulate plasma calcium concentrations and maintain skeletal health,¹⁰ but a wide variety of other nonskeletal functions for vitamin D have now been described.^{11,12} Over the past decade, vitamin D deficiency, typically defined as low serum concentrations of the major circulating form of vitamin D, 25-hydroxyvitamin D [25(OH)D], has been associated in humans with higher incidences of many medical conditions, including hypertension,¹³ diabetes,¹⁴ cardiovascular disease,¹⁵ cancer¹⁶ and infectious diseases.¹⁷ Crucially, vitamin D supplementation appears to mitigate the incidence of, and adverse outcomes from, many of these diseases.¹⁸

The role of vitamin D in influencing the pathogenesis and outcome of a range of human allergic conditions has recently received considerable attention. Several studies have indicated that vitamin D deficiency may be implicated in the pathogenesis of AD. For example, it has been

shown that infants born to mothers with low vitamin D intake^{19,20} or low fish consumption during pregnancy²¹ have an increased prevalence of AD. Moreover, cross-sectional studies have shown a greater risk of AD in infants born in autumn and winter compared with those born in spring and summer.²² A latitude effect on the prevalence of AD in children has also been reported.²³ A fivefold increase in the likelihood of AD development was found in obese patients with vitamin D deficiency compared with their vitamin D-replete counterparts.²⁴ Furthermore, Sidbury and colleagues reported beneficial effects on AD from oral supplementation with vitamin D in children with winter-related worsening of AD.²⁵ Finally, a recent study of 37 consecutively recruited children with AD found an inverse correlation between serum concentrations of 25(OH)D and severity of disease.²⁶ However, it is important to acknowledge that there is not an absolute consensus that suboptimal vitamin D concentrations are important in human AD, because Back and colleagues demonstrated that higher vitamin D intake during the first year of life was significantly correlated to atopic manifestations at 6 years of age.¹⁹

The present study had three central hypotheses, as follows: firstly, we predicted that serum 25(OH)D concentrations would be significantly lower in dogs with AD compared with healthy dogs; secondly, that there would be an inverse relationship between pretreatment serum 25(OH)D concentrations and AD severity; and finally, that pretreatment serum 25(OH)D concentrations would be predictive of the therapeutic response to prednisolone treatment. This study set out to recruit a cohort of dogs with AD, measure serum 25(OH)D concentrations pretreatment and then monitor the clinical response to a standard dose of prednisolone.

Materials and methods

Study design

This study was undertaken in the Dermatology Unit of the Royal (Dick) School of Veterinary Studies [R(D)SVS], The University of Edinburgh, between January 2009 and January 2010. Consecutive dogs with a diagnosis of AD according to well-established criteria²⁷ were considered eligible for the study. Diagnoses physically resembling AD (e.g. ectoparasitic infestations or cutaneous adverse food reactions) were ruled out using standard diagnostic and therapeutic methods prior to inclusion in the study. Dogs with physical and laboratory evidence of secondary skin infections, e.g. bacterial pyoderma or *Malassezia* dermatitis, were treated to resolution prior to inclusion and, using topical therapy with a shampoo containing 2% chlorhexidine and 2% miconazole (Malaseb®; Dechra Veterinary Products, Shrewsbury, Shropshire, UK), as required if relapses occurred during the study. In addition, dogs with AD which had received glucocorticoids by any route in the previous 12 weeks were excluded.

Following a standard therapeutic cascade, 20 consecutive atopic dogs were treated with prednisolone if the preparation of an allergen-specific immunotherapy vaccine was pending or immunotherapy had been discontinued owing to lack of efficacy. No other systemic treatments, including essential fatty acids, were allowed. Prednisolone (Prednicare®; Animalcare Limited, York, UK) was given at or as near as possible to the dosage of 1 mg/kg (range 0.93–1.06 mg/kg) every other day for 5 weeks after 7 days of treatment with the same dosage once daily. A serum sample was harvested at the time of definitive diagnosis and prior to prednisolone therapy for standard biochemical tests prior to beginning treatment, and surplus serum was retained for subsequent batch analysis of 25(OH)D.

The response to treatment was assessed by scoring the skin lesions of all dogs on days 0 and 42 using the canine atopic dermatitis extent and severity index version 3 (CADESI-03) as previously described.²⁸ All such responses were assessed by one investigator (M.K.). The owners used the Edinburgh Pruritus Scale (EPS) to score the pruritus on a numerical scale (0–5) annotated with specific behavioural descriptors as previously reported by our group.²⁹ For the purposes of this study, a dog with an optimal response was defined in the EPS scoring scale as one whose post-treatment score was 0 and in the CADESI-03 scale as one whose post-treatment score had reduced by more than 85%.

Surplus serum from blood samples taken from healthy dogs ($n = 36$) for a primary clinical purpose (e.g. routine health check, packed cell volume analysis prior to blood donation or rabies serology) were analysed as a control group. All of these dogs had no history of previous skin disease, were considered healthy by their owners and were normal on physical examination. In order to examine whether serum 25(OH)D concentrations were predictive of clinical response to a range of medications, we also measured serum 25(OH)D concentrations in a previously published cohort of atopic dogs that were treated with CsA.³⁰ This cohort of dogs was recruited in a similar time frame to the prednisolone-treated dogs, and all samples were handled in the same way. The response to CsA therapy was evaluated by the same person as the prednisolone-treated dogs (M.K.). As with the prednisolone cohort, the response to CsA therapy was assessed by scoring the skin lesions of all dogs on days 0 and 42 using the CADESI-03, and the owners used the EPS to score the pruritus. Again, as with the prednisolone group, a dog with an optimal response to CsA was defined in the EPS scoring scale as a dog whose post-treatment score was 0 and in the CADESI-03 scale as a dog whose post-treatment score had reduced by more than 85%.

Serum samples from all three groups were frozen within 2 h of collection and stored at -70°C before being sent on dry ice to the laboratory for batch analysis of 25(OH)D. Serum concentrations of 25(OH)D were measured and validated as described in detail elsewhere.^{31,32} Briefly, samples were extracted using acetonitrile and applied to C18 Silica Sep-paks (Waters Ltd, Elstree, UK). Separation of metabolites was by straight phase high-performance liquid chromatography (Waters Associates, Milford, MA, USA) using a Hewlett-Packard Zorbax-Sil Column (Hichrom, Reading, UK) eluted with hexane:propan-2-ol:methanol (92:4:4). Serum 25(OH)D₂ and 25(OH)D₃ were measured separately by application to a second Zorbax-Sil (Agilent Technologies, Stockport, UK), column eluted with hexane:propan-2-ol (98:2), quantified by ultraviolet absorbance at 265 nm and corrected for recovery [sensitivity 2 ng/mL (5 nmol/L), intra- and interassay coefficients of variation 3.0 and 4.2%, respectively].^{33,34} Results are expressed as total 25(OH)D (reference range 19.3–43.6 ng/mL). The assay laboratory is accredited to the International Organization for Standardization (ISO) 9001:2000 and ISO 13485:2003 and participates in the Vitamin D External Quality Assessment Scheme (DEQAS). All samples from prednisolone, CsA and healthy dog groups were analysed for 25(OH)D at the same time points. Analysers were blinded to CADESI-03 and EPS scores and clinicians were blinded to 25(OH)D scores until the end of the study.

Investigations were performed in client-owned dogs with owner permission. The study was approved by The University of Edinburgh's Ethical Review Committee through the R(D)SVS's Veterinary Ethical Review Committee.

Statistical analyses

Serum 25(OH)D concentrations were compared between dogs with AD and healthy dogs by Student's unpaired *t*-tests. The association between 25(OH)D concentrations and CADESI-03 and EPS scores were tested by Spearman rank correlation tests. Pretreatment 25(OH)D concentrations were compared between responder and nonresponder dogs by Student's unpaired *t*-tests. The CADESI-03 and EPS scores were compared between prednisolone and CsA cohorts by Mann-Whitney *U*-tests. The proportion of dogs which responded was compared between dogs treated with prednisolone

or CsA by Fisher's exact tests. A P -value of <0.05 was used as the criterion for statistical significance. Statistical analyses were performed with GraphPad Prism (GraphPad Software, La Jolla, CA, USA).

Results

Signalment and treatment efficacy

The 20 dogs in the prednisolone group comprised cross-bred (2), Jack Russell terrier (2), German shepherd dog (2), bullmastiff (1), West Highland white terrier (2), King Charles spaniel (1), English setter (1), boxer (3), Airedale terrier (1), Labrador retriever (1), golden retriever (1), Border terrier (1) and Staffordshire bull terrier (2). In summary, 13 were male (seven castrated) and seven female (six ovariectomized). Their ages ranged between 1.1 and 8.5 years (mean 3.4 years) and they weighed between 6.8 and 52.0 kg (mean 22.3 kg). Details of the animals in the CsA group are reported by Kovalik *et al.*³⁰ There were 16 dogs comprising 10 breeds in the CsA group. Ten were male (nine castrated) and six female (five ovariectomized). Their ages ranged between 1.1 and 9.6 years (mean 4.2 years) and they weighed between 5.6 and 56 kg (mean 25.2 kg). The healthy control group consisted of 36 dogs with ages ranging between 5 months and 10 years (mean 2.7 years). The breeds were as follows: English springer spaniel ($n = 5$), Labrador retriever (4), Cavalier King Charles spaniel (3), Staffordshire bull terrier (2), lurcher (2), German shepherd dog (2), Newfoundland (2), Hungarian vizsla (1), golden retriever (1), Pyrenean mountain dog (1), cocker spaniel (1), boxer (1), greyhound (1), Border terrier (1), Doberman pinscher (1), Rottweiler (1), beagle (1) and cross-bred (6). There was no significant difference in ages between the three groups ($P = 0.28$). The proportion of females was not significantly different between the CsA and prednisolone group ($P = 1.0$).

Serum 25(OH)D concentration and disease presentation/treatment efficacy

The mean pretreatment serum 25(OH)D concentration of prednisolone-treated dogs was 30.3 ng/mL, compared with 30.8 ng/mL in the healthy dogs, and there was no significant difference between the two groups ($P = 0.89$; Figure 1). There was no significant correlation between 25(OH)D concentrations and CADESI-03 ($r = 0.16$, $P = 0.49$; Figure 2a) and 25(OH)D concentrations and EPS ($r = 0.18$, $P = 0.44$; Figure 2b) in dogs treated with prednisolone. The serum 25(OH)D concentrations of dogs that had responded optimally to prednisolone was significantly higher when scored by both the CADESI ($P = 0.03$; Figure 3a) and EPS ($P = 0.003$; Figure 3b) compared with dogs that had a suboptimal response.

The serum concentrations of 25(OH)D pretreatment were not significantly different between the prednisolone and CsA (mean = 30.0 ng/mL) treatment groups ($P = 0.90$). The CADESI-03 scores were not significantly different between the prednisolone and CsA treatment groups, either before ($P = 0.56$) or after treatment ($P = 0.64$). Likewise, EPS scores were not significantly different between the prednisolone and CsA treatment either before ($P = 0.13$) or after treatment ($P = 0.27$). The proportion of dogs classified as responders by the CADE-

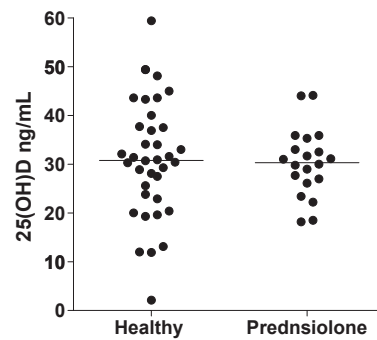


Figure 1. Serum 25-hydroxyvitamin D [25(OH)D] concentrations in healthy dogs and dogs with atopic dermatitis, which were subsequently treated with prednisolone.

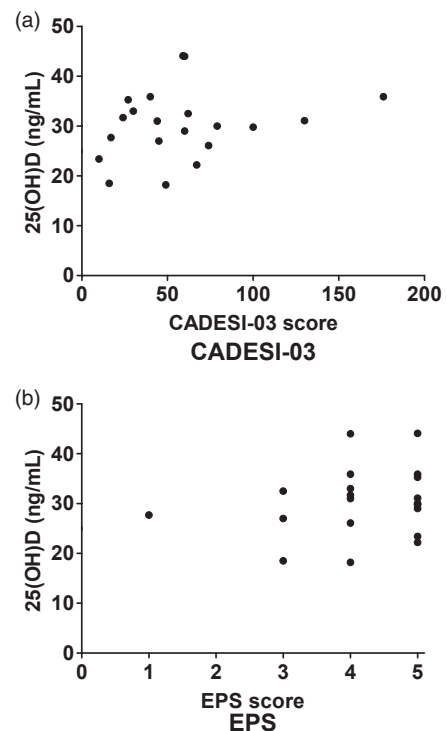


Figure 2. Plots of serum 25(OH)D concentrations and canine atopic dermatitis extent and severity index version 3 (CADESI-03 scores) (a) and Edinburgh pruritus scale (EPS) values (b) in dogs treated with prednisolone.

SI-03 (prednisolone $n = 8$ of 20, CsA $n = 4$ of 16, $P = 0.31$) and EPS (prednisolone $n = 11$ of 20, CsA $n = 7$ of 16, $P = 0.74$) was not statistically different between the prednisolone- and CsA-treated dogs. Dogs that responded optimally to CsA treatment did not have a significantly different 25(OH)D concentration to suboptimal responders as judged by the CADESI-03 ($P = 0.93$; Figure 4a) and EPS ($P = 0.47$; Figure 4b). Indeed, the mean serum concentration of 25(OH)D in CsA-treated optimal responders was lower than in suboptimal responders as measured by both the CADESI-03 and EPS scores (Figure 4a,b).

Discussion

This study has demonstrated that serum 25(OH)D concentrations in dogs with AD were not significantly

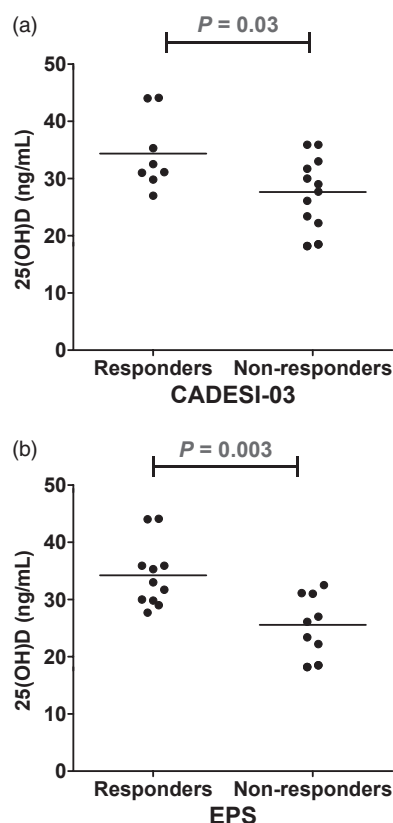


Figure 3. Serum 25(OH)D concentrations in dogs with optimal and suboptimal responses in dogs treated with prednisolone as measured by the CADESI-03 (a) and the EPS (b).

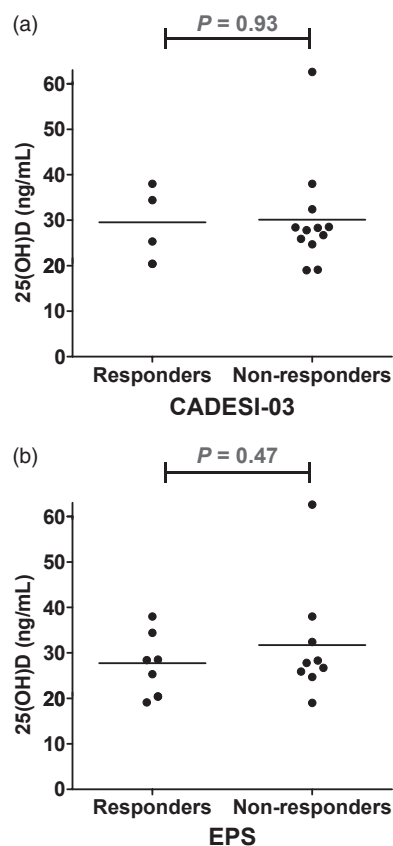


Figure 4. Serum 25(OH)D concentrations in dogs with optimal and suboptimal responses treated with ciclosporin A as measured by the CADESI-03 (a) and the EPS (b).

different from those in healthy dogs and that there was no inverse relationship between serum 25(OH)D concentrations and increasing disease severity. This contrasts with previous studies in humans,²⁶ which linked vitamin D deficiency to higher prevalence and increasing severity of AD.^{20–23} The main finding of this study is that serum 25(OH)D concentrations were higher in dogs that responded optimally to prednisolone treatment compared with dogs experiencing a suboptimal response when judged by two different clinical scoring systems. Furthermore, we demonstrated that this was not a universal finding in all treatments, because a disease severity-matched cohort of dogs with AD treated with CsA did not show such a difference in pretreatment 25(OH)D concentrations between optimal and suboptimal responders. This suggests that vitamin D and prednisolone, but not CsA, may have a synergistic effect in the management of AD.

Both glucocorticoids and vitamin D can profoundly modulate the immune response. Glucocorticoids are potent immunosuppressive and anti-inflammatory drugs, which are efficacious in the treatment of both T helper 1 (Th1)- and T helper 2 (Th2)-associated inflammatory diseases.^{35,36} They inhibit T cell proliferation and cytokine production and impair the ability of antigen presenting cells to activate T cells.³⁷ It has been shown that glucocorticoids enhance the production of the immunosuppressive cytokine interleukin (IL)-10 and reduce IL-4, IL-5 and IL-13 production in human CD4⁺ and CD8⁺ T cells.³⁸ Glucocorticoids are known to inhibit the activation and action of important transcription factors involved in cytokine gene regulation, such as nuclear factor of activated T cells, activator protein-1 and nuclear factor- κ B.^{36,39}

Vitamin D has also been shown to have a marked ability to reduce pathogenic immune responses in humans through a wide range of mechanisms.^{40–42} For example, *in vitro* studies have shown that 1,25(OH)₂D, the most metabolically active form of vitamin D, induces cathelicidin expression in keratinocytes, which enhances antimicrobial activity against *Staphylococcus aureus*.⁴⁰ In addition, cathelicidin specifically decreases T lymphocyte homing into the skin.^{43,44} Yamanaka and colleagues recently reported that 1,25(OH)₂D inhibits skin infiltration of CD4⁺ T cells by suppressing cutaneous lymphocyte-associated antigen expression on T cells.⁴⁴ Vitamin D also inhibits T cell proliferation,⁴¹ in particular the ability of Th1 cells to produce interferon- γ and IL-2 and activate macrophages,⁴⁵ and the capacity of T helper 17 (Th17) cells to produce IL-17 and IL-22.⁴⁶ This is significant because these events have been postulated to be important in the chronic and acute phases of AD,⁴⁷ respectively. In addition, CD4⁺CD25⁺ regulatory T cells (Treg) are also amplified by 1,25(OH)₂D,⁴² with consequent increased production of IL-10, which further reduces development of Th1 and Th17 responses.⁴⁸

Whilst both vitamin D and glucocorticoids individually can have an immunosuppressive effect, there are increasing data to suggest that there is a synergistic relationship between vitamin D and dexamethasone. Consistent with our study, which found that low serum vitamin D status is associated with an impaired ability of prednisolone to effect an optimal therapeutic response in dogs with AD, it has been shown that the use of inhaled and oral

glucocorticoids and the total glucocorticoid dose has a significant inverse correlation with 25(OH)D concentrations in children with asthma.⁴⁹ These findings support an earlier study which also reported that lower serum 25(OH)D concentrations are associated with increased markers of asthma severity in children.⁵⁰ In addition, Searing and colleagues found, in an experimental model of glucocorticoid resistance, that dexamethasone did not inhibit T cell proliferation, but the addition of vitamin D to dexamethasone resulted in a significant dose-dependent suppression of cell proliferation.^{49,50} The potential synergistic effect of vitamin D and glucocorticoids has been examined in patients with glucocorticoid-resistant asthma.⁵¹ This study found that the addition of vitamin D and dexamethasone to cultures of CD4⁺ regulatory T cells from patients with glucocorticoid-resistant asthma enhanced IL-10 secretion to concentrations observed in cells from glucocorticoid-sensitive patients treated with dexamethasone alone. In addition, vitamin D blocked dexamethasone-induced downregulation of the glucocorticoid receptor in CD4⁺ T cells from healthy volunteers.

Dogs with AD treated with standard dosages of prednisolone respond variably. With respect to the owner's semi-objective perception of pruritus, a post-treatment EPS score of 0, defined to the client as 'a normal dog: the dog is no more itchy than before the disease began', was taken to be an optimal response in this study. As CADESI-03 scores very rarely returned to 0, for the objective changes in physical signs, this degree of cut-off was deemed to be unhelpful in distinguishing between responders and suboptimal responders. Therefore, a cut-off of an 85% reduction in CADESI-03 score was used to distinguish between the two groups.

The finding that serum 25(OH)D concentrations are helpful in identifying good versus suboptimal responders at the time of diagnosis is encouraging and may be of prognostic value to clinicians treating canine AD with prednisolone. If larger, subsequent studies confirm our findings, additional studies to examine whether the efficacy of prednisolone therapy can be enhanced by supplementing dogs with low serum concentrations of 25(OH)D with vitamin D would be of considerable interest. Based on the findings of the present study, supplementation of all atopic dogs with vitamin D would be premature. It is also important to acknowledge that oversupplementation with vitamin D can lead to significant morbidity in dogs.⁵²

A limitation of our study is the relatively small group sizes; the CsA-treated group had slightly fewer dogs than the prednisolone-treated group; and there were a large number of different breeds within and between the three populations. In addition, it would have been optimal if dogs had been randomized to receive either CsA or prednisolone at the time of diagnosis rather than being recruited in two consecutive and distinct cohorts. However, the close matching of the two cohorts in terms of disease severity at diagnosis, time of recruitment, response to therapy and proportion of dogs that responded optimally reduces the potential risk of bias between the two treatment groups. In addition, the serum 25(OH)D concentrations in both cohorts were measured in the same batch analysis by colleagues blinded to clinical scores in an attempt to limit any chance of bias.

In summary, we found no difference in serum 25(OH)D concentrations between dogs with AD and healthy dogs and no correlation between vitamin D deficiency and severity of AD in dogs. However, dogs with an optimal response had higher serum 25(OH)D concentrations than dogs with a suboptimal response in dogs treated with prednisolone, but not CsA. Additional studies are required to establish whether vitamin D does have a synergistic therapeutic effect with prednisolone in dogs with AD. It would be particularly valuable to examine whether vitamin D supplementation improves the clinical response to prednisolone in dogs with atopy and suboptimal pretreatment serum 25(OH)D concentrations.

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Résumé Les concentrations de 25(OH)D sérique ont été mesurées chez 20 chiens atopiques avant un traitement à une dose standard thérapeutique de prednisolone (0.93–1.06 mg/kg) un jour sur deux pendant 5 semaines après 7 jours de traitement à la même dose une fois par jour. La sévérité de leurs signes cliniques a été noté avant et 6 semaines après le traitement à la prednisolone par le CADESI-3 (canine atopic dermatitis extent and severity index version 3) et l'EPS (Edinburgh Pruritus Scale). Les 20 chiens atopiques traités à la prednisolone n'ont pas eu de concentrations significativement plus basses de 25(OH)D qu'un groupe de 36 chiens sains et la sévérité clinique de la dermatite atopique n'était pas corrélée aux concentrations de prétraitement de 25(OH)D sériques. Cependant, les chiens ayant une amélioration marquée de les signes cliniques, défini par un score EPS post-traitement de 0 et/ou une réduction de 85% du CADESI-3, avaient des concentrations de 25(OH)D sériques prétraitement significativement plus élevés que les chiens avec une réponse sub-optimale ($P = 0.003$ et $P = 0.03$, respectivement). Les concentrations de 25(OH)D sérique ont été également mesurées dans une cohorte précédemment publiée de chiens atopiques traités à la ciclosporine (CsA). Cette cohorte de chiens était recrutée dans le même temps que les chiens traités à la prednisolone et tous les échantillons ont été prélevés de la même façon. A la différence des chiens recevant de la prednisolone, il n'y avait aucune différence significative entre les concentrations de 25(OH)D des chiens répondant de façon optimale à la CsA comparé aux chiens répondant de façon sub-optimale. Les études supplémentaires sont nécessaires pour établir si la vitamine D a un effet thérapeutique synergique avec la prednisolone chez les chiens atteints de dermatite atopique.

Resumen Se midieron las concentraciones en suero de D (25 (OH) D) en 20 perros con dermatitis atópica antes del tratamiento con una dosificación terapéutica estándar de prednisolona (0,93–1,06 mg/kg) en días alternos durante 5 semanas después de 7 días de tratamiento con la misma dosificación una vez al día. La severidad de los signos clínicos fue obtenida antes y 6 semanas después del tratamiento con prednisolona, de acuerdo con la versión canina 3 (CADESI-03) del grado de dermatitis atópica y del índice de severidad, y según la escala de prurito de Edimburgo (EPS). Los 20 perros con dermatitis atópica que fueron tratados con prednisolona no tenían concentraciones perceptiblemente más bajas en el suero de 25 (OH) D en comparación con un grupo de 36 perros sanos y la severidad clínica de la dermatitis atópica no se correlacionó con las concentraciones en el suero de 25 (OH) D antes del tratamiento. Sin embargo, los perros que tenían una mejora marcada de sus lesiones clínicas, definida por un valor post-tratamiento de EPS de 0 y/o una reducción del 85% en el valor de CADESI-03, tenían concentraciones perceptiblemente más altas en el suero de 25 (OH) D pre-tratamiento en comparación con perros que presentaron una respuesta sub-óptima ($P = 0,003$ y $P = 0,03$, respectivamente). Las concentraciones del suero de 25 (OH) D también fueron medidas en una cohorte previamente publicada de perros atópicos que fueron tratados con ciclosporina (CsA). Esta cohorte de perros fue reclutada en un marco de tiempo similar al grupo tratado con prednisolona y todas las muestras fueron manejadas de la misma forma. En contraste con los perros tratados con prednisolona, no hubo ninguna diferencia significativa en las concentraciones de 25 (OH) D en los perros que presentaron respuesta óptima a CsA comparado con aquellos que presentaron una respuesta subóptima. Se requieren estudios adicionales para establecer si la vitamina D puede tener un efecto terapéutico sinérgico con la prednisolona en perros con dermatitis atópica.

Zusammenfassung Es wurden Serum D (25(OH)D) Konzentrationen bei 20 Hunden mit atopischer Dermatitis vor einer Behandlung mit einer Standarddosis von Prednisolon (0,93–1,06 mg/kg) jeden zweiten Tag fünf Wochen lang gemessen, sowie nach 7 Tagen einer Behandlung mit derselben Dosis einmal täglich. Das Ausmaß der äußerlichen Symptome wurde vor und 6 Wochen nach der Prednisolon-Behandlung mittels Canine Atopic Dermatitis Extent and Severity Index Version 3 (CADESI-03) und der Edinburgh Pruritus Skala (EPS) bewertet. Die 20 Hunde mit atopischer Dermatitis, die mit Prednisolon behandelt worden waren, zeigten keine signifikante Erniedrigung der Serumwerte von 25(OH)D im Vergleich mit einer Gruppe von 36 gesunden Hunden und der physische Schweregrad der atopischen Dermatitis korrelierte nicht mit den Serumwerten von 25(OH)D vor der Behandlung. Hunde, die jedoch eine deutliche Verbesserung ihrer physischen Symptome zeigten, was durch EPS Werte von 0 nach der Behandlung und/oder einer 85%igen Reduzierung der CADESI-03 Werte definiert wurde, hatten vor der Behandlung signifikant höhere Serumkonzentrationen von 25(OH)D als Hunde mit einer weniger guten Reaktion ($P = 0,003$ bzw. $P = 0,03$). Die Serumkonzentrationen von 25(OH)D wurden ebenso in einer bereits publizierten Studie mit atopischen Hunden, die mit Ciclosporin (CsA) behandelt worden waren, gemessen. Diese Hundegruppe wurde in einem ähnlichen Zeitrahmen rekrutiert, wie die mit Prednisolon behandelten Hunde und die Proben wurden alle in der gleichen Weise gehandhabt. Im Gegensatz zu den mit Prednisolon behandelten Hunden, bestand bei den 25(OH)D Serumkonzentrationen von Hunden, die auf CsA optimal reagierten kein Unterschied zu den Hunden mit weniger guten Reaktionen. Es sind weitere Studien notwendig, um festzustellen, ob Vitamin D eine synergistische therapeutische Rolle bei der Behandlung mit Prednisolon von Hunden mit atopischer Dermatitis spielt.

要約 アトピー性皮膚炎の犬 20 頭を用いてプレドニゾロン (0.93–1.06 mg/kg) を 1 日 1 回 7 日間投与後、隔日投与を 5 週間行い、その治療前と治療後に血清ビタミン D₂₅(OH)D 濃度を測定した。臨床症状の重症度は治療前とプレドニゾロンでの治療 6 週後に犬アトピー性皮膚炎の病変範囲と重症度指数 ver. 3 (CADESI-03)、およびエジンバラ掻痒スケール (EPS) でスコア化した。プレドニゾロンで治療した 20 頭のアトピー性皮膚炎の犬の 25 (OH)D 血清濃度は 36 頭の健常犬群に比較して有意に低くはなく、アトピー性皮膚炎の臨床重症度と治療前の血清 25 (OH)D 濃度には相関はみられなかった。しかし、治療後の EPS スコアが 0、さらに/あるいは CADESI スコアが 85%低下した、すなわち臨床症状が大幅に改善した犬では、不十分な反応を示した犬(それぞれ、 $p=0.003$ and $p=0.03$)に比べて治療前血清 25 (OH)D 濃度が有意に高かった。血清 25 (OH)D 濃度はシクロスポリン (CsA) で治療したアトピー犬の報告でも測定されている。この犬群はプレドニゾロンで治療した犬と同時期に集められ、サンプルは同様に処理した。プレドニゾロンで治療した犬に比較して、CsA で最適な反応を示した犬の 25 (OH)D 濃度は不十分な反応を示した群に比べて有意な差は認められなかった。ビタミン D がプレドニゾロンで治療するアトピー性皮膚炎の犬において相乗治療効果があるか証明するにはさらなる研究が必要である。