

Vitamin D therapy in canine atopic dermatitis

Tina Kotnik

ALLERGIC diseases are caused by an exaggerated and often deleterious response of the immune system to specific antigens.¹ Canine atopic dermatitis is a genetically predisposed, inflammatory and pruritic allergic skin disease, which causes clinical signs associated with an immunoglobulin E (IgE)-mediated response towards environmental allergens. The disease may have a strong impact on the quality of life of both diseased dogs and their owners.²

The first clinical signs of canine atopic dermatitis usually begin at between six months and three years of age. Pruritus is usually the first sign noticed by the dog owners, accompanied by erythema and papules on body sites with a predilection for the disease. Trauma through scratching and biting with excoriations and alopecia follow, and recurrent skin or ear infections with lichenification and hyperpigmentation are common. Rhinitis or conjunctivitis may accompany skin inflammation, especially in response to seasonal changes. Common sites for lesions on the body are the face, concave ear pinnae and ear canals, the ventral trunk and medial and flexural aspects of extremities and paws.³

Practitioners should make a diagnosis of canine atopic dermatitis using the dog's disease history, clinical signs and by ruling out other possible conditions that can mimic the disease. The most common diseases that have similar clinical signs to canine atopic dermatitis include parasitic skin diseases (especially scabies) and infectious skin diseases (*Staphylococcus*- and *Malassezia*-provoked skin inflammation). Allergy tests should be used after the diagnosis has been made. Testing is performed only to detect the allergens to be avoided or included in allergen-specific immunotherapy (ASIT),³ which is the practice of administering gradually increasing quantities of an allergen extract to an allergic subject to improve the clinical signs associated with exposure to the causative allergen.⁴

Treatment of canine atopic dermatitis traditionally consists of symptomatic treatment, allergen avoidance and ASIT.⁵ While allergen avoidance works best for food allergies, ASIT is the treatment of choice for canine atopic dermatitis. The success rate of ASIT in canine atopic dermatitis is usually

around 70 per cent,⁶ with some dogs remaining unresponsive to therapy. ASIT cannot be used to treat dogs with atopic-like dermatitis because, although dogs with atopic-like dermatitis have the same pattern of clinical signs as those with canine atopic dermatitis, their IgE response to environmental or other allergens cannot be detected by usual methods. Consequently, it is not possible to detect the allergens that could be used for ASIT.³ For these dogs, the only treatment of choice is symptomatic therapy.

Controlled, good quality clinical trials have shown that oral and topical glucocorticoids and oral microemulsified ciclosporin are the drugs of choice in the treatment of canine atopic dermatitis.⁷ As with all drugs, these may cause adverse side effects depending on the dose and the regimen used. It has been well-established that, compared to using only one therapy, symptomatic drugs are more efficacious and have less negative side effects when they are used in combination with other drugs.⁵ Research on newly synthesised compounds or on the novel use of 'old drugs' in the treatment of canine atopic dermatitis is therefore welcome.

In a study by Klinger and others,⁸ summarised on page 406 of this week's issue of *Vet Record*, vitamin D supplementation was evaluated under controlled conditions in the treatment of canine atopic dermatitis. Vitamin D is a highly potent hormone, which is naturally produced by UV-exposed skin but can also be obtained through foods, such as fish oils or beef liver. Vitamin D has mostly been used to prevent rickets in children, a disease that was

WHAT YOU NEED TO KNOW

- Canine atopic dermatitis is one of the most common skin diseases in small animal practice.
- Vitamin D has previously not been used in the treatment of canine atopic dermatitis, but was shown to be an effective drug for the treatment of canine atopic dermatitis in this study.
- Vitamin D could be used as an adjunctive therapy in canine atopic dermatitis; however, dogs on vitamin D should be monitored regularly until further studies evaluate long term safety.

RESEARCH COMMENT



Case of chronic canine atopic dermatitis with lichenification and hyperpigmentation of the skin

formally characterised in the Victorian era.⁹ Since then, research has indicated that vitamin D might also guard against diseases such as cancer and hypertension.¹⁰

The aim of the Klinger study⁸ was to evaluate whether vitamin D (cholecalciferol) and the vitamin D receptor analogue paricalcitol improved clinical signs and skin barrier function in dogs with canine atopic dermatitis. Vitamin D seems to be involved in the skin barrier function, the immune response and the production of antimicrobial peptides.¹¹⁻¹³ Dysfunction of the skin barrier is nowadays broadly studied in human and canine atopic dermatitis¹⁴ and its role in the pathogenesis of canine atopic dermatitis can be explained by the so-called 'outside-inside-outside' theory. The theory suggests that a primary defect in the epidermal barrier leads to a higher penetration of allergens and microbes that overstimulate the local immunity (innate and adaptive) of the individual. Such excessive stimulation triggers the release of inflammatory mediators that further exacerbate the barrier dysfunction.¹⁵ Antimicrobial peptides (AMPs) also play an important role in skin barrier function through innate immunity in human and canine atopic dermatitis,¹⁶ so vitamin D might contribute to prevention of recurrent pyoderma, one of the regular

phenomenon in canine atopic dermatitis.¹⁷

The aim of the Klinger study⁸ is in agreement with recently suggested clinical trials of canine atopic dermatitis that focus on the development of drugs able to restore the skin barrier and increase natural defences against pathogenic organisms.¹⁸ The study was designed as a three-arm randomised, double-blinded, placebo-controlled, cross-over trial. This design enabled the authors to avoid biases that frequently compromise the reliability of results from clinical trials. Selection and detection biases were avoided by the use of computerised randomisation: selection bias occurs when a researcher influences allocation to comparison groups and detection bias occurs when a researcher influences the assessment of an outcome. Design of a cross-over trial enabled the authors of this study to avoid performance bias (ie, unequal provision of care) and also meant that all of the dogs included in the study received each research treatment, including the placebo, with a wash out period of eight weeks between the treatments. The adequacy of the chosen period was statistically confirmed.

The double-blinded design ensured that neither owners of the dogs or research staff were aware of the treatment they were using at each time point of the study. It also allowed research staff, as well as dog owners, to avoid attrition and detection bias, as this may happen by intentional distorted assessment of drug efficiency and side effects. The placebo control additionally prevented detection bias in this study. The design of this study is therefore to be welcome because it fulfils the highest design quality recommended for clinical trials.¹⁹

Although an advantage of the cross-over design was the possibility to include a low number of dogs, the authors pointed out that a weakness of the study was that the number of dogs completing all three arms of the cross-over study was very small. They commented that 'the main reason for the lack of compliance was the time consuming study protocol that required a multitude of visits, particularly in the first two weeks of each arm, leading to a large drop-out during the study after the first and particularly the second arm'.

As a primary outcome of the Klinger study,⁸ cholecalciferol decreased both pruritus and also acute and chronic skin lesions in dogs with atopic dermatitis. The improvement in the dogs' pruritus was significantly correlated with an increase in serum calciferol metabolite levels. No adverse clinical effects or serum electrolyte abnormalities were noticed with cholecalciferol administration. Given



Infection by *Staphylococcus pseudintermedius* in a dog with atopic dermatitis

that severe adverse effects, such as hypercalcaemia, have been associated with cholecalciferol therapy in people,²⁰ vitamin D receptor agonists, such as paricalcitol, have been introduced to human therapy, producing less hypercalcaemic side effects than cholecalciferol. However, contrary to the results from studies in people, hypercalcaemia was observed in half of the dogs treated with paricalcitol in the Klinger study. These results indicate that paricalcitol in dogs probably has a more calcaemic effect than cholecalciferol. Nevertheless, the authors recommend that dogs on vitamin D should be monitored regularly until further studies evaluate long term safety.

Given the increasing prevalence of allergic disease in people and animals, research on drugs that can improve the management of this chronic disease is to be welcomed. Klinger's study reports novel data that can influence management of canine atopic dermatitis in the future.

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