Using essential fatty acids in canine atopic dermatitis

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Canine atopic dermatitis (CAD) is a genetically predisposed inflammatory and pruritic skin disease with characteristic clinical features usually associated with IgE antibodies – most commonly directed against environmental allergens[1].

The theory on the pathogenesis of CAD suggests epidermal barrier defects might facilitate contact of environmental allergens with epidermal immune cells. This initiates the cascade of pro-inflammatory mediators' activation that eventually results in the persistent cutaneous inflammation seen in CAD cases.

A dog with atopic dermatitis. Note the erythema on axillae, groin, ventral abdomen, neck, medial aspect of elbows and muzzle.

The stratum corneum (SC) is the outermost region of the epidermis and composed of flattened, protein-enriched corneocytes ("bricks") and intercellular lipids ("mortar"). Within corneocytes are tight bundles of keratin filaments aggregated with filaggrin monomers, which provide the flattened shape and give the mechanical strength to the cells.

Ceramides, cholesterol and long-chain free fatty acids are the major lipid constituents in the SC and are critical to form the mortar and maintain the permeability of the epidermis. As a result of this bricks and mortar structure, the SC plays key roles in cutaneous barrier function in mammals[2].

Skin barrier dysfunction seen in atopic patients leads to increased water loss and, potentially, facilitates allergen penetration and sensitisation. Some of the changes are genetically inherited and some are secondary to skin inflammation and self-trauma.

In human medicine, the efficacy of emollients and moisturisers has been largely demonstrated in studies and this strategy has shown promise as a preventive function. In veterinary medicine, in vitro evidence regarding skin barrier dysfunction is building, but limited clinical evidence exists[3].

About 20% of dogs with atopic dermatitis showed decreased expression of filaggrin[4] and a filaggrin gene polymorphism (more than one allele occupies that gene's locus within a population, which may lead to the abnormal expression of the gene) has been described as being associated with CAD in Labrador retrievers in the UK[5]. Decreased lipids (ceramides) and SC ultrastructure abnormalities have also been described in dogs with atopic dermatitis.

Although it seems reasonable to think supplementing the lipid deficiency should improve the skin barrier function, it is still unknown whether this will automatically translate to an improved clinical picture[3]. The International Task Force on Canine Atopic Dermatitis recommends a multimodal approach to treat dogs with chronic atopic dermatitis, which includes:

- identification and avoidance of flare factors (food, flea and environmental allergens, *Staphylococcus* bacteria and *Malassezia* yeasts)
- skin and coat hygiene, care with bathing and dietary supplementation with essential fatty acids (EFAs)
- anti-inflammatory drugs and allergen-specific immunotherapy

On the other hand, acute flares should be treated with a combination of non-irritating baths and topical or oral glucocorticoids and antimicrobial therapy as needed. EFA supplements are unlikely to be of any benefit for acute flares of atopic dermatitis, as their mode of action requires their incorporation into cell membranes, which needs several weeks of treatment[6].

Oral EFA supplementation In normal dogs, dietary supplementation with EFAs – or feeding of EFA-rich diets (especially those rich in the omega-6 EFA linoleic acid) – has resulted in improved coat quality and gloss, and reduced transepidermal water loss (TEWL) in clinical studies[7]. Two randomised controlled trials that tested the effect of EFA-enriched diets in dogs with CAD reported improved coat quality after eight weeks[8,9].

Supplementing the diet of dogs with CAD with an EFA liquid supplement for two months improved the ultrastructure and increased the lipid content in the skin of atopic dogs. No evaluation of the correlation with clinical improvement was reported in this study[10]. At this time, no evidence exists of superiority of any particular EFA combination, dosage, ratio or formulation – although, in general, EFA-enriched diets potentially provide higher amounts of EFA than administration via oral supplements. The benefit of EFA, if any, might not be seen before two months of supplementation[11,12].

Apart from the benefit of oral EFA supplementation to improve skin barrier function, a randomised controlled trial established the daily administration of a specific EFA supplement allowed the

reduction of the dose of prednisolone needed to control pruritus in dogs with CAD[13]. EFA supplementation is, therefore, considered to have a steroid sparing effect for CAD cases.

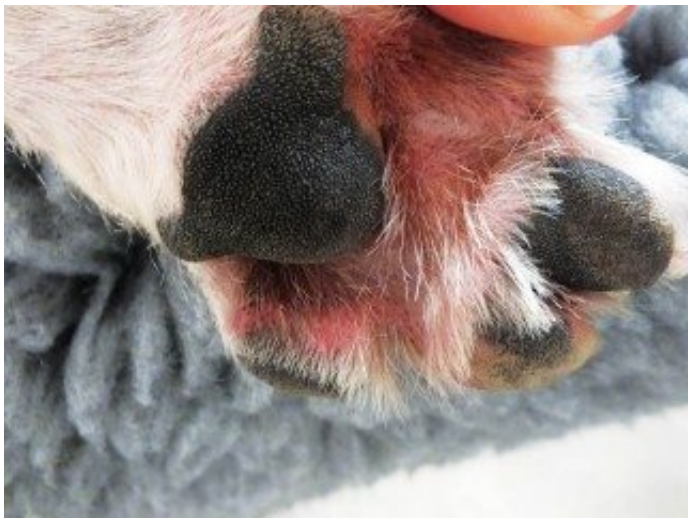
Topical lipid formulations

Ceramides

Two studies showed the levels of ceramides in lesional and clinically unaffected skin of atopic dogs were significantly lower than in healthy dogs[14,15]. Electron microscopic analysis revealed a disorganised and abnormal lipid structure in clinically non-lesional SC of dogs with spontaneous atopic dermatitis and an experimental model of CAD sensitised with house dust mites[16,17].

The application of a topical lipid complex containing ceramides, cholesterol and EFAs – every three days for six applications – was shown to normalise pre-existing SC lipid profile abnormalities in CAD[18]. Evidence supporting the relationship between these changes and clinical benefit is still limited.

TEWL



Ventral digital erythema in a dog with atopic dermatitis.

TEWL has been shown to re?ect skin barrier function in humans and dogs, and is increased in individuals with atopic dermatitis compared with normal controls[19,20].

A randomised pilot study was performed to evaluate the in?uence of topically administered EFAs on the TEWL of normal and atopic skin, and on the clinical signs of CAD. A spot-on product (applied once weekly) or a spray (applied once daily), containing essential oils and unsaturated fatty acids, for eight weeks, showed a significant decrease of clinical scores and pruritus in atopic

dogs, with both the spray and spot-on product[21].

Clinical improvement was more pronounced than the decrease in TEWL, making the authors of this study hypothesise about other mechanisms of action of these topical fatty acids, such as potential anti-in?ammatory effects.

Sphingosine-1-phosphate

A significant decrease and altered metabolism of sphingosine-1-phosphate (a constituent of ceramides) are described in lesional atopic skin compared with healthy skin[22].

A blinded, randomised, controlled trial in atopic dogs using a phytosphingosine-containing shampoo or a phytosphingosine-containing shampoo, plus spray, with similar ingredients compared to a control shampoo containing antiseptics, fatty acids and complex sugars, showed improvement in skin lesions (using a simplified Canine Atopic Dermatitis Extent and Severity Index score) and in the pruritus score (using a scale from zero to six) in all groups.

No significant difference was found between groups[23]. At this time, not enough evidence exists to support the use of topical phytosphingosine over other forms of EFAs, but a potential benefit exists of regular bathing with such products in these patients.

The International Task Force on Canine Atopic Dermatitis states topical lipid formulations can help normalise existing SC lipid barrier defects in dogs with CAD in the same way as EFA-enriched diets or EFA oral supplementation. Therefore, the benefit of topical EFA-containing formulations may be minimal in dogs already fed EFA-enriched diets or receiving EFA supplements. However, these products should not be recommended as monotherapy for CAD.

Conclusion

Skin barrier improvement is a promising approach that, if initiated early on in life, could prove to be beneficial and even alter the course of disease progression and prevent or minimise sensitisation to environmental allergens. However, large controlled studies are still needed to identify optimal treatment regimens and investigate the long-term effects on the cutaneous barrier function.

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