

# Papers

## Double-blinded, placebo-controlled study to evaluate an antipruritic shampoo for dogs with allergic pruritus

J. Schilling, R. S. Mueller

**Shampoo therapy is frequently used on pruritic dogs. However, there are few double-blinded, placebo-controlled studies of this form of therapy. This randomised, double-blinded, placebo-controlled study evaluated the efficacy of a commercial medicated shampoo (DermaTopic; Almapharm) containing chlorhexidine, lactoferrin, piroctone olamine, chitosan and essential fatty acids in 27 dogs with mild to moderate allergic pruritus without secondary skin infections. All dogs received shampoo therapy with either DermaTopic or a shampoo vehicle as placebo twice weekly for four weeks. The extent of pruritus was evaluated before the study and then on a daily basis by the owners using a visual analogue scale. Before beginning the treatment and after four weeks, the skin lesions were evaluated by an experienced clinician with a validated lesion score (Canine Atopic Dermatitis Extent and Severity Index – CADESI). The pruritus was reduced significantly by both DermaTopic and placebo. However, there was no significant difference between both groups. There was no statistically significant difference in the CADESI scores pre- and post-treatment in either group or between the two types of treatment. This study provides further evidence of the benefit of shampoo therapy for pruritic dogs.**

PRURITUS is one of the most common clinical signs in small animal practice (Hill and others 2006). Its pathogenesis is complex (Stander and Steinhoff 2002) and which pruritogenic substances are responsible for the pruritus seen in allergic dogs is not known (Carr and others 2009). The main causes for allergic pruritus in dogs are flea bite hypersensitivity, adverse food reactions and atopic dermatitis caused by environmental allergens (Scott and Paradis 1990). Recent research showed that dogs with atopic dermatitis have an increased transepidermal water loss and a decreased ceramide content in lesional and non-lesional skin (Shimada and others 2009) which may contribute to a reduced skin barrier (Marsella and Samuelson 2009). Atopic dogs are also predisposed to develop pyoderma. One reason for this may be that bacterial adherence to corneocytes of atopic dogs is reported to be higher than that of healthy dogs (McEwan and others 2006). Prednisolone and cyclosporine reduce pruritus and skin lesions in atopic dogs (Olivry and others 2002), but are more likely to show adverse effects than other treatment options such as antihistamines or essential fatty acids. Antihistamines may be effective in dogs with chronic pruritus (Scott and Miller 1999) but it may be necessary to

evaluate different antihistamines for a period of seven to 14 days each to find the most effective for the individual patient (DeBoer and Griffin 2001).

One other possibility for the treatment and prevention of acute flares of pruritus is the topical treatment with medicated shampoos (Olivry and others 2010). To achieve optimal efficacy, the contact time of shampoo with the skin must be long enough (Curtis 1998).

Some authors claim that mechanical removal of allergens, bacteria and inflammatory mediators is beneficial for atopic patients (Curtis 1998, Stroh and others 2010). One study recently showed a significant reduction of pruritus after the use of an antipruritic shampoo as opposed to the control group that was washed with water only (Loeflath and others 2007). Although many antipruritic shampoos are available, double-blinded, placebo-controlled studies on their efficacy are rare.

The aim of this double-blinded, placebo-controlled study was to evaluate the effect of a commercial medicated shampoo (DermaTopic, Almapharm) on pruritus and skin lesions of dogs with mild to moderate allergic pruritus.

### Material and methods

#### Study population

Twenty-seven dogs with a history of mild to moderate pruritus for at least four weeks were enrolled in the study. In all dogs, history and clinical findings supported the diagnosis of allergic pruritus. Before inclusion, all owners were informed about the details of the study and signed an informed consent form. All dogs were thoroughly examined and skin cytology was performed in all cases to rule out infections with bacteria and/or yeast. Skin scrapings or antiparasitic trial therapy were performed as necessary to rule out ectoparasites before inclusion in the study. Exclusion criteria were signs of pyoderma such as papules, pustules or crusts or cytological findings of inflammatory cells, bacteria or yeast. Medication and diet were not changed in the

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## Papers

six weeks before and during the study. If the dog had received antibiotics, they had to be withdrawn at least three weeks before inclusion. Immunotherapy had to be given constantly over at least half a year. Flea therapy was continued if the dogs had received it before but not necessarily initiated.

Six dogs received additional therapy. One received prednisolone on a dose of  $0.17 \text{ mg kg}^{-1}$  once daily. Three received allergen-specific immunotherapy, one of them combined with antihistamines, one with essential fatty acids, and one with both. The fifth dog was on a therapy with antihistamines and oral fatty acids, and the last received essential fatty acids topically. All of them were in the placebo group.

### Study design

The study was a randomised, double-blinded, placebo-controlled trial evaluating DermaTopic (Almapharm). DermaTopic contains lactoferrin, chlorhexidine, piroctone olamine, chitosan, essential fatty acids and glycerine.

All dogs received shampoo therapy twice weekly over four weeks with either DermaTopic or placebo. Placebo and verum were filled in identical shampoo bottles and not distinguishable by colour or smell. The animals were initially shampooed by a veterinarian. After a thorough education of owners supported by a practical demonstration and written instruction, 17 out of 27 dogs were also shampooed by the owners at home. Six of them were in the treatment group, 11 in the placebo group. The dogs' skin was rinsed with warm water for at least five to 10 minutes, depending on the length of the animal's hair coat, then shampoo was applied and massaged thoroughly into the skin. The amount of shampoo varied depending on the hair coat, enough was used to apply it to the whole body. After a period of 10 minutes, the shampoo was rinsed off completely and the dogs were dried with towels.

### Assessment of treatment efficacy

The owners evaluated the pruritus daily on a visual analogue scale (Rybníček and others 2009) from zero to 10 before the start of the study and then every evening, beginning on the day of the first bathing.

Before beginning of the treatment and after four weeks, the skin lesions were evaluated by one of three experienced clinician with a validated lesion score (Canine atopic dermatitis extent and severity index – CADESI) (Olivry and others 2007). This score evaluates erythema, alopecia, lichenification and excoriations on 62 areas of the body on a scale from zero to five.

### Statistical analyses

In addition to a per-protocol analysis, an intention to treat analysis with the last pruritus and CADESI value carried forward was performed. The CADESI and pruritus scores of the two groups before therapy and after four weeks were analysed with Kruskal-Wallis test and Dunn Post test. The pre and post CADESI scores for treatment and placebo were compared individually using the Wilcoxon matched pairs signed rank test, the pruritus scores were analysed likewise using a paired t test.

## Results

### Study population and exclusions

Twenty-seven dogs were participated in the study. Thirteen were treated with DermaTopic (group 1), six of them were washed by the owners, seven were treated by a veterinarian in the clinic. Fourteen dogs received placebo (group 2), 11 of them were treated by the owners, three were shampooed in the clinic.

Five dogs did not complete the study. Four of those dogs were in group 2. Three of the dogs that dropped out were washed in the clinic, two were treated by the owners at home. One dog developed an allergic reaction with erythema and increased pruritus to the placebo after an initial good clinical response, one dog developed a pyoderma, one dog showed excessive and prolonged scratching directly after the shampooing without any clinical signs of infection or contact allergy and the last one showed excessive hair loss without developing alopecia. One dog of group 1 was withdrawn by the owner due to lack of

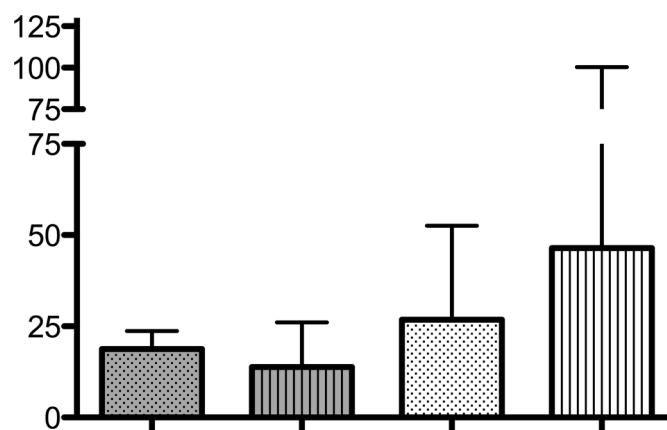


FIG 1: Mean (sd) pruritus scores before (dotted) and after (striped) four weeks of twice weekly shampoo (grey) or placebo (white) therapy in dogs with allergic pruritus.

response. All dogs discontinued the shampooing in the third week of treatment, after five and six treatments, respectively.

### Pruritus scores

Results of the intention to treat analysis and the per-protocol analysis were similar, only the results of the intention to treat analysis are listed. There was a significant reduction in pruritus (Fig 1) in the treatment group (paired t test,  $P=0.0014$ ) as well as in the placebo group (paired t test,  $P=0.0083$ ). However, there was no difference between shampoo and placebo (Kruskal Wallis and Dunn post test).

### CADESI scores

Results of the intention to treat analysis and the per-protocol analysis were similar, only the results of the intention to treat analysis are listed. There was no significant change in CADESI scores before and after four weeks of treatment (Fig 2) in the direct comparison of the values pre and post-treatment (Wilcoxon matched pairs t test,  $P=0.2892$ ) as well as placebo (Wilcoxon matched pairs t test,  $P=0.142$ ). The comparison between the pre and post values of the different groups showed no significant difference (Kruskal Wallis and Dunn post test).

### Further observations

The owners of four dogs reported the development of a poorer coat quality and a drier skin after four weeks of shampooing which was confirmed by the evaluating veterinarians. All of these animals were in the placebo group. No similar observation was made for any of the dogs in the treatment group.

However, these were not systematic and objectively measured parameters.

## Discussion

This study showed the efficacy of a commercial shampoo (DermaTopic; Almapharm) and placebo to reduce allergic pruritus in the dog. DermaTopic contains antimicrobial agents like chlorhexidine, piroctone olamine and Chitosan. Chlorhexidine has good efficacy against Gram-positive cocci, especially the most common species on the skin of dogs, *Staphylococcus pseudintermedius* (Lloyd and Lamport 1999). Piroctone olamine has antifungal activity and is a common agent in antidandruff shampoos in human medicine (Loden and Wessman 2000). Chitosan acts as a moisturiser (Illum 1998) and has additional antibacterial properties (Lee and others 2009).

The addition of antimicrobial agents in an antipruritic shampoo for allergic dogs seems sensible as those dogs are predisposed to skin infections, possibly due to a greater adherence of *S. pseudintermedius* to the keratinocytes of atopic dogs as opposed to healthy controls (Simou and others 2005). Antimicrobial substances may reduce the probability of a secondary infection. Other contents are lactoferrin and essential fatty acids which have anti-inflammatory activity (Griffiths

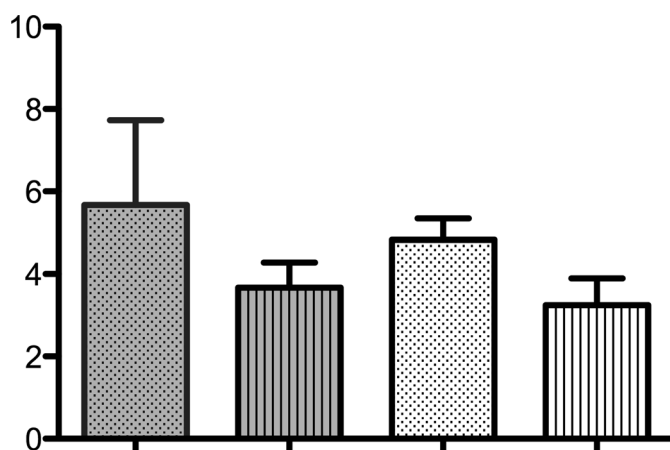


FIG 2: Mead (sd) CADESI scores before (dotted) and after (striped) four weeks of twice weekly shampoo (grey) or placebo (white) therapy in dogs with allergic pruritus

and others 2001, Stehle and others 2010). Essential fatty acids can additionally rehydrate the skin (Loden 2003). Glycerine serves as a moisturiser (Loden 2003).

A significant reduction in pruritus was achieved by both placebo and shampoo without any significant difference between the two groups. This is in accordance with claims of dermatologists that the mechanical removal of debris and allergens off the hair coat and skin and the resulting improvement in skin hygiene is the most important factor for the success of shampoo therapy (Curtis 1998, Olivry and others 2010). For the removal of bacteria, surfactants in shampoo vehicles can have a similar effect as shampoos with active ingredients (Stroh and others 2010). Loefflath and others 2007 found a significant improvement of pruritus in patients receiving an antiallergic shampoo compared with placebo (Loefflath and others 2007). However, the placebo group in that study was washed with water only, and the ingredients of the shampoo vehicle in this study may have additional effects on pruritus.

The CADESI scores showed no significant difference before and after four weeks of treatment. One possible explanation may be the low CADESI scores of the dogs enrolled in this study. Significant effects on CADESI are observed easier with higher entry scores. This observation has been made in previous studies (Ferguson and others 2006, Loefflath and others 2007). Furthermore, the duration of treatment may have been too short to improve chronic lesions such as self-induced alopecia and lichenification.

Some dogs did not complete the study, but most of these dogs were treated with placebo. Shampoo treatment is very time consuming, acceptance of such therapy vanishes quickly if there is no satisfactory outcome. One dog developed a contact allergy to the shampoo vehicle, which is rare but can be seen in any topic medication from time to time.

It has been controversially discussed, if it is possible to let the owners shampoo their dogs themselves in a double-blinded, placebo-controlled trial (Loefflath and others 2007). In this study, neither owners nor veterinarians evaluating the dogs for lesions knew which treatment the dogs received by using numbered, identical shampoo bottles. The owners were asked whether they were willing to return to the clinic twice weekly for the bath or shampoo their dogs at home. Due to the often long distance to the clinic, most owners chose the latter option. Therefore, client education was extensive and the first treatment was performed in the clinic in the presence of the owner. With this approach, the variation in shampooing was minimised. In addition, any variation would have applied to either group.

One drawback of this study was the wide definition of the trial population and the lack of an aetiological diagnosis in some dogs. It remains unanswered if efficacy of shampooing is different in dogs with pruritus caused by food adverse reactions versus environmental allergens versus combinations of the two types.

This study shows that shampooing can be an effective treatment for pruritic dogs, either as exclusive therapy in very mildly allergic dogs or as an additional therapy to corticosteroids, antihistamines or immunotherapy in more severe cases.

Our data did not show a significant benefit from the active ingredients of the shampoo. However, most of the dogs receiving the shampoo had a better skin and coat quality than those receiving placebo after four weeks of treatment. As those parameters were not measured in a systematic and objective way, these findings have to be interpreted with caution.

In conclusion, shampooing is beneficial for dogs with mild to moderate allergic pruritus. The clinician needs to consider the circumstances (coat length, skin changes and temperament of the dog, willingness of the owner to properly perform this relatively time consuming therapy) before recommending shampoo therapy for pruritic dogs.

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