Efficacy of dimetinden and hydroxyzine/chlorpheniramine in atopic dogs: a randomised, controlled, double-blinded trial

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Context
Canine atopic dermatitis is a common disease in small animal practice. The only specific treatment for atopic dermatitis is allergen-specific immunotherapy. Symptomatic treatment includes a number of options such as glucocorticoids, cyclosporine, shampoos and essential fatty acids. Due to their favourable safety profile, antihistaminic drugs are also commonly used as symptomatic therapy for atopic dermatitis in dogs; however, their clinical benefit is largely unsubstantiated and most published trials are not blinded, placebo-controlled or randomised. Currently, there is no information on the use of dimetinden in veterinary medicine, and no published placebo-controlled trials evaluating a combination of hydroxyzine and chlorpheniramine.

Main conclusion
Dimetinden and the combination of hydroxyzine and chlorpheniramine can help to reduce pruritus in atopic dogs but, in most cases, the improvement is limited and additional treatment may be needed.

Approach
In a double-blinded, placebo-controlled, crossover trial, the influence of dimetinden and of a combination of chlorpheniramine and hydroxyzine on pruritus in atopic dogs was evaluated in 19 dogs with atopic dermatitis. Dogs were treated with either product or a placebo, orally, for 14 days, followed each time by a 14-day wash-out period. Before and after each period, the dogs were examined and canine atopic disease extent and severity index (CADESI) determined by a clinician and the pruritus and general condition by the owner. Changes in CADESI and pruritus scores after treatment with the respective antihistamines were compared to placebo using a Mann-Whitney U-test. In addition, the number of dogs improving by more than 25 per cent and 50 per cent were compared between the treatment groups and the placebo group using a Fisher’s exact test. Furthermore, changes in clinical signs during the wash-out period were evaluated.

Results
Dimetinden caused significant improvement in pruritus (P=0.014) but not CADESI (P=0.037). Combined hydroxyzine and chlorpheniramine caused significant improvement in both CADESI score (P=0.049) and pruritus score (P=0.05). Ten of 17 dogs improved by more than 25 per cent in terms of pruritus with the combination of hydroxyzine and chlorpheniramine, 12 of 18 with dimetinden and only two of 19 with placebo, indicating a significant difference between the treatment groups and the placebo group (P=0.003 and P=0.001, respectively). For CADESI, the corresponding values were 11 of 17, seven of 18 and five of 19 dogs. Only the difference between placebo and treatment with the combination of hydroxyzine and chlorpheniramine was significant (P=0.023). Two thirds of the dogs deteriorated during wash-out periods while the remainder showed no changes in clinical signs. Improvement during wash-out was seen in only very few dogs. Mild drowsiness was seen in two dogs with dimetinden and four dogs with the combination of chlorpheniramine and hydroxyzine, although a dose adjustment of the antihistamine was needed in only one of those dogs.

Interpretation
Placebo treatment resulted in no improvement in the affected dogs, but treatment with the two antihistamines resulted in approximately 40 per cent improvement in mean CADESI score and more than 20 per cent improvement in mean pruritus scores. This is evidence of a limited efficacy of the oral antihistamines dimetinden and hydroxyzine/chlorpheniramine in the treatment of canine atopic dermatitis. Unfortunately, the small number of dogs with moderate to severe disease precluded a statistical comparison of success rates in dogs with mild versus moderate or severe disease. Most dogs showed perennial disease and for those that had worse clinical signs in summer than in the winter, the study took place in their pruritic season. In addition, only very few dogs improved during the wash-out periods between medication phases. However, it is possible that in some dogs clinical improvement during the last phase of the study may have been partially due to seasonal changes.

Significance of findings
The limited improvement in clinical signs of atopic dermatitis seen in dogs treated with dimetinden and hydroxyzine/chlorpheniramine warrant consideration of these antihistamines as a trial therapy in canine atopic dermatitis, particularly if the clinical signs are mild. Although most dogs seemed to respond to both antihistamines, some dogs responded just to one of the products. Thus, subsequent treatment trials with both products for 14 days each are advisable. The only adverse effect noted was drowsiness, which is in line with previous reports of antihistamine use in dogs.

| TABLE 1: Mean CADESI and pruritus scores before and after two weeks of treatment with a combination of hydroxyzine and chlorpheniramine, dimetinden or placebo |
|---|---|---|
| Hydroxyzine/Chlorpheniramine | Dimetinden | Placebo |
| CADESI (pretreatment) | 32 | 34 | 26 |
| CADESI (post-treatment) | 17 | 21 | 29 |
| Pruritus (pretreatment) | 7.2 | 6.9 | 6.4 |
| Pruritus (post-treatment) | 5.4 | 5.2 | 6.4 |

CADESI Canine atopic disease extent and severity index
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