ARTICLES

A clinical trial on the efficacy of clemastine in the management of allergic pruritus in dogs

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Abstract

Clemastine fumarate was administered to 72 atopic dogs. The pruritus in seven dogs was eliminated with this treatment. Another 14 dogs improved considerably with treatment but had some residual pruritus. Side effects were uncommon and only three dogs had to be withdrawn from treatment because of adverse reactions.

Résumé

Essais cliniques de l'efficacité du clémastine dans le traitement des allergies pruritiques chez le chien

Le fumarate de clémastine a été administré à 72 chiens présentant de l'atopie. Le prurit a cessé chez sept chiens alors que quatorze autres ont démontré une amélioration marquée avec cependant persistance d'un prurit résiduel. Les effets secondaires ont été rares et le traitement a dû être interrompu seulement dans trois cas en raison des réactions adverses.

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Introduction

Atopic disease is prevalent in the dog population (1,2). Prior to 1986, the mainstay of treatment for the atopic dog was medical management with glucocorticoids or immunotherapy. Since 1988, the results of a number of clinical trials with various nonsteroidal medications have been published which document the efficacy, or lack thereof, of these agents in the management of canine allergic pruritus (3–7). These studies have shown that the efficacy of nonsteroidal medications varies from drug to drug and dog to dog.

To date, the two drugs with the highest reported efficacy are the H_1 antihistamine clemastine fumarate (Tavist, Sandoz Pharmaceuticals Corporation, East Hanover, New Jersey, USA) and the tricyclic antidepressant amitriptyline. Clemastine has been shown to reduce pruritus by 50% or more in 9 of 30 (30%) (5) and 8 of 30 (27%) (6) dogs, while this level of control was seen in 10 of 31 (32.2%) dogs with amitriptyline (7). In the amitriptyline study, the dogs' responses were graded so that those cases where pruritus was eliminated could be identified. Comparable data are not available for clemastine. The study reported herein was done to determine the efficacy of clemastine in a large number of allergic dogs and to categorize the degree of response of each dog.

Materials and methods

Only dogs with historical and clinical data suggestive of atopic disease were included in this study. One hundred and ten dogs were entered into the study and 102 were available for follow-up. The owners of 30 dogs declined specific allergy testing and the efficacy data from these cases were excluded from further evaluation, but any adverse reactions seen were included. The 72 dogs in the final evaluation ranged in age from 1 to 15 years, included 8 mongrels and 64 purebred dogs from 32 different breeds, and consisted of 45 females and 27 males. At presentation, 60 had nonseasonal pruritus of 1–6 (mean 2.9) years' duration, five dogs had recurrent seasonal (warm weather) pruritus for 3–5 (mean 4) seasons, and seven dogs had pruritus of indeterminate seasonality with signs present for 2–10 (mean 5) months. All dogs were moderately to intensely pruritic at presentation, and the pruritus in 68 dogs was known to stop with glucocorticoid administration.

All dogs received complete clinical evaluations and various diagnostic tests as indicated or allowed by the owner. Forty-two underwent dietary restriction testing and intradermal allergy testing and were proven to be atopic. The remaining 30 dogs were fed a home-cooked hypoallergenic diet (fish and potatoes or lamb and rice) for three weeks to investigate food hypersensitivity. In no case did the pruritus disappear with dietary restriction and these dogs were given the tentative diagnosis of atopy. Any dog with fleas and/or a bacterial skin infection was treated for those disorders before the drug trial was started.

The dosage of clemastine used herein was adapted from the initial study (5). The 1.34 mg tablets were

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used and were administered orally q12h. Dogs weighing less than 9.1 kg received one-half tablet, those between 9.2 and 22.7 kg received one tablet, those between 22.8 and 34.1 kg received one and one-half tablets, and dogs over 34.1 kg received two tablets. The owners were instructed to administer the drug daily for 14 days and to record observations on the degree of clinical improvement and side effects. If a dog's pruritus was virtually eliminated during the initial trial, the drug was administered for an additional 30 days to confirm sustained efficacy.

The influence of variables of gender, seasonality of pruritus, and drug dosage on response to treatment were compared with the Chi-square test with a significance level of $p = 0.05$. The influence of duration of pruritus on response was evaluated by a one-way analysis of variance for all dogs and for dogs with nonseasonal, seasonal, and undetermined seasonality.

Results

Owners' observations were grouped into three categories of response to therapy: excellent, good, and poor. Excellent response indicated that pruritus was eliminated or reduced to an inconsequential level. Good response indicated a substantial (at least 50%) reduction of pruritus. Poor response indicated that pruritus was unchanged or worsened or that the dog had an adverse reaction which necessitated drug withdrawal.

The overall responses of the dogs and the response rate by diagnosis are shown in Table 1. One of the 51 poor responders had its pruritus intensify with treatment. That dog, along with the 21 good and excellent responders, returned to its pretreatment level of pruritus with drug withdrawal. With readministration of the drug to the seven excellent responders, all dogs duplicated their initial response and maintained it for at least 30 days.

Clinical side effects were seen in six dogs. Three were drowsy during drug administration, but completed the 14-day trial. Three dogs, classified as poor responders, had serious adverse reactions (urinary incontinence, dysuria and stranguria, profound depression) which necessitated drug withdrawal. All six dogs returned to normal within 24 hours of drug withdrawal.

The data on the influence of the variables of gender, seasonality of pruritus, drug dosage, and duration of pruritus on response are shown in Table 1. There was no significant difference in the response rate for any variable.

Table 1. Response to treatment with clemastine of pruritic dogs, tabulated by variable

Variable	Total	Excellent	Good	Poor
Overall	72	7	14	51
Diagnosis				
Atopy	42	3	11	28
Atopy (tentative diagnosis)	30	4	3	23
Gender				
Female	5	0	1	4
Female-neutered	40	5	8	27
Male	8	0	1	7
Male-neutered	19	2	4	13
Seasonality				
Nonseasonal	60	5	13	42
Seasonal	5	1	1	3
Undetermined	7	1	0	6
Drug Dosage				
½ tab q12h	24	4	3	17
1 tab q12h	20	1	6	13
1½ tab q12h	8	1	2	5
2 tab q12h	20	1	3	16
Duration of pruritus		Mean duration (years) of signs[a]		
Nonseasonal	60	2.3	2.8	3.0
Seasonal	5	5.0	4.0	3.7
Undetermined	7	0.3	0.0	0.5

[a]Indicates the group mean duration of clinical signs

Discussion

Although atopic disease appears to be the second most common allergic skin disease of dogs (1,2), it can be the most difficult to manage because sensitization in life-long and progressive and the offending allergens usually cannot be avoided (8). By design, this study was limited to atopic pruritus. Based on the clinical evaluations, intradermal skin testing, and dietary restriction testing, the diagnosis of atopy was proven or strongly supported in these dogs.

In this study, 7 (9.7%) of 72 dogs showed an excellent response, 14 (19.4%) a good response, and 51 (70.9%) a poor response. Seventy of the study dogs had previously been treated with a glucocorticoid steroid and 68 had shown an excellent response to that treatment. The data presented herein, coupled with our inability to identify any variable which positively or negatively influenced the dogs' ability to respond, again show categorically that antihistamines are not as effective as glucocorticoids in the management of canine atopic pruritus and that a dog's response to an antihistamine is very individualistic. However, when an animal shows an excellent response to an antihistamine, its pruritus is just as well controlled as it would be with a glucocorticoid, while clinical side effects are far less common. The seven excellent responders described herein showed no adverse reactions to clemastine administration while a rate of at least 10% would be expected with a glucocorticoid (5).

Since the mid-1980s, there has been increased interest in the efficacy of antihistamines or drugs with antihistaminic activity in the management of atopic pruritus. To date, reports on diphenhydramine, chlorpheniramine, hydroxyzine, trimeprazine, astemizole, clemastine, amitriptyline, and doxepin have been published; their efficacy and the frequency of adverse reactions vary greatly (3,5,7). If the combination of good and excellent response is considered, the reported efficacy of the drugs mentioned above is: diphenhydramine 22.3%, chlorpheniramine 17.8%, hydroxyzine 24.5%, trimeprazine 3.3%, amitriptyline 32.2%, and doxepin 0%. The combined efficacy of 29.2% found in this study exceeds that reported for those drugs, except amitriptyline, and duplicates that previously reported for clemastine (5,6).

Although a good response can be recognized by owners, it is usually not sufficient to manage the dog's

pruritus without the addition of some other form of treatment. Accordingly, excellent responses are more important to owners. For diphenhydramine, chlorpheniramine, hydroxyzine, and amitriptyline, excellent response rates of 6.7%, 8.9%, 6.7%, and 13.1%, respectively, have been reported (3,7). Comparable figures are not available for the other drugs discussed previously. The rate of 9.7% for clemastine reported herein exceeds all of those above, except amitriptyline, and confirms the usefulness of clemastine in the nonsteroidal management of allergic pruritus in dogs.

Clemastine fumarate belongs to the benzhydral ether group of H_1 antihistaminic compounds and is indicated in humans for the relief of symptoms of allergic rhinitis and mild, uncomplicated allergic skin manifestations of urticaria and angioedema (9). Clemastine, like other traditional H_1 antihistamines, has anticholinergic (drying) and sedative side effects. Transient drowsiness occurs relatively frequently, and other adverse reactions include sedation, sleepiness, urinary frequency, difficult urination, and urinary retention. Clemastine fumarate is not licensed for use in dogs.

Six of the 102 dogs showed some adverse reaction to drug administration. Three dogs were mild to moderately drowsy, while three dogs had serious reactions (urinary incontinence, dysuria and stranguria, profound depression) which necessitated drug withdrawal. Because of the expense of clemastine, only three of the seven excellent responders have continued with treatment for periods of 8–12 months. None of these dogs have shown any clinical adverse reactions to chronic administration.

This study was not blinded or placebo-controlled and, as such, could be considered a case series where no claim for efficacy of treatment should be made. However, since the clinical signs in 65 dogs were chronic in nature, all dogs were pruritic at the start of the treatment, and the owners' assessment of response was confirmed by withdrawal and subsequent readministration of the drug, we feel that each dog acted as its own control during this short clinical trial. Accordingly, the improvement in symptomatology in the 21 dogs, especially the seven excellent responders, can probably be attributed to the clemastine.

Although clemastine is available as an over-the-counter drug in Canada and is less expensive than prescription antihistamines, it is still expensive, especially when used for large dogs. This study, coupled with the two previous studies (5,6), shows that approximately 30% of treated dogs will respond with a 50% or greater reduction in pruritus, making clemastine the most effective antihistamine studied to date. The 9.7% excellent response rate reported herein is less impressive, but still superior to that reported for all other antihistamines. Since only three dogs showed drowsiness, a frequent side effect in humans (8), our dosage may be suboptimal and further studies with increased dosages are indicated. CVJ

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