

An open clinical trial on the efficacy of cetirizine hydrochloride in the management of allergic pruritus in cats

Joya S. Griffin, Danny W. Scott, William H. Miller, Jr., Michelle M. Tranchina

Abstract – Cetirizine hydrochloride was administered orally at 5 mg/cat, q24h, to 32 cats with allergic skin disease. Pruritus was reduced in 41% (13/32) of the cats. The antipruritic effect was repeatable and sustainable. There was no significant association between patient age, disease severity, or cutaneous reaction pattern and improvement during cetirizine administration. No adverse side effects were reported.

Résumé – Étude clinique ouverte sur l'efficacité du chlorhydrate de cétirizine dans la gestion du prurit allergique chez les chats. Le chlorhydrate de cétirizine a été administré par voie orale à une dose de 5 mg/chat, q 24 h, à 32 chats atteints d'une maladie allergique de la peau. Le prurit a été réduit chez 41 % (13/32) des chats. L'effet antiprurigineux a été répétable et durable. Il n'y avait pas d'association significative entre l'âge du patient, la gravité de la maladie ou le schéma de réaction cutanée et l'amélioration durant l'administration de la cétirizine. Aucun effet indésirable n'a été signalé.

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Introduction

Allergic skin diseases (atopic dermatitis, food allergy) are common causes of pruritus in cats (1–3). Management is often difficult due to the temperament of some cats and the adverse side effects associated with some medications (1–3). Treatment options include allergen avoidance, allergen-specific immunotherapy (ASIT: for atopic dermatitis), glucocorticoids, cyclosporine, antihistamines, essential fatty acids, and combinations of these (1–3). Allergen-specific immunotherapy is associated with few adverse side effects, and has been reported to be beneficial in 60% to 78% of cats with atopic dermatitis (1–4). Although ASIT is one of the most effective and specific treatment options for atopic dermatitis, many cat owners do not choose this therapeutic option due to financial concerns, their cat's temperament not being amenable to injections, or their own fear of needles (trypanophobia).

Management with orally administered medications can be difficult in cats. Cyclosporine has been reported to be as effective as prednisolone; however, it is not registered for use in cats and should be avoided in cats with underlying viral disease or at risk for toxoplasmosis (5). Glucocorticoids are an effective and

inexpensive treatment for atopic dermatitis, but are less reliable for food allergy (1–3). Although cats are fairly resistant to the adverse side effects of glucocorticoids, long-term and high-dose corticosteroid use are known to have the potential to potentiate insulin resistance, adrenal hormone resistance, cutaneous fragility, and may result in congestive heart failure (1,6,7).

Oral antihistamines are a viable treatment option for allergic cats and can be used for their steroid-sparing property (1–3,8,9). As in the human and canine patient, antihistaminic effect in felines is individualized and unpredictable. Trial courses of different antihistamines may be required. Published studies investigating the efficacy of individual antihistamines in cats with allergic pruritus are limited and include evaluation of chlorpheniramine (10), oxatomide (11), clemastine (12), and cyproheptadine (13).

Cetirizine is a second generation H1-receptor antagonist that is well-tolerated in dogs (14) and cats (15). Because cetirizine is known to affect eosinophil function, and eosinophils appear to play an important role in cats with allergic dermatitis, this antihistamine may be particularly beneficial in this species (1,16,17). Cetirizine acts as an inverse agonist and stabilizes the inactive conformation of H1 receptors (18). It also has non-H1-dependent activities such as inhibition of preformed mediators of inflammation such as histamine, tryptase, and leukotrienes from basophils and mast cells; inhibition of eosinophil chemotaxis; reduction of eosinophil survival; and alteration of adhesion molecule expression (17,19,20). All of these elements are involved in the pathogenesis of allergic inflammation. Cetirizine is nonsedating at therapeutic doses in humans due to efflux from the central nervous system via the P-glycoprotein pump system (15,21). Sedation can occur at higher doses in humans (15,21) and was reported to occur transiently in

Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, New York 14853-6401, USA.

Address all correspondence to Dr. Danny W. Scott; e-mail: shb3@cornell.edu

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Table 1. Clinical data on 32 cats with allergic dermatitis

Case	Breed	Gender	Age (y)	Diagnosis	Cutaneous reaction pattern
1	DSH	MC	7.5	Undetermined allergic dermatitis	SIA
2	DSH	FS	16	Undetermined allergic dermatitis	NP
3	DSH	FS	8	Atopic dermatitis	NP
4	DSH	MC	7	Atopic dermatitis and food allergy	NP
5	DSH	MC	7	Atopic dermatitis	SIA
6	DLH	FS	7	Atopic dermatitis	NP
7	DSH	FS	11.5	Undetermined allergic dermatitis	NP
8	DSH	FS	6.5	Atopic dermatitis	SIA/EGC
9	DSH	MC	3	Atopic dermatitis	SIA
10	Persian	FS	4	Atopic dermatitis	SIA
11	DSH	MC	11.5	Undetermined allergic dermatitis	SIA
12	DSH	MC	6	Atopic dermatitis	SIA/EGC
13	DSH	MC	3.5	Atopic dermatitis	SIA
14	DSH	MC	5	Undetermined allergic dermatitis	SIA
15	DSH	MC	10	Undetermined allergic dermatitis	SIA
16	Bengal	MC	6.5	Atopic dermatitis	SIA
17	DLH	MC	3	Undetermined allergic dermatitis	SIA
18	DSH	FS	5	Atopic dermatitis and food allergy	SIA
19	DSH	MC	13	Atopic dermatitis	NP
20	DSH	MC	3	Undetermined allergic dermatitis	SIA
21	DLH	MC	8	Atopic dermatitis	SIA/NP
22	DSH	MC	7	Undetermined allergic dermatitis	NP
23	DSH	MC	6	Undetermined allergic dermatitis	SIA
24	Bengal	FS	4.5	Atopic dermatitis	EGC
25	DSH	FS	7	Undetermined allergic dermatitis	NP
26	DSH	MC	4.5	Undetermined allergic dermatitis	NP/EGC
27	DSH	FS	6	Undetermined allergic dermatitis	NP
28	Devon rex	MC	6.5	Atopic dermatitis	SIA
29	DSH	MC	3	Undetermined allergic dermatitis	EGC
30	DSH	FS	2.5	Atopic dermatitis	NP
31	DSH	FS	7	Undetermined allergic dermatitis	SIA
32	DSH	MC	9.5	Undetermined allergic dermatitis	EGC

DSH — Domestic shorthair, DLH — Domestic longhair, MC — Castrated male, FS — Spayed female, EGC — Eosinophilic granuloma complex, NP — Nonlesional pruritus, SIA — Self-induced alopecia.

dogs (18). Sedation has not been reported in cats given cetirizine (15). Papich et al (15) found cetirizine to have a half-life of 10.06 h after oral administration in cats, allowing for once-daily administration in this species. This makes cetirizine a drug that can be administered by cat owners with greater compliance than drugs which require multiple daily dosing (15).

Cetirizine was found to be effective in 18% of dogs with atopic dermatitis in 1 small study (14). Although anecdotal information (3,16) indicates that cetirizine may be beneficial in the treatment of cats with allergic skin disease, we could find no published studies that corroborate or refute this information. The purpose of this paper is to report the results of an open clinical trial on the efficacy of cetirizine for the management of allergic pruritus in the cat.

Materials and methods

Thirty-two cats with cutaneous reaction patterns typical of allergic skin disease were enrolled into the study as they were examined by the Dermatology Service at the Cornell University Hospital for Animals (CUHA) if their owners agreed to the protocol (Table 1). The cats included 20 castrated males and 12 spayed females and ranged in age from 2.5 to 16 y. There were 25 domestic shorthairs, 3 domestic longhairs, 2 Bengals, 1 Devon rex, and 1 Persian. Cats ranged in weight from 3.6 to 8.5 kg.

All cats exhibited one or more of the following cutaneous reaction patterns typical of allergic cats (1–3): self-induced alopecia (bilaterally symmetrical, self-induced hair loss, especially on the ventral surface of the abdomen and medial aspect of the thighs, wherein the underlying skin appears normal), nonlesional pruritus (bilaterally symmetrical pruritus which initially involves clinically normal skin, but results in self-excoriation, especially on the face, neck, and pinnae), eosinophilic plaques (raised, flat-topped, red, intensely pruritic lesions, especially on the ventral surface of the abdomen and medial aspects of the thighs), and eosinophilic granulomas (firm, well-circumscribed papules and nodules, especially on the lips, chins, and caudal aspect of the thigh) (Table 1) (1). Twenty-eight cats were presented with nonseasonal clinical signs and 4 cats (cases 5, 6, 8, and 28) with seasonal clinical signs. The duration of the clinical signs varied from 6 wk to 15 y. Twenty-three of the 32 cats had previously been treated with various medications to control their clinical signs. These medications included topical, oral, and injectable glucocorticoids; antihistamines; antibiotics; and monthly ectoparasitides. None of the cats were reported to be anxious, and none had identified environmental stressors that might have provoked behavior-induced skin disease.

All cats were free of bacterial, fungal, and parasitic dermatoses based on physical examination and appropriate laboratory investigations. Skin biopsies were not performed. Fourteen cats

(cases 3, 5, 6, 8–10, 12, 13, 16, 19, 21, 24, 28, 30) failed to improve while being fed an appropriate commercial or home-prepared novel protein diet for at least 4 wk and received a diagnosis of atopic dermatitis (Table 1) (1). In 16 cats (cases 1, 2, 7, 11, 14, 15, 17, 20, 22, 23, 25–27, 29, 31, 32), completing a strict novel protein diet was impossible due to one or more of the following reasons: patient intolerant to dietary changes; the patient was living in a multicat household; the client was unable to confine the patient indoors during dietary trial. Thus, these cats may have had atopic dermatitis, food allergy, or both. Two cats (cases 4 and 18) had both atopic dermatitis and food allergy (1). Two cats underwent intradermal and/or serologic allergy testing (cases 4 and 9). Case 4 had a positive reaction to *Acarus siro* on intradermal testing and positive reactions to short ragweed, alfalfa, red cedar, perennial rye, *Penicillium*, *Aspergillus*, *Fusarium*, *Rhizopus*, *Mucor*, and *Malassezia* on serology. Case 9 had the following positive results on serology: plantain, lamb's quarters, yellow dock, pine, sweet vernal grass, June grass, *Aspergillus*, *Fusarium*, *Rhizopus*, *Epicoccum*, *Helminthosporium*, *Curvularia*, house dust, and *Tyrophagus*. Case 9 received ASIT prior to and during the cetirizine trial.

Each client was given a consent form detailing the inclusion criteria of the study and a 14-day follow-up questionnaire. No other anti-inflammatory medications were administered during the cetirizine trial. Clients were asked to evaluate the severity of pruritus experienced by their cats on a scale of 1 to 10: 1 representing no pruritus, and 10 representing the maximum pruritus exhibited by the patient. Excessive scratching, licking, chewing, grooming, or combinations of these were obvious to the owners of all cats prior to the initiation of the cetirizine trial.

Each cat was treated with cetirizine hydrochloride (Mylan Pharmaceuticals, Montgomery, West Virginia, USA) 5 mg, PO, q24h, for 2 wk. A 2-week treatment period was selected based on observations made in other studies in which nonsteroidal agents were given to pruritic cats (12,13). Reduction in pruritus on the pruritus scale was assessed to be nonexistent, mild (< 25% reduction), moderate (25% to 50% reduction), or marked (> 50% reduction). If there was a reduction in pruritus after the initial 2-week trial, the cetirizine was discontinued for 2 wk. If pruritus returned, the cetirizine was readministered for an additional 30-day period in order to document a repeatable and sustainable response (8).

Statistical analysis

All statistical methods were performed using Statistix® 7.0 (Statistix 9.0 Analytical Software, Tallahassee, Florida, USA).

In order to determine whether or not there was an association between a cat's major cutaneous reaction pattern and improvement while receiving cetirizine, the data were evaluated in 2 Fisher's exact tests. In each, the patterns with the smaller numbers of cats were compared to the pattern with the most cats (self-induced alopecia) so that there was greatest possible precision in these 2 tests. In order to determine whether or not the age of a cat or the severity of the pruritus was associated with improvement while receiving cetirizine, the data were evaluated using Wilcoxon's rank-sum test using all 32 cats. Significance was declared at $P = 0.0125$.

Table 2. Evaluation of response to cetirizine in 32 allergic cats

Case	Severity score pre-treatment	Severity score post-treatment	Response to cetirizine
1	10	10	None
2	5.5	5.5	None
3	8	1.5	Marked
4	10	10	None
5	6.5	6.5	None
6	6	6	None
7	5	5	None
8	8	8	None
9	4	3	Mild
10	10	10	None
11	5	5	None
12	7	6	Mild
13	8	4	Moderate
14	2	2	None
15	6.5	6.5	None
16	9	5	Moderate
17	5	4	Mild
18	7	8	None
19	5.5	4.5	Mild
20	6	2	Marked
21	7.5	6	Mild
22	3.5	3.5	None
23	4	2	Moderate
24	5	1	Marked
25	5	2.5	Moderate
26	5	2.5	Moderate
27	5	5	None
28	5	5	None
29	5	5	None
30	5	5	None
31	5	5	None
32	5	5	None

Mild = < 25% reduction in severity score.

Moderate = 25% to 50% reduction in severity score.

Marked = > 50% reduction in severity score.

Results

All 32 cats completed the study. The owners of 13 cats [13/32 = 41%; 95% confidence interval (CI) is 24% to 59%] recorded a reduction in their pet's pruritus (Table 2). The reduction in pruritus in these 13 cats was recorded as marked in 3 cats (cases 3, 20, 24), moderate in 5 cats (cases 13, 16, 23, 26, 27), and mild in 5 cats (cases 9, 12, 17, 19, 21). The median pruritus score reduction for these 13 cats was 2.5 (range 1 to 7) (Table 2). In all 13 cats that improved while receiving cetirizine, the improvement was lost when the cetirizine was stopped and regained after the cetirizine was readministered. Of the cats that responded to cetirizine, 8 had atopic dermatitis (8 of 14 atopic cats, 57%), and 5 had allergic dermatitis of undetermined origin (5 of 16 cats, 31%).

There was no association between cutaneous reaction pattern and improvement while receiving cetirizine; both P were ≥ 0.69 in the Fisher's exact tests. Neither the age of the cat nor the severity of pruritus was associated with improvement while receiving cetirizine; both P were ≥ 0.25 in Wilcoxon's rank-sum test.

No adverse side effects were observed during the trial.

Discussion

Cetirizine hydrochloride is a second generation, nonsedating, selective H1-receptor antagonist that is used to treat atopic dermatitis, asthma, allergic rhinitis, and idiopathic urticaria

in humans (17). It has also been reported to be effective for the prevention of the development of asthma in atopic children (22). Cetirizine lacks the anticholinergic effects of first-generation antihistamines at therapeutic doses in humans, and its long half-life allows once-daily dosing (21). It has also been used as a treatment for canine atopic dermatitis, and has been associated with rare and mild adverse side effects in this species (14).

Anecdotal sources indicate that cetirizine may be useful in the treatment of cats with allergic and eosinophilic skin diseases (12,16). To our knowledge, this study is the first published clinical trial evaluating the efficacy of cetirizine for the management of feline allergic skin diseases.

In our study, 41% of the allergic cats responded favorably to cetirizine. In previous studies, 73%, 50%, 50%, and 35% of allergic cats responded to chlorpheniramine, oxatamide, clemastine, and cyproheptadine, respectively (10–13). Thus, in spite of cetirizine's wide range of anti-inflammatory effects, especially its effects on eosinophils, it does not appear to be more effective in allergic cats than the antihistamines previously evaluated.

In our study, there was no significant association between patient's age, disease severity, or cutaneous reaction pattern and improvement with cetirizine administration. These findings are consistent with those in previous studies using other antihistamines in allergic cats (10,12,13). No adverse side effects were reported in the allergic cats in our cetirizine study, which is consistent with the findings of Papich et al (15) in healthy cats. In a pharmacokinetic study of cetirizine in normal cats (15), therapeutic drug concentrations were achieved with an oral dose of 1 mg/kg BW. An identical dose was used in atopic dogs (14). In this study of allergic cats, at a dose of 5 mg/cat, the cetirizine dosage varied from 0.6 to 1.4 mg/kg BW.

In conclusion, under the conditions of this study, cetirizine was a useful nonsteroidal antipruritic agent for cats with allergic skin disease. Once-daily dosing, lack of adverse side effects at therapeutic doses, and affordability (7¢ US/cat/d) make cetirizine an attractive treatment option for allergic cats. CVJ

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