Observations on the use of tetracycline and niacinamide as antipruritic agents in atopic dogs

Karyn E. Beningo, Danny W. Scott, William H. Miller, Jr., Emily Rothstein

Abstract — Tetracycline and niacinamide were administered in combination to 19 atopic dogs to determine their effectiveness in controlling pruritus. The pruritus was controlled successfully in only one dog. One dog experienced diarrhea that was severe enough to warrant stopping the medication.

Résumé — Observations sur l'utilisation de tétracycline et de niacinamide comme agents antiprurigineux chez des chiens atopiques. Tétracycline et niacinamide ont été administrées à 19 chiens atopiques pour déterminer leur efficacité à contrôler le prurit. Le prurit a été contrôlé de façon satisfaisante chez un seul chien. Un chien a présenté une diarrhée suffisamment grave pour justifier une interruption de la médication.

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Atopy is the second most common hypersensitivity skin disease of the dog (1). Glucocorticoids are effective in treating dogs with atopy; however, due to their side effects and some owners' reluctance to use these agents, they may be undesirable. Antihistamines and omega-3/omega-6 fatty acid supplements have been useful in some atopic dogs (1).

Tetracycline, a bacteriostatic antibiotic, has many biologic properties at certain dosages, including inhibition of leukocyte chemotaxis, inhibition of prostaglandin synthesis, inhibition of the complement system, inhibition of lipases and collagenases, and suppression of lymphocyte blastogenic transformation and antibody production (2). Niacinamide (the amide of niacin) has been shown to prevent degranulation of mast cells, block antigen IgE-induced histamine release, and decrease protease release (3). Tetracycline has been used in human dermatology for the treatment of acne, rosacea, telangiectasia, pityriasis lichenoides, panniculitis, and pustulosis palmaris and plantaris (2). The combination of tetracycline and niacinamide has been used to treat canine and human patients with bullous pemphigoid and the pemphigus complex, and human patients with linear IgA dermatosis (2–5). In canine patients, this combination has also been used successfully for discoid lupus erythematosus, the sterile pyogranuloma/granuloma syndrome, and lupoid onychodystrophy (3,6,7).

The purpose of this paper is to report our observations on the use of tetracycline and niacinamide for controlling the pruritus of atopic dogs.

Nineteen dogs were randomly entered into this study. All of the dogs were examined at the Companion Animal Hospital at the College of Veterinary Medicine and the owners agreed to and complied with the protocol. Various breeds were represented of which 11 were female and 8 were male. Their body weights varied from 4 kg to 58 kg and their ages ranged from 2.5 y to 7 y. The duration of clinical signs varied from 1 y to 6 y. All dogs exhibited nonlesional pruritus that involved one or more of the following areas: face, paws, elbows, distal extremities, ventrum, ears, and lumbosacral area.

Sixteen of the dogs had nonseasonal pruritus. Thirteen of these dogs were placed on a 4- to 6-week, home-prepared, hypoallergenic diet. One of these dogs (case 8) showed a partial improvement on the diet and was determined to have a concurrent food hypersensitivity. Three dogs (cases 3, 11, and 14) were placed on a 4- to 6-week trial with a commercial novel protein diet with no response. The remaining 3 dogs had seasonal pruritus. All of the dogs had multiple positive reactions on intradermal skin testing and were known to respond completely to anti-inflammatory doses of glucocorticoids.

Any dog found to have a bacterial pyoderma, *Malassezia* dermatitis, or ectoparasites, based on physical examination, skin scrapings, flea combing, and cytology, was treated appropriately prior to starting the clinical trial. No dog had received glucocorticoids or antihistamines 3 wk or 10 d, respectively, prior to the beginning of the trial, and all of the dogs were pruritic.

The dogs were treated with tetracycline and niacinamide for 2 wk. Previous studies that assessed the efficacy of nonsteroidal agents in controlling pruritus had used 1- to 2-week trial periods (1). Based on the past studies, a 2-week trial period was considered sufficient. Dogs weighing less than 10 kg received 250 mg of tetracycline and 250 mg of niacinamide every 8 h. Dogs greater than 10 kg received 500 mg of each every 8 h. This protocol was previously used for the treatment of other immune-mediated dermatologic conditions (3). No other treatments were allowed.

After the 2-week period, the owners were asked to classify the reduction in pruritus as either poor (0–25% reduction), fair (26–50%), good (51–75%), or excellent (76–100%). If there was a good or excellent response, the owners were asked to give tetracycline alone for 2 wk,

Departments of Clinical Sciences and Pathology, College of Veterinary Medicine, Cornell University, Ithaca, New York USA 14853.

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Table 1. Clinical data and response to tetracycline and niacinamide in 19 atopic dogs

Case #	Breed	Sex	Age (years)	Duration of disease (years)	Response to tetracycline and niacinamide	Side effects
1	Boston terrier	F/S	5.5	5	Excellent	None
2	Labrador retriever	MC	7	6	Poor	None
3	German shorthaired pointer	FS	5	4	Poor	None
4	Bichon frise	MC	3	2.5	Poor	None
5	Irish setter	FS	5	3	Poor	None
6	Cocker spaniel	FS	6.5	4	Poor	None
7	Mixed	FS	6	5	Poor	None
8	Welsh terrier	MC	6.5	5.5	Fair	None
9	Golden retriever	FS	4	3.5	Stopped due to side effect	Diarrhea
10	Lowland sheepdog	MC	4	3.5	Poor	None
11	Golden retriever	MC	6	4	Poor	None
12	Labrador retriever	M	5	3	Poor	None
13	Golden retriever	MC	4.5	3.5	Poor	None
14	Golden retriever	FS	2.5	2	Fair	None
15	Shar-pei	FS	5	2	Poor	None
16	Mixed	FS	5	1	Poor	None
17	Shih tzu	FS	3.5	3	Poor	None
18	Golden retriever	MC	4	3	Poor	None
19	Labrador retriever	FS	4	1	Poor	None

FS = Female spayed MC = Male castrated M = Male

then niacinamide alone for an additional 2 wk. If either drug or the combination was effective, that protocol was to be given for an additional 30-day period to document repeatable and sustainable efficacy.

Only one dog (case 1) had an excellent response to the tetracycline and niacinamide combination. The owner additionally reported that the niacinamide alone also gave excellent results; however, the tetracycline given alone resulted in a poor response. A 30-day trial of tetracycline and niacinamide showed a repeatable and sustained response in this dog.

Fifteen dogs had a poor response (cases 2–7, 10–13, 15–19) to tetracycline and niacinamide, and 2 dogs (cases 8 and 14) had fair responses. One dog (case 9) developed a side effect (diarrhea) that was severe enough to warrant stopping treatment. No other dogs experienced any side effects.

Tetracycline and niacinamide have been used for the treatment of immune-mediated skin diseases of the dog, but to the authors' knowledge no prior clinical trials have looked at this combination to assess its efficacy in pruritic dogs. Only one dog had an excellent repeatable and sustained response to the combination of tetracycline and niacinamide. This dog (case 1) also had an excellent response to niacinamide alone, but not to tetracycline alone. Arguably, it was the niacinamide that this dog responded to, and not the combination. However, the owner felt that the combination worked better, and was not interested in doing a 30-day trial with niacinamide alone. Two dogs (cases 8 and 14) had fair responses to the combination of tetracycline and niacinamide, but the owners of the latter 2 dogs did not feel that the reduction in pruritus was enough to warrant further use of the drugs. In a previous study, another tetracycline drug (doxycycline) was not effective as an antipruritic agent in dogs (8). The single dog response does not compare favorably with those in studies using antihistamines and omega-3/omega-6 fatty acid supplements as antipruritic agents. Good to excellent results were seen in up to 30% of dogs receiving clemastine, 24% receiving hydroxyzine, 22% receiving diphenhydramine, 17.8% receiving chlorpheniramine, and 25% receiving omega-3/omega-6 fatty acid supplements (1). Amitriptyline produced a response in 30% of dogs in one clinical trial (1).

The most common side effects reported for tetracycline include nausea, vomiting, anorexia, and diarrhea. Other side effects reported include hepatotoxicity, photosensitivity reactions, and blood dyscrasias (3,9). Niacinamide can cause diarrhea, anorexia, and lethargy (3). Only one dog in this study developed a side effect (diarrhea) with the combination of these 2 drugs.

Based on previous trials (3,6), the dosage of tetracycline and niacinamide should be acceptable. A 2-week period was chosen for the study. However, in other diseases where the combination of tetracycline and niacinamide is used, it can take 8 to 12 wk for a good clinical response (3,6). Therefore, a lengthier study may have produced different results. It is very difficult to convince owners of pruritic dogs to wait for 8 to 12 wk for an antipruritic therapeutic regimen to work.

A placebo was not used in our study. However, with the poor response to the study and the sustained and repeatable response of case 1, a placebo effect would be unlikely. In addition, other studies have failed to demonstrate a repeatable and sustainable placebo effect in pruritic dogs (10).

Based on this study, the combination of tetracycline and niacinamide at this dose and frequency was not useful in controlling the pruritus of atopic dogs. CVJ

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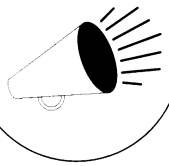

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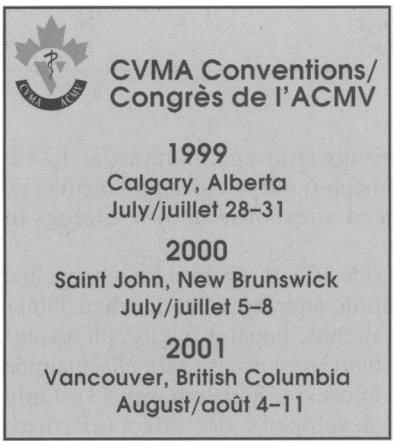

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