Case Report of Afoxolaner Treatment for Canine Demodicosis in Four Dogs Naturally Infected with Demodex Canis

Fernando Chávez, DVM

C.M.V.P. 2983
Veterinaria Bertchi S.A.
Clinical Veterinaria Bertchi
Lima, Peru
Phone: +5114518077
Email: Fernando@bertchi.com

KEY WORDS: Afoxolaner; demodicosis; demodectic mange; Nexgard

ABSTRACT

Background

Afoxolaner is currently used for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of the black-legged tick (*Ixodes scapularis*), American dog tick (*Dermacentor variabilis*), lone star tick (*Amblyomma americanum*), and the brown dog tick (*Rhipicephalus sanguineus*). No claims of activity against mange mites are presently available in the product indications. This paper describes four cases of naturally occurring generalized demodectic mange that were diagnosed and treated with afoxolaner (Nexgard®; Merial, Inc., Duluth, Georgia, USA) using the standard flea and tick control doses.

Materials and Methods

Four dogs, including three intact males and one intact female, ranging in ages from 8 months to 10 years, were presented at the clinic exhibiting clinical signs of demodectic mange infestations. The clinical diagnosis was confirmed using deep skin scrapings, identifying the mites and counting the number of mites per microscopic field. On Day 0, each dog was given a single dose (tablet) of Nexgard, achieving the minimum dosage of 2.5 mg afoxolaner/kg (1.14 mg/lb). Dogs were re-treated at the same dose 4 and 8 weeks after the initial visit. Deep skin scrapings and clinical evaluations were performed at each treatment visit, and final evaluations were performed at 12 weeks.

Results

Clinical improvement and dramatic reduction in recovery of live mites was observed at 4 weeks after initiation of treatment with afoxolaner. All four dogs were clear of clinical lesions, and were negative for live mites in all skin scraping sites at 8 and 12 weeks after the initial treatment.

Conclusions

Afoxolaner was an effective and practical treatment for canine generalized demodectic mange in these four dogs and demonstrated effective reduction of live mites in skin scrapings and clinical improvement in skin lesions. Based on results of the present study, additional work is justified to gather further evidence of afoxolaner for the treatment of canine generalized demodicosis.

BACKGROUND

Canine demodicosis (demodectic mange) is a skin disease of dogs consisting of greater than normal numbers of *Demodex* mites.[1,2] Although most *Demodex* spp. are considered normal mammalian fauna, overgrowth of mites may be associated with development of patchy hair loss or mild to severe dermatitis in dogs and, infrequently, in cats.[2-4]

Canine demodicosis may be localized or generalized, and both forms may present in either juvenile or adult dogs.[1,2,4]

Localized demodicosis is characterized by a mild, nonpruritic, patchy alopecia on the head or limbs. This form usually develops in puppies younger than 6 months of age, and most of these cases resolve spontaneously without treatment.[2,4] Generalized canine demodicosis is a moderate to severe disease that is generally attributable to an overgrowth of mites, which may occur as a result of underlying systemic disease or immunosuppression from various causes, possibly including malnutrition or endoparasitism in juveniles or chemotherapy, neoplasms, hypothyroidism, or hyperadrenocorticism in adult dogs.[2,4]

Although demodicosis has been recognized as a global parasitic disease that can be easily diagnosed, treatment options are few, and to achieve an adequate response to treatments extended, aggressive therapy is required.[2,4] Deep skin scrapings are the most reliable and frequently used method to diagnose demodicosis. Generalized demodicosis is also frequently accompanied by secondary bacterial skin infections.[2] The most common organism present is *Staphylococcus pseudintermedius*.However, *Escherichia coli* or *Pseudomonas aeruginosa* may be the predominant species in some cases.[2] An appropriate antimicrobial must be initiated according to product recommendations and continued for 1 to 2 weeks beyond clinical and microscopic resolution of the bacterial skin infection.

Amitraz dip at 250 ppm applied topically every 2 weeks for three to six treatments is the only approved miticidal treatment for generalized demodicosis in the United States.[2,4,5] Several series of treatment may be required to eliminate the mites for severe cases. In clinical studies conducted in approximately 1,100 dogs with generalized demodicosis, efficacy of amitraz dip was 96% after one or two treatment series, and 99% after 3% to 4% of the dogs received a third or fourth series of dips.[5] However, treatment concentrations of amitraz and intervals vary from country to country.[2] Despite the reports of high efficacy, variable efficacy and the potential for toxicity also have been reported.[2-5] Persons handling animals, animals that have been treated with amitraz solutions, or amitraz concentrate, are warned to avoid eye and skin contact as well as ingestion or inhalation of amitraz.[2,4]

Other miticidal treatments used off-label include high-dose oral ivermectin,[2,4] oral milbemycin oxime,[2] topical 2.5% moxidectin + 10% imidacloprid,[6] injectable doramectin,[7] and topical combination of fipronil 6.26%, amitraz 7.48%, (S)-methoprene 5.63%.8 Currently, no approved treatment exists that will provide consistent clinical and/or microscopic remission, or that is considered safe and acceptable to pet owners.

Fluralaner, a long-acting, systemic insecticide, and acaricide, of the isoxazoline family, are approved by the FDA for treatment of flea and tick infestations.[9] This class of parasiticides exhibits selective inhibition of arthropod γ–aminobutyric acid and L-glutamate-gated chloride channels.[9]

In a study of fluralaner chewable tablets against generalized demodicosis in dogs, Fourie and colleagues found the oral dose used to control fleas and ticks was highly effective against canine generalized demodicosis.[9] As a result of this observed efficacy of fluralaner, a study was initiated to evaluate the efficacy of afoxolaner in a clinical setting in dogs presented with canine demodicosis.

Afoxolaner (Nexgard®; Merial, Inc., Duluth, Georgia, USA) is another member of the newly introduced isoxazoline family that bind to chloride ion channels of arthropods inhibiting the activity of γ-aminobutyric acid (GABA) and L–glutamate.[10] Its long half-life enables afoxolaner to cause the death of insects and acarines.[9,10] Afoxolaner is currently approved in the United States by the Food and Drug Administration (FDA), and has been used in clinical practice for more than 1 year for the treatment and prevention of flea infestations (Ctenocephalides felis),

Table 1. *Dog identification and afoxolaner treatment information for dogs with generalized demodectic mange presented to the clinic*

Patient No.	Breed	Age (y)	Sex	Lesions	Weight (kg)	Tablet size (mg)
1	Shih-tzu	10	Male	Left hind limb	6.1	28.3
2	Jack Russell Terrier	0.67	Male	Generalized	7	28.3
3	Pitbull Terrier	1.5	Female	Generalized	27	68.0
4	Mongrel	11	Male	Generalized	3.3	11.3

and the treatment and control of black-legged tick (Ixodes scapularis), American dog tick (Dermacentor variabilis), lone star tick (Amblyomma americanum), and the brown dog tick (Rhipicephalus sanguineus).[10] Afoxolaner also has recently been introduced in Peru. To the author's knowledge, no studies have been conducted to date describing the efficacy of afoxolaner as a treatment for demodicosis.

METHODS

Afoxolaner was tested as a potentially effective treatment for demodicosis in four dogs presented with clinical evidence of naturally occurring generalized demodectic mangement. The dogs included three intact males and one intact female. All four dogs had been clinically ill for at least 2 months before presentation at the clinic. The dogs had all been prescribed to have a 2% chlorhexidine shampoo weekly. Two of the dogs had received oral cephalexine antibiotic at 22 to 26 mg/kg BID for 21 days. No other illnesses were observed at the time of presentation. Additional descriptive information about the dogs is presented in Table 1.

The clinical diagnosis of generalized demodicosis was confirmed using deep skin scrapings, identifying the mites and counting the number of mites/eggs per microscopic field. The owners were informed about all other possible treatment options, and were given the opportunity to allow the use of afoxolaner as an alternative treatment. Owners also were informed that this would be an off-label use of the product, and that it would be administered to their dog at the recommended standard dose and frequency for flea/tick treatment.

TREATMENT

Each dog received a single dose (tablet) of the commercially available afoxolaner chewable (Nexgard) achieving the minimum dosage of 2.5 mg afoxolaner/kg (1.14 mg/lb) on Day 0 and again at 4 and 8 weeks after the initial treatment.

EVALUATIONS

Initial deep skin scrapings were taken for microscopic examination to detect the presence and number of live mites prior to the initial visit and at 4, 8, and 12 weeks after the initial visit. For three of the dogs, five sites were scraped at each evaluation. However, Dog 1 had only two sites scraped because only one leg exhibited clinical signs of mite infestation. Clinical evaluation of the initial skin lesions were performed at each visit. Percentage efficacy was calculated at each follow-up visit using the formula total adults Day 0 – total adults at follow-up/total adults Day 0 × 100. At 16 weeks after the initial treatment, a clinical evaluation was performed. No skin scrapings were taken for microscopic examination.

RESULTS

All dogs were clinically improved at 4 and 8 weeks after treatment was initiated, and one dog even showed remarkable improvement at a clinical evaluation requested by the owner 1 week after treatment (Figure 1). Efficacy of the clearance of adult mites at Week 4 ranged from 99.4% to 100% (Table 2). At the 8-week evaluation, no live mites, immatures, or eggs were observed. At 12 weeks, the dogs still remained free of lesions and live mites.

Table 2. *Total number of demodectic mange mites and eggs from sampling sites for dogs treated orally with 2.5 mg afoxolaner/kg on Day 0 and at 4 and 8 weeks after the initial treatment*

Time of evaluation	Total No. of mites and eggs from skin scrapings/field			
	Dog 1[a]	Dog 2	Dog 3	Dog 4
Day 0 (pretreatment)	391 adults	1305 adults	612 adults	181 adults
	92 immature	325 immature	94 Immature	0 immature
	102 eggs	87 eggs	238 eggs	0 eggs
4 weeks	3 adults[b] (99.4%)	8 adults[c] (99.4%)	0 (100%)	0 (100%)
8 weeks	0 (100%)	0 (100%)	0 (100%)	0 (100%)
12 weeks	0 (100%)	0 (100%)	0 (100%)	0 (100%)

[a]Only 2 sites counted because this dog had only 1 limb affected
[b]7 fields scraped at this evaluation to be able to find any live mites
[c]12 fields scraped at this evaluation to be able to find any live mites
[d]1 mite exoskeleton was observed in the entire slide
% efficacy = total adults Day 0 – total adults at follow-up/total adults Day 0 × 100

DISCUSSION

This is the first publication reporting the use of afoxolaner for the treatment of canine demodicosis. The use of afoxolaner (Nexgard) as a sole treatment against generalized demodicosis was 99% to 100% effective 1 month after a single treatment, and was 100% for all four dogs following the second and third treatments 1 and 2 months after the initial treatment. In one case (Dog #3), the rate of improvement was dramatic, with all skin scrapings for this dog negative for live mites 7 days after receiving the first oral treatment of afoxolaner. As of the preparation of this paper 6 months after the initiation of treatment with afoxolaner, all four[4] dogs remain clinically free from clinical signs of demodicosis.

In a study conducted by Fourie and colleagues, a single oral dose of fluralaner was >99% effective in reducing mite numbers by Day 28 and 100% on Days 56 and 84.[9] In the present study with afoxolaner, three treatments were administered at monthly intervals, according to the recommended treatment regimen for year-round flea and tick control.[10] Prescribing information for afoxolaner (NexGard) indicates the product is indicated for monthly administration to dogs and puppies 8 weeks of age and older, weighing at least 4 lb for treatment and prevention of fleas and the treatment and control of Ixodes scapularis, Dermacentor variabilis, Amblyomma americanum, and Rhipicephalus sanguineus tick species. No adverse reactions were observed with the concomitant use of afoxolaner with other medications, including vaccines, anthelmintics, antibiotics, steroids, NSAIDS, anesthetics, and antihistamines.[10]

It is expected that a single treatment with afoxolaner will be effective against Demodex spp mites on dogs, and will provide clinical improvement of dermatologic signs associated with canine generalized demodicosis for at least 12 weeks after treatment. However, studies with larger numbers of animals will be required to provide statistical evidence of the efficacy of a single dose and the duration of the efficacy.

CONCLUSIONS

Afoxolaner administered orally at 3 monthly intervals to client-owned dogs exhibiting evidence of generalized demodicosis demonstrated effective reduction of live mites in skin scrapings and clinical improvement in skin lesions for 12 weeks. Based on results of the present study, additional work is justified to gather further evidence of afoxolaner for the treatment of canine generalized demodicosis.

Figure 1. *Skin condition on ventral aspect of Dog #3 before treatment with afoxolaner on Day 0 (a); 1 week after treatment (b); 4 weeks after treatment (c); 8 weeks after treatment (d).*

COMPETING INTERESTS

Dr. Chávez has received consulting and speaker funding from Merial and Zoetis.

ACKNOWLEDGEMENTS

The author thanks Kathleen Newcomb, Blythewood Consulting, LLC for editorial assistance with the preparation of this manuscript.

REFERENCES

1. Miller WH Jr, Griffin CE, Campbell KL. Parasitic skin disease. In: Muller and Kirk's small animal dermatology. 7th edition. St Louis, MO: Elsevier, 2013; 284–342.
2. Mueller RS, Bensignor E, Ferrer L, et al. Treatment of demodicosis in dogs: 2011 clinical practice guidelines. *Vet Dermatol* 2011; 86–96.e21.
3. Ravera I, Altet L, Francino O, et al. Small Demodex populations colonize most parts of the skin of healthy dogs. *Vet Dermatol* 2013, 24:168–172.e37.
4. Demodex (mange mite) CAPC Vet. Available at http://www.capcvet.org/capc-recommendations/demodex-mange-mite. Accessed March 12, 2016.
5. Mitaban for Animal Use. Available at http://www.drugs.com/vet/mitaban.html. Accessed March 12, 2016.
6. Paterson TE, Halliwell RE, Fields PJ, et al. Canine generalized demodicosis treated with varying doses of a 2.5% moxidectin + 10% imidacloprid spot-on and oral ivermectin: parasiticidal effects and long-term treatment outcomes. *Vet Parasitol* 2014; 205:687–696.
7. Hutt JH, Prior IC, Shipstone MA. Treatment of canine generalized demodicosis using weekly injections of doramectin: 232 cases in the USA (2002–2012).*Vet Dermatol* 2015;26:345–349.e73.
8. Fourie J, Dumont P, Halos L, Beugnet F, Pollmeier M. Efficacy of a topical application of Certifect® (fipronil 6.26% w/v, amitraz 7.48% w/v, (S)-methoprene 5.63% w/v) for the treatment of canine generalized demodicosis. *Parasite* 2013; 20:46.
9. Fourie J, Liebenberg JE, Horak IG, Taenzler J, Heckerorth AR, Frénais R. Efficacy of orally administered fluralaner (Bravecto™) or topically applied imidacloprid/moxidectin (Advocate®) against generalized demodicosis in dogs *Parasit Vectors* 2015; 8:187.
10. Merial, Inc. NexGard® (afoxolaner) Chewables. Prescribing information. 2015.
11. Dryden MW, Smith V, Chwala M, et al. Evaluation of afoxolaner chewables to control flea populations in naturally infested dogs in private residences in Tampa, FL, USA. *Parasit Vectors* 2015;8:286.
12. Beugnet F, Leibenberg J, Halos L. Comparative speed of efficacy against Ctenocephalides felis of two oral treatments for dogs containing either afoxolaner or fluralaner. *Vet Parasitol* 2015;207:297–301.
13. Beugnet F, Leibenberg J, Halos L. Comparative efficacy of two oral treatments for dogs containing either afoxolaner or fluralaner against Rhipicephalus sanguineus sensu lato and Dermacentor reticulatus. *Vet Parasitol* 2015;209:142–145.