

Efficacy of Simparica Trio® against Natural Lice Infestations on Dogs Presented as Veterinary Patients

Research Article

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Abstract

Many parasites can infest dogs, and some are more prevalent than others. In Canada, lice are anecdotally considered to be the most common ectoparasite in Alberta by most veterinarians. For compliance reasons, all-in-one oral medications are considered preferred preventative treatment for parasite control in dogs. As such, a field study was performed to evaluate the clinical efficacy of a monthly oral treatment with Simparica Trio against naturally acquired lice infestations in dogs in Alberta. For this study, dogs presented with a naturally acquired lice infestation on initial examination were recruited. All dogs were treated with Simparica Trio. Dogs received the oral chewable tablet treatment on day 0 and day 30. Lice counts on all dogs were performed before treatment (day 0), and were repeated on days 7, 30 and 45. On day 30 of the study, no lice were detected on any of the Simparica Trio treated animals, and the infestation did not recur during 45 days of the study duration. All dogs were successfully treated with a single dose administration. The data provided in this study suggests that Simparica Trio might be an alternative treatment for use in lice infestations in dogs affected by *L. setosus*.

Keywords: Parasitology; Lice; Simparica Trio; Isoxazoline.

Background

Many parasites can infest dogs, and some are more prevalent than others. Lice are considered occasional ectoparasites and they are commonly reported in colder climates [1]. In Canada, no publications have been available to report the prevalence of lice. However, lice are anecdotally considered to be the most common ectoparasite in Alberta by most veterinarians. Many different species of lice are reported in the literature, and they are considered to be host specific [1]. For canines, two main species have been reported, *Trichodectes canis* and *Linognathus setosus*. *T. canis* is considered a chewing or biting louse since it feeds on epidermal tissue debris and sebaceous secretions. *L. setosus* is a sucking louse because it feeds on blood [2]. Both depend on their host to survive and as such will spend their entire life on their host. The life cycle for

these parasites from egg to adult takes 3-6 weeks, and all phases occur on the host. Each female lays a couple of eggs per day, and those eggs are attached to the fur with an insoluble cement. The nymphs hatch after 1 to 2 weeks and then develop into subsequent developmental stages to eventually become an adult over a period of 1 to 3 weeks [1]. Lice are considered to be an 'active' parasite, and animals affected by this parasite can potentially develop clinical signs such as pruritus, alopecia, cutaneous erythema, dermatitis, and secondary bacterial skin infections [1]. In severe infestations, or with young animals, cases of anemia secondary to infestation by *L. setosus* have been reported [1]. Lice generally spread by direct contact, or by secondary contact via contaminated grooming tools such as brushes or combs [1].

Multiple insecticides including permethrin [3], macrocyclic lac-

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tones [4] (including selamectin) and isoxazolin [5-7] have been reported to be effective against lice infestations. A novel chewable oral tablet (Simparica Trio[®], Zoetis, Parsippany, NJ, USA) containing unique dosage of sarolaner, moxidectin and pyrantel has shown marked efficacy to treat external parasite infestation such as fleas and ticks [8, 9]. For compliance reasons, all-in-one medications are the preferred preventative treatment for parasite control in dogs [10]. As such and taking into consideration that no publication was made to evaluate the efficacy of sarolaner at a dosage of 1.2-2.4 mg/kg, a field study was performed to evaluate the clinical efficacy of a monthly oral treatment with Simparica Trio against naturally acquired lice infestations in dogs in Alberta, Canada.

Methods

The study was a multicentered field case report study conducted between March 2021 to December 2022 in Alberta. A total of 6 veterinary practices in the Calgary and Edmonton areas participated. Privately-owned dogs diagnosed with lice infestation of any breed and gender were recruited.

Inclusion Criteria: For this study, otherwise healthy, non-breeding dogs presented with a naturally acquired lice infestation on initial examination were recruited. One louse present was sufficient for the dog to be included in the study. To be eligible for the study, the dogs needed to weigh more than 1.3kg and be eight weeks of age or older. Also, if the dog was living in a multi animal household, only dogs living with a maximum of three animals (dogs and/or cats) were allowed to participate. Of those, all dogs in the household could be recruited. Dogs participating in the study could not have been treated during the last 30 days prior to study entrance with any parasiticide products, bathed in an insecticidal treatment, or housed with dogs that had been exposed to any of the above mentioned treatments. To be included in the study, all pet owners had to sign an informed consent form stating that the above exclusions were not present.

Dogs were excluded from the study if they were living in a household with more than three animals (dogs and/or cats), if they were treated with an ectoparasite product in the last month (or the last three months if the patient received a treatment with a fluralaner-based product). No topical treatment was allowed during the study period unless the dog was presented with bacterial pyoderma. In such case, the prescribed dermatological treatment should not have had any insecticidal activity.

Treatment: All dogs were treated with Simparica Trio. Dogs received the oral chewable tablet treatment on day 0 and day 30. Dosing was performed according to the manufacturer recommendation based on the patient weight. This represents a dosage of 1.2-2.4 mg/kg of sarolaner, 24-48 mg/kg of moxidectin and 5-10mg/kg of pyrantel. Doses were determined based on the body weight of the patient at days 0 and 30. The treatment was administered by the veterinarian or a registered veterinary technician/technologist. There was no restriction regarding the prandial state at the time of treatment administration. Dogs were observed after each dose administration to ensure that the entire dose was consumed. If the dog was living with a cat, a treatment with Revolution[®] Plus was recommended to ensure cats were not acting as a potential fomite to reinfest the dog(s). Doses of Revolution Plus

were based on the body weight of the cat available in the cat's medical record.

Lice assessment and clinical findings: Lice counts on all dogs were performed before treatment (initial examination) on day 0, and were repeated on days 7, 30 and 45 post treatment. At each count, the number of nits, live nymphs, live adults, dead nymphs and dead adults were counted without magnification by a veterinarian or a registered veterinary technician in approximately 5 cm long coat partings at 25 predetermined locations. The locations assessed were the same for all animals and based on the common predilection sites of the parasites, including shoulders, neck and back. The technique used was consistent with the protocol described by Pollmeier et al [11] (Table 1). Additionally, one parasite for each patient was sampled on day 0 to be sent to a referral laboratory for definitive parasite identification. The referral laboratory was the same for all submissions.

A dermatological assessment was also performed by the veterinarian at days 7, 30 and 45. The assessment was made using the VAS dermatological assessment tool utilizing the protocol described by Olivry et al [12]. Using this tool, the veterinarian attributed a score based on the severity of the dermatological lesions detected during the physical exam. The bottom of the scoring chart represented normal skin. Equally distributed on a line of 10 cm, skin conditions were evaluated up to the upper limit which represented an extremely severe dermatitis. Scoring was calculated as the distance from the bottom of the chart to the veterinarian's mark as a percentage of the total length on the chart.

The dog owner was asked to assess the dog's pruritus level using the Pruritus Visual Analogue Scale chart, using the protocol described by Olivry et al [12]. This system allowed the owner to characterize the level of pruritus of the dog via a validated model. The pruritus score was calculated as the distance from the bottom of the chart to the owner's mark on the scale, as a percentage of the total length of the chart.

Data analysis: The animal was the experimental unit in this trial which was conducted as a completely randomized design (CRD). Variables of interest included total lice counts as well as visual analog scores (VAS) over time for each of animals.

Total lice counts were transformed by the log (total lice count + 1) transformation prior to statistical analysis to stabilize the variance and normalize the data. Total counts were analyzed by a linear mixed model (LMM) approach. Using the SAS Proc Mixed Procedure (SAS 9.4, Cary, NC) total counts were analyzed with a model that considered Day 0 as the fixed effect and animal and the residual error as random effects. Least Squares Means (LSMeans) were calculated and compared for each day by the two-sided Student's t-test at the 5% level of significance. Total lice count LSMean for each day were then back-transformed by the $10^{\text{AMean}^{-1}}$ calculation and presented as geometric means.

Arithmetic and geometric means along with % reduction from Day 0, based on both arithmetic and geometric means for total lice counts were calculated as follows:

Arithmetic Mean % Reduction = $(A \text{ Mean Day } 0 - A \text{ Mean Day } x) / A \text{ Mean Day } 0$

and

$$\text{Geometric Mean \% Reduction} = (\text{GMean Day } x - \text{GMean Day } 0) / \text{GMean Day } 0$$

were

$$x = \text{Day } 7, 30 \text{ or } 45.$$

VAS scores collected over time on the same animal were analyzed by the LMM approach for repeated measures. Using the Proc Mixed Procedure, these variables were analyzed with a model that considered the fixed effect of day, and the random effect of the residual error. Day was the repeated factor, and animal was the subject.

The covariance structure in the repeated measures analysis was investigated using five structural assumptions, namely, compound symmetry (CS), power [SP(POW)], first order autoregressive [AR(1)], heterogeneous first order autoregressive [ARH(1)] and unstructured (UN). The assumption giving the minimum value of the Akaike's Information Criterion (AIC) was selected in the final analysis.

LSMeans for each day were calculated and compared by the two-sided Student's t-test at the 5% level of significance.

Ethical evaluation: This study has been reviewed and approved by the Zoetis Kalamazoo Ethical Review Board prior to initiation.

Results

Nine dogs (five male and four females between 6 months and 13

years old), weighing between 4.2 and 46.3kg on the day of treatment and living in eight households were enrolled in the study over a 21-month period. Four dogs were purebred and 5 were mixed breed. Three dogs were affected by co-morbidities including heart murmur, chronic allergic skin disease, hypothyroidism and osteoarthritis.

Five dogs completed the study, and four dogs partly completed it. Three dogs were not presented back for their day 30 and day 45 post-treatment assessment. Of those, two were from the same household. Those three patients showed a significant reduction in their lice counts however they were not considered lice free on day 7, which represents the last time point they were presented. One dog did not return for its evaluation 45 days post-treatment. That patient was lice free on day 30.

Samples from eight patients were submitted to the laboratory for parasite identification purposes. From those samples, seven confirmed the presence of *L. setosus*. The other submitted sample was detected as a positive result, but the species of lice was not specified.

Table 2

The evaluation of pruritus reduction between day 0 and day 7, 30 and 45 showed a statistical difference at all timepoints. The results showed that dogs were significantly less pruritic at all timepoint following treatment with Simparica Trio (P-value of 0.0010 on day 7 and 0.004 on day 30 and 45).

Table 3

Seven dogs received a score reflecting dermatitis by their veteri-

Table 1: Body sites investigated for the parasites counts.

Body Site	No. of sites
Top of the head	1
Caudal to the right pinna	1
Right lateral neck	1
Caudal to the left Pinna	1
Left lateral neck	1
Dorsal spine (cervical)	2
Dorsal spine (thoracic)	2
Dorsal lumbar region and rump	2
Ventral abdomen	2
Ventral Neck	2
Total	15

Table 2: Mean lice counts and efficacy after administration of sarolaner/moxidectin/pyrantel to dogs naturally infested with lice *L. setosus*

Study Day	Number of dogs	Count range	Arithmetic mean lice count	Geometric mean lice count (log)	Efficacy (%)	P-Value
0	9	5-218	39	2.92		
7	9	0-35	7.44	1.31	84.58	0.0001
30	6	0	0	0	100	0.0001
45	5	0	0	0	100	0.0001

Table 3: Dermatological and pruritus assessment scoring for each dog at each timepoint.

	Start Day	End Day	Diff	Error	P-Value	Test
Statistically significant	0	7	1.663	0.36	0.001	Two-sided
Statistically significant	0	30	2.648	0.502	0.000	Two-sided
Statistically significant	0	45	2.648	0.502	0.000	Two-sided

narian on day 0 using the VAS dermatological scoring tool. All of those dogs improved their VAS score with treatment. Five of the patients improved by 50% after 7 days of treatment, and two dogs showed 50% improvement after 30 days of treatment.

Eight dogs were perceived as pruritic by their owner on day 0 using the Pruritus Visual Analogue Scale tool. All eight dogs improved with treatment. Seven improved by more than 50% after 7 days of treatment, and one improved by more than 50% after 30 days of treatment. Of the six dogs that completed the assessment performed on day 30, five were pruritus free. The dog that was still had mild signs of pruritus was also affected by a comorbidity (allergic skin disease) that could explain the symptoms.

Over the study period, one dog developed drowsiness and lethargy on day 45. The patient recovered quickly without treatment. Due to the time between the administration of the medication and the development of the symptoms, it is considered unlikely that the symptoms were treatment related.

Discussion

On day 30 of the study, no lice were detected on any of the sarolaner/moxidectin/pyrantel (Simparica Trio) treated animals, and the infestation did not recur during 45 days of the study duration. The 45 days duration of this study was chosen to ensure that the period would have allowed for the hatching of any eggs laid prior to the treatment being applied. The reduction in lice counts for all patients suggests that Simparica Trio can be considered as an alternative treatment for parasitic lice infestations. The treatment of lice bearing dogs with Simparica Trio resulted in significant reduction of pruritus in all animals showing clinical signs, as well as improvement of their skin condition. Another case study was published recently in the literature that reported the successful treatment of a lice infestation caused by a different louse, *Heterodoxus spiniger*. The dog in that study was lice-free at day 28 following treatment [13]. In this case the standalone formulation of Simparica was used and the dosage is higher compared to the dosage of sarolaner in Simparica Trio. To the best of the authors' knowledge, this is the first article published reporting a case series of successful treatments of lice infestation (*L. setosus*) in canine patients with a broad spectrum oral parasiticide product.

This study was designed to evaluate the possible efficacy of the treatment of naturally acquired lice infestation using the animal as its own control. Lice live their entire life on a host, and do not have the ability to survive in the environment for more than a couple of days. As such, natural cure of infestation is not expected, and infested animals should be quarantined and treated prior to coming into contact with other pets [1]. However, some evidence of an effective immune response to lice has been reported in the literature with lice [14]. Consequently, more research, including a randomized positive controlled study, should be conducted to

complete the assessment.

Previous study performed with fluralaner (Bravecto™) [5] and Afoxolaner (NexGard®) [6] also showed positive treatment results for dogs affected by lice infestation. The isoxazoline class of drug is therefore considered as a promising new class of medication to help in the treatment of these parasites. In Canada, the only products labeled for the treatment of lice in canine patients are permethrin- or imidacloprid-based and are available only in a topical formulation [15]. There is concern with the usage of permethrins about its neurotoxicity incats that cohabitate with a treated dog. Some cases of mortality have been reported following administration of permethrin-based products inducing neurotoxicity [16]. The alternative usage of isoxazoline-based products such as Simparica Trio could lead to the adoption of new treatment options without these toxicity concerns when dogs are sharing the same household with cats.

During this 21-month study, only nine dogs were recruited. This number of enrolled patients is lower than the authors expected. Even though prevalence data is not available in regard to *L. setosus* for the region studied over the period of time the research was conducted, the feedback from local veterinarians was that few animals were presented with lice infestation during this specific timeframe. One hypothesis that could explain this phenomenon is in the fact that over the years, more dog owners have adopted isoxazoline based products for the prevention of commonly seen parasites. Therefore, less lice infestations could have been seen in animals receiving this class of medication. Also, this study was conducted during the COVID-19 pandemic. Consequently, some legislations limiting contact between individuals might have also reduced the contact between dogs. Being a parasite that is transmitted primarily by direct contact, it is suspected that lice infestations might have been reduced during the COVID-19 pandemic.

Conclusion

The data provided in this case-based study suggests that Simparica Trio might be an alternative treatment for use in lice infestations in dogs affected by *L. setosus*. All dogs were successfully treated with a single dose administration. A repeated treatment was undertaken to ensure that all enrolled patients were covered over the potential six-week period of time representing the life cycle of this parasite as reported in the literature. Further studies including a positive control are recommended to fully confirm the efficacy of Simparica Trio for the treatment of lice infestation.

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