SMALL ANIMALS

Evaluation of efficacy of selamectin and fipronil against *Ctenocephalides felis* in cats

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Objective—To evaluate efficacy of monthly administration of selamectin and fipronil against *Ctenocephalides felis* in cats.

Design—Randomized controlled trial.

Animals—36 healthy cats.

Procedure—Cats known to be free of fleas were infested with 100 unfed adult fleas on days –28 and –21. On days 0, 30, 60, 90, and 120, sixteen cats (8 pairs/treatment group) were treated by topical administration of selamectin (6 mg/kg [2.7 mg/lb] of body weight) or fipronil (7.5 mg/kg [3.4 mg/lb]). Four control cats (2 pairs) were not treated. On day –6 and every 2 weeks after initial treatment, comb counts were performed to detect fleas. Flea counts were recorded, and fleas (≤ 50) that had been removed were replaced onto the cat. On day 89, fleas were not replaced. On day 91 and every 7 days until the end of the study (day 150), cats were challenged with 20 adult fleas. Flea counts were compared between and within treatments.

Results—14 days after treatment, geometric mean flea counts were reduced by 71.2% by fipronil treatment and 35.3% by selamectin treatment. Both treatments resulted in 97 to 98% reduction in flea counts on day 29 and 99.8 to 100% reduction from day 44 to the end of the study.

Conclusions and Clinical Relevance—Selamectin is as effective as fipronil in treating infestation in cats housed for 3 months in a flea-infested environment under conditions known to support the flea life cycle and in protecting against subsequent weekly challenges with *C felis* for an additional 2 months. (*J Am Vet Med Assoc* 2000;217:1666–1668)

Strategies for control of flea infestation in cats have focused on disruption of the flea life cycle at various stages. Lufenuron,[a] a benzoyl-urea compound, inhibits the synthesis of chitin, thereby preventing the development of flea eggs.[1,2] Compounds that have been developed with flea adulticidal activity include fipronil,[b,3] a phenylpyridazole, and selamectin, a novel semisynthetic avermectin.[c,4] Fipronil blocks the **gamma-aminobutyric acid (GABA)**-gated chloride channel in insects.[5] The mechanism responsible for the parasiticidal activity of selamectin is not fully known but may involve, as with other avermectins, an increase in permeability to chloride ions through interaction with GABA binding sites.[6] The purpose of the study reported here was to compare the efficacy of selamectin with that of fipronil against infestation by *Ctenocephalides felis* in cats.

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Materials and Methods

Cats—The study included 18 male and 18 female 10- to 36-month-old domestic shorthair cats that weighed from 2.5 to 10 kg (5.5 to 22 lb). Cats had been reared indoors from birth and were fed once daily with a maintenance ration of commercial cat food. Water was provided ad libitum. Cats had been vaccinated against rhinotracheitis virus, calicivirus, and panleukopenia virus during the period between 1 year and 60 days before initial treatment and had not been treated with ectoparasiticides or avermectins for at least 60 days prior to the first experimental infestation with fleas.

Daily general health observations were made for each cat throughout the study as well as additional observations before and after each treatment administration. Physical examinations were conducted by a veterinarian on day –31, on each day of treatment, and on each day following treatment.

Animal housing—For the selection phase of the study, cats were housed individually in 1.1 × 0.6 × 0.75-m aluminum pens with solid walls, grid doors, and a grid floor with a collecting tray beneath. Each pen contained a raised metal grid (approx 0.2 m^2) and a litter box. For the main phase of the study, cats were housed (2/pen; 1 treatment/pen) in 3.0 × 1.55-m pens constructed of 3 solid walls and 1 timber wall of which the upper part was wire mesh, sisal-carpeted flooring, and a wooden door. A 0.9 × 0.4-m sisal-carpeted shelf and a litter box were provided in each pen. The room in which the pens were contained was controlled for temperature, humidity, and ventilation.

Separate coveralls and gloves were used by investigators who entered pens for each of the treatment groups. Additionally, investigators changed overboots between pens to avoid transfer of fleas.

Pharmaceuticals and initial infestation—Fipronil[b] is available commercially. Fipronil was administered topically as a 9.7% solution in the commercial-unit dose of 0.5 ml to approximate a dose rate of 7.5 mg/kg (3.4 mg/lb) of body weight.

Selamectin[c] is available commercially. It was prepared as a 12% solution (60 mg/ml) in glycol ether and isopropyl alcohol and administered topically in a unit dose to provide a minimal dose rate of 6 mg/kg (2.7 mg/lb).

Adult fleas (*C felis*) used for the initial infestation and subsequent challenges were reared on-site and provided to the animal facilities in transport vials. On receipt, fleas were inspected for viability, counted within vials, and applied to the cats, typically within 48 hours or less. Viability was judged on the basis of the fleas' ability to maintain normal posture or jump. Approximately half of the fleas in each vial were males.

Experimental design and procedure—The study compared the 2 treatments by use of a mixed-model repeated-measures design in a single study composed of 2 parts. The first part tested the treatments against chronic flea infestation for 3 months. The second part tested the treatments against weekly challenges with fleas for 2 months.

Selection for study—On day –40, cats were combed free of fleas and moved to clean noninfested housing. Combing was performed by investigators, using a separate fine-tooth comb for each cat. Investigators were unaware of treatment allocation. Combing was conducted in single strokes for at least 15 minutes and continued until 5 minutes after the last flea was found. Cats were combed again on day –39 to ensure that they were free of fleas, then infested with 100 viable unfed adult fleas. Fleas were applied to each cat by parting hair in the dorsal lumbosacral area and turning the uncapped warmed vial of fleas upside down in the parted hair, allowing the fleas to disperse into the hair. On day –36, 72 hours after infestation, cats were combed, and fleas collected from the combing were counted and removed. Technicians who performed the comb counts were unaware of treatment assignments. Cats were selected for the study on the basis of retention of a flea burden, as assessed by results of flea counts performed on day –36 and satisfactory results of physical examinations performed on day –31. In addition, 4 untreated cats (2 males, 2 females) with typical flea burdens were selected as sentinels. The pens that housed the sentinel cats were placed at opposite ends of the rows that housed the treated cats. Cats of the same sex and with similar numbers of fleas were housed together.

Chronic infestation and assignment to treatments—On days –28 and –21, each cat was infested with 100 viable unfed adult fleas, as described. On day –6, flea counts were conducted, and collected fleas were placed in covered glass jars. Fleas were then replaced to aid in maintaining the infestations (up to a maximum of 50 fleas) on the cats from which they were removed. Cats were randomly assigned to treatments on the basis of sex and stratified counts of fleas made on day –6. Treatments (selamectin or fipronil) were administered on days 0, 30, 60, 90, and 120. Selamectin was applied at a single site to the skin of the cats' back at the base of the neck and in front of the scapulae. Fipronil was administered according to label directions. Fleas were counted and replaced on days 14, 29, 44, 59, and 74. On day 89, fleas were counted but not replaced. Nontreated (sentinel) cats were combed free of fleas whenever excessive flea burdens were detected.

Flea challenges—On days 91, 98, 105, 112, 119, 126, 133, 140, and 147 of the study, 20 unfed adult fleas were applied to each cat. Fleas were counted and replaced on days 94, 101, 108, 115, 122, 129, 136, and 143. The study concluded on day 150 when fleas were counted but not replaced.

Statistical analysis—Flea counts were analyzed by use of a mixed-model repeated-measures ANOVA of ln (count + 1).[7] Pairwise comparisons between treatments were made for each data collection time point, using the Fisher protected least squares difference. Geometric means, calculated by back-transforming the least-squares means, were used to estimate percentage reductions in flea counts at each time point within all treatments, according to the formula:

% reduction = ([geometric mean, day –6] – [geometric mean, day X] × 100) / (geometric mean, day –6)

Significance was set at $P \leq 0.05$.

Results

Flea infestations resulted in geometric mean flea counts that were not different between treatments 6 days before the first treatment. Fourteen days after the first treatment, flea counts decreased in the selamectin and fipronil treatment groups (compared with respective means of counts determined on day –6; **Table 1**). Geometric mean flea count of the fipronil-treated group was reduced 71.2% on day 14 and was significantly lower than geometric mean of the selamectin-treated group, which was reduced by 35.3%.

Table 1—Percentage reductions in geometric mean flea counts for *Ctenocephalides felis*-infested cats (n = 16/group) treated with selamectin or fipronil on days 0, 30, 60, 90, and 120. Cats were infested with 100 fleas on days –28 and –21; these fleas were removed on day 89. Cats were reinfested with 20 fleas/d on days 91, 98, 105, 112, 119, 126, 133, 140, and 147

Day of study	Selamectin	Fipronil
−6	0.0	0.0
14	35.3	71.2
29	97.3	98.0
44	99.8	99.8
59	99.9	99.9
74	100.0	100.0
89	100.0	100.0
94	100.0	100.0
101	100.0	100.0
108	100.0	100.0
115	100.0	100.0
122	100.0	100.0
129	100.0	100.0
136	100.0	100.0
143	99.9	100.0
150	99.6	100.0

However, on day 29, prior to administration of the second treatment, the selamectin- and fipronil-treated groups had geometric mean flea counts reduced by 97.3 to 98%, and from days 44 through 150, counts were reduced 99.8 to 100%, compared with their respective counts determined on day –6. Geometric means of the selamectin and fipronil groups did not differ significantly from each other on days 29 to 150.

Sentinel cats had flea counts that indicated housing conditions were able to support a chronic increasing flea burden after infestation. In consideration of their welfare, sentinels were combed free of fleas, without replacement, whenever cats appeared uncomfortable because of flea burdens. Therefore, no direct comparisons were made between treated and sentinel cats.

In addition to observations of the cats made during daily care, health observations were made once daily (minimum) and more frequently on days before and after treatment administration. No mydriasis, vomiting, hyperactivity, tremors, convulsions, coughing, tachypnea, dyspnea, ataxia, excessive salivation, or any sign of intolerance was seen in any of the treatment groups for the duration of the study. Scratching was observed with an incidence of 5.9% in the sentinel cats and 0% in the selamectin- and fipronil-treated groups. Incidence of scratching corresponded with the flea counts in each of the groups for the duration of the study.

Discussion

Results of the study reported here indicate that selamectin was as efficacious as fipronil in reducing flea burdens during experimental infestations with *C felis* in cats. Selamectin and fipronil are effective and lead to a rapid reduction in flea counts. In the study reported here, these adulticidal treatments caused > 97% reduction in fleas by day 29 and 99.8% reduction by day 44. Hutchinson et al[8] reported similar results with fipronil, with 100% reduction in flea counts 24 weeks after treatment. Selamectin, like fipronil, is also effective against fleas on dogs.[4] The cats in the study reported here, however, had a slower rate of reduction in flea counts, compared with that in dogs, for both treatments. Dogs treated with selamectin or other adulticides had 99% reductions in flea burdens by day 29 after treatment, whereas cats did not have this amount of reduction until day 44. This difference between species may reflect differences in the housing of the animals. Dogs were housed in a smaller area than the cats and slept directly on the carpeted area where the flea eggs, larvae, and pupae were developing. In addition to the carpeted area on the floor of the cat pens, a carpeted shelf above the floor was provided for cats to use. For dogs, stimulation of hatching of pupae was likely to have occurred more completely and in a shorter time than for cats housed in larger pens. For dogs treated with either selamectin or fipronil, this would result in a more rapid clearance of the environment flea infestation.

[a]Program, Novartis, Basal, Switzerland.
[b]Frontline Top-Spot, Merial Animal Health Ltd, Harlow, UK.
[c]Revolution, Pfizer Inc, New York, NY.

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