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Efficacy of Afoxolaner in the treatment of otodectic mange in naturally infested cats

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HIGHLIGHTS

- Afoxolaner was effective in the treatment of otoacariasis in cats.
- The cats were negative for the presence of the mite 48 hours after the treatament.
- The cats presented no adverse reaction to the use of afoxolaner.

ABSTRACT

Afoxolaner is a drug belonging to the isoxazolines' family, and it is recommended for ectoparasite control in dogs. The objective of this study was to evaluate the efficacy of afoxolaner in the treatment of otodectic mange in naturally infested cats. Sixteen cats were divided into two groups (treated and control). The treated group (n = 8) underwent a single oral presentation of afoxolaner at a dose of 2.5 mg / kg. The control group (n = 8) received no antiparasitic treatment. The detection of mite infestations were performed by video otoscopy before the medication, 48 hours after the medication and at weekly intervals up to 35 days after treatment (+7, +14, +21, +28, +35). In the treated group, the animals were negative for the presence of the mite 48 hours after the medication and throughout the evaluation period. The control group remained positive throughout the experiment, demonstrating 100% efficacy ($p < 0.05$) for the treated cats naturally infested with *Otodectes cynotis* in a single dose over a period of 35 days. The animals were reintroduced into their natural habitat, allowed to regain contact with other cats and then reassessed for possible reinfestation. It was found that afoxolaner was effective in the treatment of otodectic mange the animals presented no adverse reaction to the use of afoxolaner

Key words: Antiparasitic, control, isoxazolines, otoacariasis, *Otodectes cynotis*

1 INTRODUCTION

Otodectic mange, also called "ear mange", is caused by the *Otodectes cynotis* mite that belongs to the Psoroptidae family. These mites are considered highly contagious (SOTIRAKI et al., 2001), and inhabit the skin surface and ear canals of most felines and canines (MILLER et al., 2013). These on average, are responsible for 50 to 80% cases of otitis externa in cats (YANG and HUANG, 2016).

Among the clinical signs observed in parasitized animals, pruritic and/or erythematous otitis are common, with the presence of dark brown exudates, popularly known as "coffee grounds", ulcerated and alopecic lesions in the area around the ear and cervical regions (MILLER et al., 2013). Diagnosis can be made through parasitological examinations of the cerumen or by video-otoscopy (NEVES et al., 2015). As a topical treatment option, reference can be made to products formulated with selamectin (SANKS et al., 2000), fipronil in association with eprinomectin (BEUGNET et al., 2014), ivermectin (FOSTER, 2006), imidacloprid associated with moxidectin (ARTHER et al., 2015) and fluralaner (TAENZLER et al., 2017).

Afoxolaner is an insecticidal and acaricidal drug belonging to the class isoxazoline. It acts systemically on the gamma-aminobutyric acid receptor (GABA) of arachnids to regulate the absorption of chloride ions, thereby resulting in increased neural stimulation and death of the parasites (Beugnet et al., 2015). Its efficacy has been proven against *Sarcoptes scabiei* (BEUGNET et al., 2016), *Demodex canis* (BEUGNET et al., 2016; SIX et al., 2016), and *O. cynotis* (CARITHERS et al., 2016) in dogs.

According to Letendre et al. (2014), afoxolaner is rapidly absorbed, has high bioavailability and moderate distribution in tissues; hence, its monthly use is recommended. However, commercial formulations are available only for use in dogs.

This is the first study to investigate the use of afoxolaner in cats against *O. cynotis* only.

2 MATERIALS AND METHODS

The present study was approved by the ethics and animal use committee of the Federal Rural University of Rio de Janeiro (CEUA / UFRRJ) under number 6041210417 and was conducted in compliance with the good standards of animal husbandry,

according to the criteria defined by ISFM - Feline- Friendly Handling Guidelines (RODAN et al., 2011). During the study period a commercial diet was offered twice daily and water was available 24 hours to all animals, with the contents refreshed twice a day.

To evaluate the efficacy of afoxolaner, a clinical, randomized, longitudinal and negative control study was conducted.

2.1 Experimental animals

Sixteen felines originally from the Laboratory of Experimental Chemotherapy in Veterinary Parasitology, aged between 2 and 6 years were selected. The animals weighed between 2.6 and 4.7 kg, were naturally infested with *O. cynotis*, presented clinical manifestations of erythema, as well as the presence of otic exudate, crusts and alopecia in the auricular pavilion.

The animals were kept in individual cages, measuring about 2 m^2, with visibility to other animals. To be included in the study, laboratory analisys (erythrogram, biochemistry, ALT, AST, albumin, urea and creatinine) were performed 7 days prior to the beginning of the experiment. The animals were also kept on those cages for a period of 7 days after the end of the study. Felines, identified by microchips did not receive any ectoparasiticide therapy for at least 30 days before the start of the experimental period.

The diagnosis of otoacariasis was confirmed by bilateral video-otoscopy, and by evaluating the presence of mites. This was used to define and classify the score from one to three, based on the number of mites found. Animals classified with scores of one, two and three; respectively, presented less than five, five to 10 and more than 10 mites respectively. The mean of the control group was 2.3 and for the treated group of 2.0, presenting no statistically significant difference before the start of treatment.

Cats were allocated into two groups: control (untreated) and treated (medicated with 2.5 mg / kg afoxolaner, orally, in a single dose, respectively).

At day 0 the animals were observed daily on a general clinical base for 35 days. At day 0, after receiving medication, the treated group remained under observation for three hours to assess the occurrence of possible adverse events.

After 48 hours, and on days +7, +14, +21, +28 and +35, the animals in both groups were reevaluated for the presence of mites by video-otoscopy at the end of the 35-day trial period. The following formula was used to evaluate the efficacy of the treatment, (number of animals infested with live mites prior to treatment - number of animals infested with live mites after treatment) / (number of animals infested with live mites prior to treatment) x 100 (Adapted from Marchiondo et al., 2013).

For data analysis, after the application of the Shapiro-Wilks normality test, the Kruskal-Wallis test was used between the groups followed by the Student-Newman-Keuls test for analysis of variance at 5% significance level. Calculations were performed using the Bioestat program version 5.3.

3 RESULTS

Animals from the control group and those treated with afoxolaner, presented bilateral otitis externa at the beginning of the experiment with dark brown cerumen, hyperemic pinna and intense pruritus. One cat presented with an ulcerated lesion at the base of the ear, which presented resolution soon after therapy.

The results obtained for the treated and control groups are presented in Table 1. After 48 hours, the animals in the treated group, which did not receive afoxolaner, did not present visible mites by video-otoscopy, different from the control group that remained infested throughout the experiment. In subsequent evaluations, the treated animals remained negative, suggesting 100% cure of afoxolaner for the treatment of *O. cynotis* infestation

The control group mean scores varied between 2 to 3 from 7 to 14 days, and between 1 and 3 from 14 to 35 days. After 35 days, all cats were reintroduced into their habitats, to regain contact with other cats, and the treated group was evaluated weekly and no reinfestation was observed for a period of 30 days. The efficacy of afoxolaner was maintained for 65 days.

Throughout the experiment, no adverse effects were observed in cats receiving afoxolaner therapy at a dose of 2.5 mg / kg.

4 DISCUSSION

At a single oral dose of 2.5 mg / kg, afoxolaner was effective in the treatment of natural infestations by *O. cynotis*, resulting in the complete elimination of parasites within 48 hours, with no apparent side effects for 30 days. Despite being recommended for monthly use in dogs, as a result of the lack of studies of the molecule in cats, it was not possible to determine the length of action of the drug in the body. As reported by Letendre et al. (2014), it can be ascertained that the drug has a rapid action, since the animals were negative after 48 hours.

In addition to the control of fleas and ticks, other studies have emphasized the efficacy of afoxolaner in the treatment of parasitic diseases such as canine demodicosis (BEUGNET et al., 2016; SIX et al., 2016), canine scabies (BEUGNET et al., 2016) and canine otoacariasis (CARITHERS et al., 2016). This is the first study on the use of afoxolaner for the treatment of otodectic mange in cats.

In the class of isoxazolines, sarolaner provides a good efficacy in the treatment of otodectic mange in felines (BECSKEI et al., 2017). Also, good results have also been reported after two monthly administrations in cases of canine otoacariasis (SIX et al., 2016), confirming efficacy as demonstrated in the study.

The 100% efficacy obtained with oral afoxolaner is similar to that observed by Taenzler et al. (2017) with topical fluralaner and by Shanks et al. (2000) with selamectin at 14 and 30 days post treatment, respectively. The difference between those andthe present study was the time of elimination of the mites, since the group treated with afoxolaner was negative, 48 hours after the medication.

Guaguère and Prélaud (2006) and Foster (2006) observed good results with topical therapy using terpineol, crotamiton, carbaryl and fipronil, two to three weeks after treatment of otocariasis in cats. As performed in this study, oral therapy has advantages to the treatment period, since afoxolaner was a single dose. Additionally, no adverse effects were observed in cats treated with a single dose of afoxolaner during the evaluation period, indicating a good therapeutic option compared to ivermectin, which has potential for intoxication in cats (MAGALHÃES et al., 2015).

Reinfestations were not observed during the evaluations, but their activity against other parasites has not yet been clarified, as well as the availability of the drug in the organism.

5 CONCLUSION

Afoxolaner, at a dose of 2.5 mg/kg, was effective in treating cats naturally infested by *O. cynotis*, from 48 hours onwards. It successfully prevented reinfestation for up to 65 days.

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Figure and table

Table 1. Presence of *O. cynotis* in the auditory canal of cats belonging to the control group and treated with afoxolaner, before and after treatment.

Group/Animal	D+7	D+14	D+21	D+28	D+35
Control					
Average	**2.3**	**2.3**	**1.9**	**2.3**	**2.1**
SD	**0.5**	**0.5**	**0.8**	**0.5**	**0.6**
Treated					
Average	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
SD	**0**	**0**	**0**	**0**	**0**
Effect (%)	**100**	**100**	**100**	**100**	**100**
p-value	**0.0008**	**0.008**	**0.008**	**0.008**	**0.008**

SD: standard deviation

Averages differ from each other when p-value ($p \leq 0.05$).