Efficacy of a Formulation Containing Imidacloprid and Moxidectin Against Naturally Acquired Ear Mite Infestations (Psoroptes cuniculi) in Rabbits

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ABSTRACT
The purpose of this study was to evaluate the efficacy of a topical formulation containing imidacloprid and moxidectin for eradication of Psoroptes cuniculi in rabbits. Fourteen adult rabbits from a rabbit hutchery were enrolled in the study. Rabbits were treated with 40 mg imidacloprid and 4 mg moxidectin monthly as spot-on on Days 0, 30, and 60. No other treatment or environmental decontamination was performed during the trial. On Days 0, 30, 60, and 90, all rabbits were examined, and epidermal debris was collected from both auricular areas and the external ear canal for microscopic examination. Clinical signs had subsided by Day 30 in 13/14 rabbits and almost no signs of recurrence were apparent in the following weeks. All epidermal samples were negative by Day 90. No adverse reactions were observed. Under the conditions of our study, topical formulation of imidacloprid and moxidectin was a practical and well-tolerated means of treatment for ear mange in rabbits.

INTRODUCTION
Astigimated Psoroptes mites are cosmopolitan external parasites of mammalian hosts and are of economic significance as the agents of mange in several domesticated animals, particularly with regard to the psoroptic mange of sheep caused by Psoroptes ovis (Hering).¹-³ Another ear mite, Otodectes cynotis (Hering), causing otocariosis, is an obligate parasite that inhabits the vertical and horizontal ear canals of dogs and cats,⁴ although other species such as ferrets may become infested.⁷ A fairly frequent species of veterinary importance is Psoroptes cuniculi (Delafond) responsible for otoacariosis in different farm animals, mainly affecting rabbits, goats, horses,
antelopes, cattle, and sheep.6–9 The ear mite is mainly found in the external auricular meatus of the ear and inside the ear pinnae; it is common to discover that only one ear is affected. *Psoroptes cuniculi* infestations in domestic rabbits are recognized in 2 clinical pictures: characteristic psoroptic “ear canker” causing puff pastry-like crusts, excoriations, massive pruritus, and occasionally aural hematomas due to intense head shaking or scratching10,11; and “extra-auricular” mange extensively described by Ribbeck and Ichmann12 and Guilhon.13 Cutler14 reported an ectopic *P. cuniculi* infestation in a pet rabbit, with severe lesions on the skin of the caudoventral abdomen. Bates15 observed the ectopic form in 5% of all *P. cuniculi*-infested rabbits of his study, showing lesions extending to the base of the ears, the cheeks, dewlap, face, and between the digits of both hind feet.

A new dermal product has been developed containing imidacloprid and moxidectin (Advocate®, Bayer) that is administered as a viable topical application to the skin at a single site on dogs and cats. No information is available on the efficacy of this preparation in rabbit “ear canker.” There are currently no licensed veterinary products specifically indicated for the therapy of ectoparasites in rabbits. Thus, veterinarians need to re dedicate pharmaceuticals normally used for other animal species. The present clinical study was conducted to evaluate the efficacy and tolerance of a spot-on formulation with imidacloprid and moxidectin in the treatment of *P. cuniculi* mange in naturally infested rabbits.

**MATERIALS AND METHODS**

Fourteen adult rabbits with a naturally occurring *P. cuniculi* infestation were enrolled in this field study. All rabbits were from the same rabbit husbandry in the western Bodensee area (Baden-Wuerttemberg) and kept exclusively in cages indoors during the treatment period. Ages ranged from 6 months to 1 year with a mean age of 9 months. On Day 0, all animals were individually weighed. Body weight of the measured rabbits ranged from 2.1 to 3.7 kg with a mean body weight of 2.65 kg. In the course of this study, one female was pregnant. Owners reported about reduced appetite and increasing restlessness in their animal husbandry over the last weeks. Moreover, remarkable crusts in the pinnae were observed.

**Treatment**

Each rabbit received 3 spot-on treatments 30 days apart on study Days 0, 30, and 60. Dermal application was performed using a 40-mg imidacloprid and 4-mg moxidectin topical solution (Advocate®, Bayer) at the base of the neck. Due to the animal welfare within this field trial of heavily mite-infested animals, a placebo treatment group was not enrolled. No other treatment or environmental decontamination was performed during the trial. The success of the treatment was assessed by clinical as well as parasitological examination.

**Clinical Examination**

General health of all treated animals was observed daily by the farm owners from Day 0 for the duration of the study, except for Days 30, 60, and 90 when a detailed clinical check-up was conducted by the veterinarian. At these particular assessment dates, ear lesions were judged for each rabbit. During the course of the trial, ear lesion evaluations and observed side effects were recorded. Clinical signs were evaluated by scoring from absent (–), mild (+), moderately (++), or profoundly (+++) on Days 0, 30, 60, and 90 with respect to appearance of scaling and crusting in the pinnae and in the external auricular meatus.

**Parasitological Examination**

On Days 0, 30, 60, and 90, all rabbits were examined, and epidermal debris was collected from both auricular areas and the external ear canal for microscopic examination. The ear canal swabs sampled were examined for mites, their eggs, and other developmental stages each time by at least 2 of the following methods: (1) stereomicro-
scope: epidermal debris and hairs were placed in a petri dish and examined at 25× magnification; (2) epidermal debris and hairs from one sample, respectively, were diluted in ~1 mL of a 10% KOH solution and heated for 20 minutes to macerate scales and hairs. The mixture was stirred, centrifuged, and the supernatant discarded. A concentrated sucrose solution was then added to the sediment, a cover slip was applied to the surface of the solution, the samples were again centrifuged, and, finally, the cover slip was transferred to a slide and inspected under a microscope at 40× magnification; or (3) direct check up under the microscope: epidermal debris and hairs were applied directly onto a microscope slide, covered with a few drops of mineral oil and a cover slip, then inspected at 40× magnification. The KOH and flotation technique was used in all rabbits on Day 0, because a relatively large portion of pattern material was collected with a sharp spoon.

RESULTS

On Days 30, 60, and 90, the quantity of ear canal swabs sampled was generally much less than on Day 0, which appeared to correlate with clinical improvement. Clinical signs were absent by Day 30 in 13/14 rabbits, and no signs of recurrence were apparent in the following weeks (Figures 1 and 2). Thus, for all further examinations performed on Days 30, 60, and 90, the stereomicroscope and direct microscopic procedure were the only techniques used.

The eggs and mites recovered from the ears were documented for each rabbit to produce geometric mean egg and mite counts on each assessment day (0, 30, 60, and 90). For each treatment and/or assessment day within the study, the number of rabbits with or without eggs/mites in the skin scrapings was established in order to specify the efficacy of the used antiparasiticide (Table 1). Live mites and eggs were numerous in all animals on Day 0, but had declined on Day 30 prior to the second treatment. A moderate recurrence of mean mite counts was observed from Day 30 to Day 60 despite repeated treatment. Only 4/14 rabbits still harbored eggs and/or mites on Day 30 and Day 60. Thus the evaluated efficacy of the imidacloprid/moxidectin combination was 71.4%. No eggs or mites (dead or alive) in any rabbit were detected on assessment Day 90. Efficacy of the imidacloprid/moxidectin spot-on formulation rated 100% at this point of time, accordingly. Clinical signs of the rabbits during the study are summarized in Table 2. There were no adverse drug experiences or treatment-related mortalities during the trial.

DISCUSSION

Although our study does not allow us to conclude where the mite infestation is usually acquired, the fact that new rabbits are
purchased permanently in this husbandry may be seen as a constant source of infestation with *P. cuniculi* mites. Twelve of the 14 rabbits showed a mild form of “ear canker” accompanying moderate pruritus and head shaking. There had been no evidence for ectopic ear mite infestation. The skin lesions were margined to the pinnae and the external ear canal. All animals suffered from bilateral otitis externa parasitaria. On Day 0, all 14 rabbits showed a clinical picture compatible with “ear canker.”

Pruritus, which was present in 14/14 rabbits, was considered mild to moderate in 12 rabbits and severe in 2 rabbits. Fourteen rabbits presented mild to moderate ear scaling and crusting. Alopecia, excoriations, or hematomas were not detectable. On Day 30, a great clinical improvement was noted. Only one rabbit still exhibited mild scaling. Pruritus and head shaking had resolved in all of the small mammals. On Day 60, with the exception of 2 rabbits, all clinical signs disappeared, even though a total of 4 rabbits still harboured eggs and mites on this day.

On Day 90, all rabbits were free from clinical signs and mites or developmental stages. Significantly increased mite counts from Day 30 to Day 60 may be due to reinfestation from the contaminated environment. This might be supported by the ability of *P. cuniculi* to survive off the host for 4 to 21 days at relative humidities between 20% and 99% and temperatures between 5°C and 30°C. Smith and colleagues quantified the probability of transmission of psoroptic mites from the environment to the animal and emphasized its fundamental importance for the design and implementation of effective control strategies.

In this trial, the spot-on formulation containing imidacloprid and moxidectin was 100% effective against naturally acquired aural infestations of *P. cuniculi* mites in rabbits. Although there was no control group, the treatment regimen appeared effective and tolerable in the clinical control of ear mite infestations. A lack of licensed antiparasiticides for this indication in rabbits requires an off-label use of adequate pharmaceuticals. The simple dosing protocol used here, with a spot-on
formulation topically administered at the base of the rabbit’s neck, facilitates owner compliance with the treatment protocol. “Ear canker” is seen predominantly in large agricultural rabbit husbandries. It is in contrast to the otic preparations currently available for the therapy of ear mites that demand applications into the external auricular meatus once or twice daily for up to 4 weeks. Because of more applications and a higher incidence of recurrence, topical administration into the ear canal is much more time-consuming and laborious. The off-label use of another macrocyclic lactone of the avermectin subclass, ivermectin, administered subcutaneously, has been reported to be successful in the control of P. cuniculi in rabbits.18–22 Although there are topical and injectable acaricidal products available for the treatment of psoroptic mange in rabbits, most of them require frequent and careful application to control or eradicate the mites. Several authors report that efficacy of injections with the preferred ivermectin appears to vary with several populations of P. cuniculi in rabbits. According to Wilkins and colleagues23 in Texas, USA, and Pandey19 in the UK, a single injection of ivermectin (200 µg/kg body weight) eliminated all P. cuniculi mites. Animals studied by Wright and Riner18 required injections at a higher dose rate of 400 µg/kg body weight to cure psoroptic “ear canker.” In a German trial, neither 200 nor 400 µg/kg body weight failed to eradicate P. cuniculi completely.24 Moreover, the injection route seems to be a determining factor. Rabbits infested with P. ovis and P. cuniculi were injected intramuscularly (IM) or subcutaneously (SC) with ivermectin. A single application of 200 µg/kg body weight either IM or SC was inadequate to eliminate all mites in the ears of the rabbits. However, a single injection of 400 µg/kg body weight, regardless of the route of application, eradicated all P. cuniculi mites, but eliminated P. ovis in only 50% of the rabbits.18 Results of a study from McTier and colleagues25 suggest that a single topical application of selamectin at a dose of 6 or 18 mg/kg body weight can completely eliminate mites from rabbits naturally infested with P. cuniculi. Wagner and Wendelberger26 treated rabbits with psoroptic mites with moxidectin 0.2 mg/kg body weight SC and orally twice 10 days apart, respectively. After this period, neither excessive cerumen nor mites could be identified in the external ear canal. All rabbits were cured and did not show clinical signs during the next 6 months. No side effects occurred in any of these rabbits. Fourie and colleagues4 figured out that a single therapy with an imidacloprid/moxidectin solution applied at a dosage of 0.1 mL/kg body weight resulted in a treatment success rate of 80% as assessed 50 days after application in O. cynosis-infested cats. Two treatments with the imidacloprid/moxidectin combination 4 weeks apart and at the same dosage was efficacious in curing all cats from the ear mites as assessed 22 days after the second application (Day +50). Pullium and colleagues27 found that in mice infested by Myocoptes musculinus, there was a total eradication of mites without any toxic effect or clinical signs of illness in the patients after one topical treatment with moxidectin 0.5%. Avermectins are not currently approved for use in rabbits in Germany or elsewhere in the world. Interest is developing in the use of biocompatible products such as lavender oil for the therapy of external parasites in rabbits.28 Macchioni and colleagues29 tested acaricidal activity of aqueous extracts of camomile flowers against P. cuniculi and showed its efficacy.

**CONCLUSIONS**

Under the conditions of our trial, topical formulation containing imidacloprid and moxidectin was a practical and well-tolerated means of treatment for ear mite infestation in rabbits. The results indicate that imidacloprid in addition to moxidectin at a dosage of 10 and 12 mg/kg body weight, respectively, percutaneously thrice 4 weeks apart is effective and a good alternative for the control of “ear canker” in rabbits.


