

Assessment of the Ear Mite (*Otodectes cynotis*) Infestation and the Efficacy of an Imidacloprid plus Moxidectin Combination in the Treatment of Otoacariosis in a Hungarian Cat Shelter

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Abstract

Two separated field studies were carried out in Hungary to assess *Otodectes cynotis* infestation and to evaluate the efficacy of 10% imidacloprid and 1.0% moxidectin spot-on for cats against ear mites in a cat shelter. Mite infestation was studied with direct, otoscopic examination of the external ear canals and with the presence or absence of live mites in samples taken with cotton-tipped swabs from both ears of each animal. Fifteen out of 100 cats selected randomly were found to be infested. Seven animals showed severe clinical signs of otitis externa consistent with *O. cynotis* infestation. These cats were restless, shaking their heads and scratching their ears. Alopecia, wounds caused by self-injuries and dermatitis were seen in and around the ears of the two cats having most severe clinical signs. The other infested cats did not show any clinical signs, only dark brown exudates rang-

ing from moist and waxy to crumbly and flaky accumulated at the deeper part of the external ear canals.

Ten cats were randomly assigned to the treatment group and five animals to the untreated control group. Each cat of the treated group was weighed and treated with the recommended dosage of 10% imidacloprid and 1.0% moxidectin spot-on on day 0. Only those three cats were found to be infested with live ear mites on day 9, which had showed the most severe clinical signs of otitis externa before treatment. The black-brown cerumen or scab was drier in their ear canals than nine days earlier. Some live and dead mites were found only by microscopic examination of aural debris. The efficacy of 10% imidacloprid and 1.0% moxidectin against *O. cynotis* was 100% on days 16 and 30. Direct and otoscopic examinations of both ears of treated animals could not reveal mite movement. A very small amount of

dry material was found in the ear canals of the formerly most affected cats. No or some dried up mites occurred in samples taken with cotton-tipped swabs from all cats which had no clinical signs of otoacariosis. The external ear canals of untreated cats continued to contain large amounts of dark brown, waxy cerumen and their ear swab samples contained live ear mites until the end of study.

Introduction

Worldwide, several ectoparasites can infest domesticated cats, of which an obligate, relatively large, non-burrowing mite, *Otodectes cynotis* seems to be one of the most common species. Kittens and adult animals can be infested to the same extent but the young cats seem to be more susceptible (Six *et al.* 2000, Sotiraki *et al.* 2001). The main route of infestation is from infested dams to their kittens. The mites can also spread with contaminated combs, brushes, bedding and other grooming accessories, especially where cats are bred or sheltered. Transmission through cerumen or crusts expelled from infested ears is rare (Kraft *et al.* 1988). No connections were observed between infestation and age, sexual activity or lifestyle of infested cats (Sotiraki *et al.* 2001). The overall infestation is referred to as “otoacariosis” (Rose 1976, Roth 1988). The ear mites which live and breed in the external and the internal ear canal cause irritation during feeding on superficial debris and cerumen, piercing the skin surface and moving around. Their secretions may account for the intense inflammatory and hypersensitivity reaction soon after infestation, and chronic cases in cats may result in Arthus-type hypersensitivity (Weisbroth *et al.* 1974, Kraft *et al.* 1988). However, cats appear to tolerate a significant population of otodectic mites. Therefore, the earliest lesions are not detected in most cases (Roth 1988). It has been speculated that these cats in their young age developed “immunity” against

mites and this would explain why the ear mites quite rarely cause clinical signs (Lane 1994). Weisbroth *et al.* (1974) suggested that older cats developing clinical manifestations of otoacariosis represent a minority, with defective immune response relating to predisposing factors (e.g. poor body condition due to malnutrition). The cats suffering from otitis externa usually show marked pruritus, mild or severe dermatitis, frequent scratching of the ears and head shaking. The intense pruritus may result in self-mutilation, bleeding and haematomas (Kraft *et al.* 1988). Otodectic mange accounts for more than 50% of all feline otitis externa. Scott (1980) found that 75% of affected cats had bilateral involvement. There is a typical sign of mite excretory products in the ears that have a coffee grounds appearance with a waxy consistency (Scott 1980). In most severe cases the invasion of Gram-positive bacteria are involved and may lead to ulceration of the tympanic membrane resulting in otitis media. There is a great variety of type of discharge present in the ears; its colour can be yellow, brown or black. The consistency of discharge can be watery, tenacious, cheesy or dry. The number of mites does not correlate well with the severity of the lesion, as hypersensitivity responses are suspected to play a significant role (Roth 1988). Sometimes mites move away from the external ear canal onto the skin and hair of the interscapular area, and they can also be found on other parts of the body, mainly on the head, interscapular area, base of the tail and paws. However, clinical signs of mite infestation are rarely seen at these areas. *O. cynotis* might be a zoonotic agent when humans have contact with infested animals (Kraft *et al.* 1988). Although rare, there have been some reports of *O. cynotis* being found in the external ear canal of humans causing intense irritation (Lopez 1993).

In order to eliminate ear mites it is important to treat the cat's ears. Effective treatment aims at killing and/or removing every mite and returning

the lining of the ear to normal. There are a number of approved medications for ear mites. Most of these products can be applied directly into the external ear canal once or twice daily for up to four weeks (Curtis 2004). This method is very tedious and demanding for the owner, plus it often causes pain and discomfort for the animal. Ear cleaning is also recommended only prior to treatment. Therefore, spot-ons applied to the skin only monthly offer more practical control measures against *O. cynotis*, without cleaning of the ears, treating the hair coat and the cat's environment and, in most cases, without the concurrent use of antimicrobial drugs (Six *et al.* 2000, Shanks *et al.* 2000). Advocate[®], Advantage Multi[™] (Bayer AG, Leverkusen, Germany) is a spot-on formulation of moxidectin and imidacloprid in a solution containing 10% imidacloprid and 2.5% moxidectin for dogs, and 10% imidacloprid and 1.0% moxidectin for cats (The Technical Manual Advocate[®] 2005).

The aims of these studies were to investigate the occurrence of *Otodectes cynotis* and to evaluate the efficacy of a 10% imidacloprid plus 1.0% moxidectin spot-on combination in the treatment of otocariosis in naturally infested cats of a Hungarian shelter.

Materials and methods

Assessment of the ear mite infestation

The privately owned cat shelter is located in a suburb of a small town approximately 30 kilometres from Budapest, Hungary. The majority of animals of different breeds and age were kept indoors and outdoors where they could have contact with each other. The number of cats changed slightly from time to time because new cats arrived and other animals were adopted by families. Most cats were neutered young adults under five to six years old, and there were a few dozen kittens at the time of the field studies. The shelter was visited in Octo-

ber 2005 when there were 154 animals. The owner mentioned that some cats had been restless, shaking their heads, scratching their ears several times a day. The clinical examination and sampling from the ears were performed on 100 cats selected randomly for assessing their ear mite infestation. The behaviour of these cats was observed and recorded. Visual examination of the inner surface of each cats' ears was done to note any presence of signs of ear mite infestation (e.g. coffee grounds-like cerumen) and otitis externa. After that, bilateral otoscopic examination was performed to observe any motile ear mites. Finally, samples were taken with cotton-tipped swabs from both ears of each animal. The swabs were inserted deep into the external ear canal and a circular motion was used to collect samples. The samples were checked immediately at the site for the presence of *O. cynotis* (adults, larvae, nymphs and eggs) under a dissecting microscope. The presence of even one mite, in any development stage, was deemed to have been a positive result.

Trial with imidacloprid/moxidectin spot-on

On 9 May 2006, the shelter was visited to start the field study to evaluate the efficacy of the imidacloprid/moxidectin spot-on combination on naturally infested cats with *O. cynotis*. Prior to enrolment, the ear mite infestation was confirmed in all animals by otoscopic examination of the external ear canal, or if no mites (adults, larvae or nymphs) were observed by this method, by microscopic examination of aural canal debris. If a cat was found to be infested with *O. cynotis*, a plastic collar was placed around the cats' neck with a number for individual identification. Fifteen cats had natural ear mite infestations in either one or both ears. A brief description of the cats' sex, approximate age, colourings and their overall health status was recorded. These animals had not received any systemic or aural ectoparasiticide for at least eight weeks prior to enrolment. Ten cats were randomly assigned to the treatment group and five animals to the

untreated control group. Each cat of the treated group was weighed with a portable scale to determine the appropriate dosage of treatment. The test product spot-on was administered as a single treatment according to the bodyweight of cats on day 0. One single-dose pipette of the drug, containing 0.4 ml for cats equal to or less than 4 kg or 0.8 ml for cats 4–8 kg, was applied to the base of the neck in front of the shoulder blades. The treatment provided minimum doses of 10 mg/kg body weight of imidacloprid and 1 mg/kg body weight of moxidectin, which is equivalent to 0.1 ml/kg of the spot-on solution for cats. After the individual treatments, the cats were kept amongst the other cats. During the study, cats could not be treated with concurrent medications and ear cleaning was not allowed in any treated and untreated animal because of the potential to remove mites.

All the treated cats were observed for the first four hours, and daily up to day 30, in order to check for any possible side effects from the treatment. Clinical inspections, including direct and otoscopic examination of the ear canals and sampling for checking the presence or absence of ear mites by microscopic examination of aural debris, were performed on days 9, 16 and 30 on the treated cats, to regulate the efficacy of the treatment and any improvements in the clinical signs. The untreated control animals were also evaluated with the same methods.

Data were compared by using Fisher's exact test, and differences were regarded significant when $P \leq 0.05$.

Results and discussion

Assessment of the ear mite infestation

Fifteen cats were found to be infested during the assessment of the ear mite infestation of 100 cats

selected randomly. This is the first report on the prevalence of *O. cynotis* infestation of cats in Hungary. The ear mite is the most common mange mite species of cats worldwide, its prevalence ranges from 5 to 50%, depending on many factors. The age, condition and keeping system of animals, social and grooming behaviour and immunologic factors (e.g. development of hypersensitivity) may constitute a reasonable explanation. Two studies carried out in the United States have reported low prevalence of ear mite infestation of the cat, 5% (McCallum 1967) and 7% (Murphy *et al.* 1982). In comparison with these results the infestation rate was higher in the cat population studied, but it was lower as it has been reported elsewhere (Beresford-Jones 1955, Gram *et al.* 1994). A study of 161 domestic cats in Greece reported that 25.5% of animals were found to be infested with *O. cynotis* (Sotiraki *et al.* 2001). A higher prevalence (37%) of ear mite infestation was detected in Florida (Akucewich *et al.* 2002).

Seven animals showed severe clinical signs of otitis externa, consistent with *O. cynotis* infestation. These cats were restless, shaking their heads and scratching their ears. Erythema of the inner pinna and a greater or lesser amount of ear discharge, having the classic coffee-grounds appearance, were seen in their both ear canals by visual examination, as has been previously reported (Saridomichelakis *et al.* 1999). This kind of clinical picture is not rare amongst cats infested with ear mites. Although usually more than one pathogen species is isolated from otitis externa in cats, many papers have reported that *O. cynotis* is responsible for up to 50% of these cases (Griffin 1981, Merchant 1993, Scott *et al.* 1995, 2001). It might be possible that the hypersensitivity reaction of cats to mites is responsible for poor correlation between the severity of clinical signs and the burden of mites (Curtis 1995, Little 1996). However, many live mites (larvae, nymphs and adults) and eggs were found on the



Fig. 1 Live ear mites can be seen on the cotton-tipped swabs of a cat with otitis externa

cotton-tipped swabs of these cats (Fig. 1). Alopecia, wounds caused by self-injuries and dermatitis were seen in and around the ears of the two cats having the most severe clinical signs (Fig. 2). This phenomenon might be explained with the behaviour of mites, which usually leave the ear canal as soon as the inflammation and exudates create a hostile environment for them (Scott *et al.* 1995). The severe clinical manifestation of ear mite infestation in these two cats might be related to their poor body condition due to malnutrition, resulting in defective immune reaction (Weisbroth *et al.* 1974).

Eight out of 15 infested cats did not show any clinical sign. Their behaviour was normal, and dark

brown exudates ranging from moist and waxy to crumbly and flaky accumulated only at the deeper part of the external ear canal. Except for two cats, no mites could be observed with otoscopic examination because copious amounts of cerumen hindered any viewing of mites. Therefore, bilateral ear swab samples were taken from the external ear canals of 13 animals. Live mites were found in all the samples with qualitative microscopic examination, confirming otoacariosis of cats. It is known that many cats can be carriers of the mites without any clinical sign. Sotiraki *et al.* (2001) reported that many infested cats were asymptomatic, having normal ear canal appearance with mild ceruminous. It may be possible that these cats had a more recently



Fig. 2 Alopecia and wounds on and around the ear of a cat suffering from severe otitis

acquired ear mite infestation or the mites could not multiply in the ear canals and there were not secondary infections causing inflammation and typical ear discharge. In most cases, therefore, the examination of ear swabs is needed for an accurate diagnosis of *O. cynotis* infestation.

The efficacy of imidacloprid/moxidectin spot-on in the treatment of otocariosis

At the beginning of the study, on day 0, three of the mite-infested cats randomly assigned to the treatment group showed clinical signs of otitis externa. These animals had black-brown cerumen in their both ear canals; they shook their heads and scratched their ears. The other animals of this

group had only a small amount of dirty cerumen located in the deeper part of one or both auditory canals, which was hardly recognisable to the naked eye. It was easy and quick to treat the animals with the imidacloprid/moxidectin spot-on solution. Neither local nor general side effects were observed amongst the cats compared to the signs of transient pruritus observed during previous studies with the test product (European Medicines Agency 2005). The cats showed some discomfort due to the wetness of the circumscribed area of treated skin, but that disappeared once the solution evaporated in a few hours. Large amounts of ear discharge having the classic coffee-grounds appearance were seen in both ears of two untreated control cats by visual

examination on day 0. In spite of the presence of ear mites in the auditory canals, the other animals of this group showed no or mild clinical signs.

The efficacy of imidacloprid/moxidectin spot-on was 70% on day 9, because three of the treated cats were found to be still infested with live ear mites (Tab. 1). However, the percentage of animals with live *O. cynotis* mites was significantly ($P < 0.01$) lower compared with that on day 0. All of these animals had showed severe clinical signs of otitis externa before treatment. At this assessment date none of the mite-infested cats showed abnormal behaviour. The black-brown cerumen or scab was drier in their ear canals than nine days earlier and no mites could be seen by direct or otoscopic examination. Some live (adults and larvae) and dead mites were found by microscopic examination of aural debris. There could be a number of explanations as to why these cats still harboured live mites. Since the treated cats were residing with the rest of the cats of the shelter, they may have been re-infested with ear mites shortly before the follow-up samples taken on day 9. It is also possible that they were newly hatched larvae, most likely from those eggs which were not yet affected by the treatment. The other reasonable explanation is that those mites remained alive in the ear canals of three cats having clinical otitis externa, which could not ingest any or enough moxidectin because of the thick layer of black-brown cerumen or scab. The other cats of the treated group had very small amounts of dry and dark material in their ear canals. No live mites were found in samples taken with cotton-tipped swabs from these animals. The results obtained nine days after treatment indicated that the imidacloprid/moxidectin combination reached the ear canals. It is known that the high lipophilicity of the acaricide ingredient of the product, moxidectin contributes to its extensive tissue distribution. The maximum serum concentration of moxidectin was already detected in cats approximately a day after

the application (The Technical Manual Advocate® 2005). It means that ear mites die soon after the treatment of cats if they pierce the skin surface of the ear canals for feeding on epidermal debris and body fluids. French scientists have also found a similar quick efficacy of another avermectin. Selamectin killed ear mites within three days after administering topically in a single spot to the base of the neck in front of the scapulae, at a minimum dosage of 6 mg/kg^{-1} (Blot *et al.* 2003). The untreated five control cats remained infested with live mites. They contained copious amounts of dark brown exudates that were usually moist and sticky and sometimes crumbly.

The efficacy of the single treatment with the imidacloprid/moxidectin combination spot-on was 100% on day 16 and two weeks later, on day 30 against *O. cynotis* (Tab. 1). Direct and otoscopic examination of both ears of treated animals could not reveal mite movement. Very small amounts of dry material were found in the ear canals of most affected animals. No or some dried up mites occurred in samples taken with cotton-tipped swabs from all the cats having no clinical sign of otoacariosis. The external ear canals of untreated cats continued to contain large amounts of dark brown, waxy cerumen and their ear swab samples contained live ear mites (Tab. 1). These results indicate that the acaricide efficacy persisted for about a month. It is related to the long elimination half-life of moxidectin, which is longer than other approved macrocyclic lactones. No live mites infested the treated animals or they died after getting on these cats before laying any eggs. This period of efficacy allows time for any remaining viable life cycle stages of the parasite to have developed to the adult stage and to have been affected by the treatment (Shanks *et al.* 2000).

Topical preparations containing different active ingredients (e.g. acaricide, antimicrobial and anti-

	Days post-treatment			
	0	9	16	30
Treated group¹				
Proportion	0/10	7/10	10/10	10/10
Percentage	0.0 %	70.0 %	100 %	100 %
P-value²		<0.01	<0.0001	<0.0001
Untreated group				
Proportion	0/5	0/5	0/4 ³	0/4
Percentage	0.0 %	0.0 %	0.0 %	0.0 %

Tab. 1 Proportions and percentages of cats without live mites
¹ treated with imidacloprid/moxidectin spot-on on day 0, ² compared with day 0, ³ one cat missed

inflammatory) currently used for treatment of otitis externa related to ear mites require several applications for many days or weeks, and tend to be tedious for the owners, and otitis externa causes pains whenever the ears are handled of the affected animals. For these reasons scientists have been searching for safer products which are long-acting and effective against ear mites, and that do not cause difficulties for the pet owners to apply and stress for the animals. The first macrocyclic lactone, ivermectin was evaluated against *O. cynotis* administered as a subcutaneous injection. It has been reported to be effective in the treatment of feline otoacariosis (Schneck 1988, Jeneskog and Falk 1990). However, others have reported that more than one subcutaneous injection was needed to reach complete cure and sometimes severe adverse effects, including death, had been associated with the off-label usage of ivermectin in cats (Gram *et al.* 1994, Lewis *et al.* 1994). At the beginning of 2000, some papers reported the efficacy of a novel avermectin, selamectin, which had been evaluated against naturally acquired aural infestations of *Otodectes cynotis* on cats. It was found that selamectin administered in a single spot to the

skin of each animal's back at a minimum dosage of 6 mg/kg⁻¹ was safe and 100% effective against ear mites of all cats on day 30 post-treatment (Shanks *et al.* 2000). In another field study, selamectin administered at the same dosage in a topical preparation applied to the skin of cats eliminated ear mites in 94–100% by day 30 (Six *et al.* 2000). French scientists have reported no mites (dead or alive) or eggs were detected after day 17 (Blot *et al.* 2003). Three independent laboratory and one field studies have been conducted in cats naturally infested with *Otodectes cynotis* to evaluate the efficacy of imidacloprid/moxidectin (Fourie *et al.* 2003). On day 30 after treatment, according to label instructions the efficacy of imidacloprid/moxidectin was 98.6%, based on mean numbers of ear mites. In another study when mite counts and clinical cure were evaluated, one animal from ten cats naturally infested with *Otodectes cynotis* had evidence of live mites at day 28 post-treatment. In a follow-up study, ten cats in each group with natural ear mite infestation received a single treatment of imidacloprid/moxidectin or selamectin. The combination of imidacloprid/moxidectin proved to be as effective as selamectin, with 99.5%. In the field study carried

out in the private vet clinics of three European countries 28 days after treatment the efficacy rate was 85.7% for imidacloprid/moxidectin and 87.1% for selamectin.

Although many of the products applied directly into the external ear canal are eventually effective, the efficacy of an otic treatment against *O. cynotis* is slightly lower when compared to using spot-on treatment such as imidacloprid/moxidectin. The results have shown that imidacloprid/moxidectin spot-on is safe and effective against otodectic mites of cats and provides easy use for the owners. However, the efficacy of imidacloprid/moxidectin has differed slightly from each other in the laboratory and field studies. It is not surprising because the outcome of the treatment with imidacloprid/moxidectin, as well as with selamectin or other drugs, depends on many factors. The dosage and application of spot-on, the severity of ear mite infestations of cats and the risk of re-infestation of treated ani-

mals can influence the time of the eradication of parasites and the number of requested treatments. Besides the acaricide efficacy of the spot-on combination its active ingredients, imidacloprid and moxidectin are also effective against many common external and internal parasites of cats including fleas, lice, heartworm (*Dirofilaria immitis*), roundworm (*Toxocara cati*) and hookworm (*Ancylostoma tubaeforme*) (Reinemeyer and Charles 2003, Arther *et al.* 2005, European Medicines Agency 2005).

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