Chapter 7

Anthelmintic efficacy of oxibendazole against some important nematodes in dogs and cats

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Abstract

The anthelmintic efficacy and safety of the oxibendazole component in a combination oxibendazole-niclosamide paste were investigated in dogs and cats and in litters of pups with naturally acquired nematode infections. A single dose of 15 mg oxibendazole/kg body weight given to 70 dogs and to 29 cats reduced faecal worm egg counts (EPG) by 97.6% for *Toxocara canis*, 95.7% for *Trichuris vulpis*, 94.6% for *Ancylostoma caninum* and 100% for *Toxascaris leonina*. In cats, 96.7% efficacy was demonstrated against *Toxocara cati*. In a second trial, 119 pups in 22 litters were treated with the same dosage at 2, 4 and 6 weeks of age. After treatment on two consecutive days, 95% of the pups did not shed *T. canis* eggs, compared with 85% after only a single treatment. Side effects were rare and only recorded in young animals. A two day treatment schedule is recommended for unweaned pups.

Introduction

In spite of the availability of numerous anthelmintics, intestinal nematode infections of dogs and cats continue to be a significant problem, particularly in relation to the zoonotic significance of *Toxocara* ascarids and *Ancylostoma* hookworms. Anthelmintic strategies, consisting of a combination of treatment schedules and the choice of appropriate anthelmintics, are therefore considered to be important and deworming schedules directed against such parasites have been published (4). The purpose of an anthelmintic treatment directed against gastrointestinal nematodes is to stop egg output and to expel worms from the pet. Due to a poor solubility in gastro-intestinal secretions, benzimidazoles have minimal gastrointestinal absorption except for thiabendazole, albendazole and oxfendazole (20). They have significant larvicidal effects (1, 13) and are virtually without toxicity at therapeutic dose rates (7, 9). Oxibendazole (methyl 5-n-propoxy-2-benzimidazole-carbamate; OBZ), was first synthesised in 1973 (24). It is used against many endoparasites in a wide range of hosts. Toxicology studies in companion animals support a wide margin of safety for OBZ (2, 3). Attempts to determine an LD50 for OBZ in small laboratory animals failed because rats and mice tolerated the maximum quantities (10,000 mg/kg) that could be physically given (20). Oxibendazole is indicated for several nematodes of dogs and cats, such as *Toxocara, Toxascaris, Trichuris, Ancylostoma* and *Uncinaria* (6, 8). The efficacy of OBZ against endoparasites in dogs and cats after single administration, however, has been little
investigated, in contrast to larger animals such as cattle, sheep and horses (7, 20, 21). This
report describes trials in dogs and cats to investigate the anthelmintic efficacy of OBZ,
administered in a combination with niclosamide, based on faecal egg count reduction. Co-
incidental observations relating to treatment safety were made. Niclosamide is a taeniacidal
drug and not reported to have any action against nematodes (20).

Material and methods

Animals

Trial 1. In the period between 1993 and 1996, 55 naturally infected dogs (23 male and 32
female, average age 2.1 years, range 0.1 - 7 years) and 28 cats (15 male and 13 female,
average age 2.5 years, range 0.1 - 11 years) were used in this trial, conducted in the
Netherlands. The animals were of different breeds and body weights, and located at veterinary
practices, breeder kennels, catteries and in a colony of purpose bred beagles. Eleven pups
from Surinam with A. caninum infections (6 male and 5 female, average age 7 weeks, range 4
- 10 weeks) were included since hookworm infections are not common in the Netherlands
(19). All dogs and cats were healthy.

Trial 2. A second group consisted of 119 newborn pups in 22 litters (20 pure bred and 2
mixed breed) at breeders in different locations in the Netherlands.

Drug formulation and treatment

Because OBZ is not licensed as a single active ingredient for pets, a registered combination
paste of 3% oxibendazole and 24% niclosamide (Vitaminthe®, Virbac Laboratories SA,
France) was used.

The animals in both trials were treated at a dose rate of 15 mg OBZ/kg body weight,
corresponding to 1 ml of paste/2 kg b.w., applied on the back of the tongue. In trial 1 only a
single dose was administered.

The pups of trial 2 were treated, either once or twice on consecutive days, when 2, 4 and 6
weeks old (3 or 6 treatments in total, respectivily). The anthelmintic was administered by
either a veterinarian or the owner and the treated animals were fed ad libitum before and
during treatment.
**Faecal examination**

Faecal samples from animals of trial 1 were taken 1-3 days before and 7 days after treatment and in trial 2 only at 7 days after each treatment (sampling at 3, 5 and 7 weeks of age). A first pre-treatment faecal examination at 2 weeks of age was not performed, because prenatally infected puppies may be passing eggs in the faeces not earlier than by 3 weeks of age (22). The faeces were stored in plastic tubes at -20° C until examined. Faecal worm egg counts (eggs per gram; EPG) were performed as described by Overgaauw (19). Species differentiation of hookworm eggs was performed by measuring dimensions.

**Efficacy evaluation**

Efficacy calculations were based both on faecal egg count reduction and by calculating the percentage of animals with negative (EPG <10) egg counts after treatment. Individual animals served as their own controls.

An average percentage reduction in mean egg counts of 90% or more was considered effective, 80-89% moderately effective and 60-79% low efficacy. Values below 60% were considered ineffective (14).

**Palatability and side effects**

After each treatment, the animals were observed to evaluate whether the paste formulation was palatable. The animals were monitored by the owner/attendant for general behaviour, appetite and excretions.

**Statistical analysis**

The significance of the difference in mean egg counts in the 2 groups of pups was determined by ‘Pearson’s Chi Square’, in Statistix 3.5 (NH Analytical Software, St. Paul MN), applying a significance level ≤ 5%.

**Results**

**Efficacy in dogs in trial 1**

The results of the mean egg counts in dogs are shown in Table 1. Single treatment reduced mean egg counts of ascarids (Toxocara, Toxascaris), hookworms (Ancylostoma) and whipworms (Trichuris) by between 94.6% and 100%. All hookworms were determined as A. caninum. Five of 11 dogs infected with this parasite were still positive, but with a
considerably lower egg count. These dogs were younger than 3 months. Four dogs were infected with both *Ancylostoma caninum* and *Toxocara canis*. After deworming, they were all negative for *T. canis*, but only pup negative for *A. caninum* as well. The 6 dogs that were still shedding *T. canis* eggs after deworming had an average age of 11 months while the 5 remaining dogs with persistent *Trichuris vulpis* eggs were 4 years old. *Toxascaris leonina* was the most susceptible worm species since the treatment was 100% effective.

<table>
<thead>
<tr>
<th>parasite</th>
<th>no. negative/ no. treated</th>
<th>mean epg before treatment</th>
<th>mean epg after treatment</th>
<th>EPG reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Ancylostoma caninum</em></td>
<td>6/11</td>
<td>1246</td>
<td>67</td>
<td>94.6%</td>
</tr>
<tr>
<td><em>Toxascaris leonina</em></td>
<td>4/4</td>
<td>745</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td><em>Toxocara canis</em></td>
<td>22/28</td>
<td>889</td>
<td>21</td>
<td>97.6%</td>
</tr>
<tr>
<td><em>Trichuris vulpis</em></td>
<td>22/27</td>
<td>699</td>
<td>30</td>
<td>95.7%</td>
</tr>
</tbody>
</table>

*Table 1. Results of a single treatment of 15 mg oxibendazole/kg b.w. against some nematodes in dogs.*

**Efficacy in cats in trial 1**

The results of the mean egg counts in cats are shown in Table 2. One cat was infected both with *T. leonina* and *T. cati*, all others were infected only with *T. cati*. Substantial reductions in *T. cati* egg counts were observed, although five of the 28 cats remained positive (all single infections). The average age was 2 years.

<table>
<thead>
<tr>
<th>parasite</th>
<th>no. negative/ no. treated</th>
<th>mean epg before treatment</th>
<th>mean epg after treatment</th>
<th>epg reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Toxascaris leonina</em></td>
<td>1/1</td>
<td>30</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td><em>Toxocara cati</em></td>
<td>23/28</td>
<td>1137</td>
<td>38</td>
<td>96.7%</td>
</tr>
</tbody>
</table>

*Table 2. Results of a single treatment of 15 mg oxibendazole/kg b.w. against some nematodes in cats.*
Efficacy in puppies in trial 2

The results of treatment of the 119 pups are shown in Table 3. It was not possible to collect faecal samples from every pup every two weeks, since some pups had already been delivered to the new owner at 7 weeks of age. Until 7 weeks of age, eighty-five percent of the pups that received a single treatment at 2, 4 and 6 weeks did not shed *T. canis* eggs after treatment, while ninety-five percent of the pups treated on 2 successive days were cleared during this period. The difference (i.e. number of pups negative) was significant in pups sampled at 5 weeks of age ($\chi^2 = 4.5$ and $p < 0.05$) and also comparing single and double treatment values ($\chi^2 = 7.0$ and $p < 0.01$).

<table>
<thead>
<tr>
<th>Treatments</th>
<th>3 weeks of age</th>
<th>5 weeks of age</th>
<th>7 weeks of age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. negative/ no. treated</td>
<td>mean EPG</td>
<td>no. negative</td>
</tr>
<tr>
<td>1 treatment</td>
<td>40/49</td>
<td>242</td>
<td>31/40</td>
</tr>
<tr>
<td>2 treatments</td>
<td>48/53</td>
<td>13</td>
<td>26/27</td>
</tr>
<tr>
<td>$p$-value ($\chi^2_{df=1}$)</td>
<td>0,19</td>
<td>0,03*</td>
<td>0,21</td>
</tr>
</tbody>
</table>

* significant difference

Table 3. Results of a single or double treatment of 15 mg oxibendazole/kg b.w. against some nematodes in unweaned puppies

Palatability and side effects

Information was recorded from 55 animals in trial 1 (23 dogs and 32 cats). Two 8 weeks old cats spat out the paste. One 10-week-old cat was described as sleepy and one 16-week-old dog and two 8 week old cats vomited after treatment. In trial 2, five Dachshund pups in the same litter showed persistent mild diarrhoea throughout the study, although the relationship to treatment was uncertain.

Discussion

The results demonstrated a mean egg count reduction for ascarids, whipworms and hookworms of between 95% and 100% after treatment with the oxibendazole-niclosamide paste. Niclosamide was not considered to have contributed to efficacy since it is a taeniacidal drug and has not reported as having an action against nematodes (20) and OBZ was therefore
considered the active agent. Except for the hookworm infections (all in young pups), the faeces of more than 80% of the animals were free of nematode eggs after treatment, while the others had considerably diminished egg counts. Further research may be merited to investigate efficacy after double treatment on 2 consecutive days in older animals.

The results of the egg counts in pups in trial 2 showed that considerably more pups were cleared after treatment on two consecutive days (91% - 98%) than after single treatment (78% - 91%). A better efficacy after repeated administration can be explained by the relatively short gastrointestinal tract of carnivores with a short transit time as result.

Occasional and rare diarrhoea and vomiting in our study may be attributed to the niclosamide component (20). Lower efficacy values can be a consequence of diarrhoea since this will alter the rate of passage of the anthelmintic (15). Diarrhoea can be exacerbated by physiological instabilities associated with the stress of weaning, change of diet and being moved to a new environment (12).

Oxibendazole (in combination with diethylcarbamazine) at the low daily dosage of 5 mg/kg continued for at least 7 days, has been shown to be effective against *T. canis, T. leonina, T. vulpis, Uncinaria stenocephala* and *A. caninum* infections. Several groups of authors confirmed this efficacy: McCall et al. (18) in a double-blind controlled critical challenge study, Stromberg et al. (23) in a critical study with naturally infected pups and Armstrong et al. (5) and Marley et al. (17) in clinical trials where pups were included. Fenbendazole administered in comparable schedules with treatments of 50 mg/kg on three consecutive days to unweaned puppies also reduced the overall numbers of *T. canis* by 90% to 94% (9) and, compared with untreated control pups, reduced *T. canis* egg output by 88% - 95% after a single treatment of 100 mg/kg (10). A single treatment with a combination of febantel, pyrantel and praziquantel induced 85% reduction in egg-output when given to pups at 2, 4 and 6 weeks (10).

The risk of toxocarosis in man and animals can be minimised by reducing contamination of the environment with *Toxocara* eggs. This should be a primary objective of any control programme (13). Efficacy of anthelmintics for dogs and cats is often evaluated only in adolescent or adult dogs (11), although nursing pups and kittens are more frequently and heavily infected and hence present the greatest potential risk to the environment and trials on them should be included if possible. The population dynamics of *Toxocara* in unweaned puppies (somatic migration of larvae at the moment of deworming and re-infection throughout the suckling period) require repeat dosing of anthelmintics after 10 to 14 days. Efficacy of anthelmintics can be influenced by diarrhoea (increased intestinal passage) and
the fat contents of the bitches’ milk (16, 13). Treatment efficacy should be measured in several geographical locations in order to address variability in environmental conditions and possible worm strain variations (14).

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References


