

## Anthelmintic efficacy of three doses of an association of pyrantel pamoate plus, oxantel pamoate and praziquantel in naturally infected cats

Eficácia anti-helmíntica de três doses de uma associação de pamoato de pyrantel, pamoato de oxantel e praziquantel em gatos naturalmente infectados

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### SUMMARY

The purpose of this study was to evaluate the anthelmintic activity of three different doses of an association of pyrantel pamoate, oxantel pamoate and praziquantel in a single oral dose, in naturally infected cats. Animals were obtained from the Centro de Controle de Zoonoses, from Diadema, São Paulo, and divided in four groups each of eight cats, based on pre-treatment faecal examination. Group 1: untreated control cats; Group 2: 5 mg of pyrantel pamoate, 5 mg of oxantel pamoate and 2.5 mg of praziquantel/kg body weight (BW); Group 3: 10 mg of pyrantel pamoate, 10 mg of oxantel pamoate and 5 mg of praziquantel/kg BW and Group 4: 20 mg of pyrantel pamoate, 20 mg of oxantel pamoate and 10 mg of praziquantel/kg BW. The percentage of reduction in egg counts and percentage of efficacy were calculated. Mean egg counts from all treated cats decreased significantly from the second day after treatment on. The number of immature *Toxocara cati* and *Ancylostoma* spp. worms also decreased, however it was not significant. The number of adult worms decreased significantly in the treated groups. The percentage of efficacy for *Toxocara cati* was 93.0%, 97.6% and 100.0% and for *Ancylostoma* spp. was 96.5%, 99.0% and 100.0%, for groups 2, 3 and 4, respectively. The compound was effective against *Dipylidium caninum* and ineffective against *Physaloptera* spp. and *Strongyloides stercoralis* in a single dose.

UNITERMS: Cats; Pyrantel pamoate; Oxantel; Praziquantel; Helminths.

### INTRODUCTION

Pyrantel is a tetrahydropyrimidine compound with high activity against a variety of nematode parasites in domestic animals<sup>4,10</sup>. Pamoate form is commonly used in carnivorous, like dogs and cats<sup>2</sup>. Oxantel pamoate is a pyrantel analogous (moxiphenol), that showed high activity against *Trichuris* sp<sup>5</sup>. Praziquantel has a well established cestocidal activity and it is normally used in combination with other anthelmintic compounds<sup>3,1</sup>.

The purpose of this study was to evaluate the anthelmintic activity of three different doses of an association of pyrantel pamoate plus, oxantel pamoate and praziquantel<sup>6</sup>, in a single oral dose, against the most common helminths affecting cats.

### MATERIAL AND METHOD

#### Experimental design

Thirty-two cats (9 males and 23 females) of mixed breed

and various ages, obtained from the Centro de Controle de Zoonoses of Diadema, São Paulo, were used in this trial. They were captured from the streets and were naturally infected by helminths.

Infected cats were randomly assigned to one of four treatment groups, based on pre-treatment faecal examination. Group 1, untreated control; group 2, treatment with 1 tablet containing 5 mg of pyrantel pamoate, 5 mg of oxantel pamoate and 2.5 mg of praziquantel/kg body weight (BW); group 3, treatment with twice group 1 dose (10 mg of pyrantel pamoate, 10 mg of oxantel pamoate and 5 mg of praziquantel/kg BW) and group 4, treatment with 4 tablets containing 20 mg of pyrantel pamoate, 20 mg of oxantel pamoate and 10 mg of praziquantel/kg BW.

Of each group of eight cats, six were positive both for *Ancylostoma* spp. and *Toxocara cati* and the remainder two were only positive for *Toxocara cati*. Few cats were also positive for *Dipylidium caninum*, *Physaloptera* spp. and *Strongyloides stercoralis*.

Cats were monitored twice a day for a period of seven days after treatment to detect any adverse reaction. Faeces were collected daily during the three days prior to treatment and on day 0, 2, 4, and

\* Basken plus<sup>®</sup> - Lab. König do Brasil Ltda.

6 after treatment. Cats were necropsied on day 7 for worm recovering.

### Housing and management

The study was conducted according to World Association for the Advancement of Veterinary Parasitology guidelines for evaluating the efficacy of anthelmintics in dogs and cats<sup>6</sup>.

Cats were individually housed during the acclimation period (at least 3 days prior to treatment) and during the study. Fresh water was given *ad libitum* and they received commercial cat food once daily.

Tablets were administered orally, hidden in a small amount of meat, just before routine feeding.

### Parasitological techniques

Cats were selected based on pre-treatment faecal examination by flotation-centrifugation technique and faecal egg counts (EPG) were performed by means of a modified McMaster technique<sup>13</sup>, using 2 g of faeces. The percentage of reduction in egg counts after treatment was calculated by the formula:

$$\% \text{ of EPG reduction} = \frac{\text{Mean EPG before treatment} - \text{Mean EPG after treatment}}{\text{Mean EPG before treatment}} \times 100$$

Cats were humanely euthanased on day 7 after treatment, and gastrointestinal tract was entirely removed and segments were isolated and tied off separately. Stomach, small intestine, large intestine and cecum of each cat were removed, separated, opened, the contents collected and the mucosae washed and placed in beakers containing a 2% HCl solution for two hours. The contents of each segment were then gently washed over a No. 65 tyler sieve\*. Helminths collected from the contents and mucosae of each section were preserved in 10% formalin and examined in order to verify the species and stage of development.

The percentage of the efficacy against each parasite species was determined by the formula:

$$\% \text{ efficacy} = \frac{\text{Mean no. of worms in controls} - \text{Mean no. of worms in treated cats}}{\text{Mean no. of worms in controls}} \times 100$$

### Statistical analysis

Statistical analysis was carried out using SAS software<sup>12</sup>. A general linear model for analysis of variance was used and least squares means were compared using Tukey test for parametric observation (EPG and adult stages). For immature stage it was used a non-parametric test (Kruskal Wallis) for comparisons among groups. Data from worm burdens and EPG were logarithmically transformed to stabilize variance. P values less than 0.05 were considered to be significant.

## RESULTS

The dose rates used did not present any toxicity problem in single oral doses.

*Ancylostoma* spp. and *Toxocara cati* egg counts (mean  $\pm$

standard deviation) and percentage of reduction after treatment are presented in Tab. 1. Worm burdens recovered at necropsy and treatment efficacies are summarized in Tab. 2.

*Ancylostoma* spp. and *Toxocara cati* egg counts from all treated cats decreased significantly ( $P < 0.0001$ ) from the second day after treatment on. The three doses of the product reduced hookworm EPG by at least 99.8% (group 4) and *Toxocara cati* EPG by at least 96.2% (group 2). In the control group, both *Toxocara cati* and *Ancylostoma* spp. EPG increased approximately 100% during the 7-day period of observation.

The mean number of adult *Ancylostoma* spp. recovered from the controls at necropsy were significantly higher ( $P < 0.0001$ ) than the worms recovered from the other three treatments. The percentages of efficacy of the formula on adult *Ancylostoma* spp. were 96.5%, 99% and 100% respectively for group 2, 3 and 4, with three, one and none infected cats from the six that were positive for hookworm in each group. The two species of *Ancylostoma*, *A. braziliense* and *A. tubaeforme* were found. In group 1, 81% (101 worms) were from the genera *A. braziliense* and 19% (23 worms) were *A. tubaeforme*. Treated cats from groups 2, 3 and 4 presented only 4 *A. tubaeforme* and 1 *A. braziliense*.

*Toxocara cati* adult worm in the control cats also presented significant differences when compared to the treated groups ( $P < 0.0001$ ) and the percentage of reduction in group 2, 3 and 4 was 93.0%, 97.6% and 100% respectively, with two, one and no cats presenting the nematode from the total of eight per group by the end of the treatment.

Data on immature stages were not normally distributed and a non-parametric test (Kruskal-Wallis) was used. No differences in the number of immature stages recovered at necropsy, were observed between groups, neither for *Ancylostoma* spp. nor for *Toxocara cati* ( $P > 0.05$ ).

Efficacy against *Ancylostoma* sp. immature stages was 13.3% for group 2 (one tablet of the compound) and 100% and 86.6% for groups 3 and 4 respectively (two and four tablets of the compound). In relation to the immature *Toxocara cati* stages, the formula presented efficacy of 4.7%, 86.7% and 52.3% for groups 2, 3 and 4.

*Dipylidium caninum* segments were observed in the faeces of three cats from group 1, and in two cats from groups 2, 3 and 4 during experimental period. However, at necropsy, all the eight control cats presented *Dipylidium caninum* (mean 17.5 scolex) and two cats from group 3 were also positive (mean 6.5 scolex).

*Physaloptera* spp. was found at necropsy in cats from all groups. In group 1, one cat presented the parasite, in groups 2 and 3, three cats presented it and in group 4, two cats presented it, with a mean of 1.0; 2.3; 2.0 and 6.5 worms respectively.

*Strongyloides stercoralis* was also present at necropsy in 1, 2 and 2 of the eight cats from groups 1, 3 and 4 respectively.

## DISCUSSION

The major purpose of this experiment was to evaluate the efficacy against adult stages, however, despite the low amount of immature stages presented at necropsy, the results showed that the latter stages are more resistant. Probably a second dose of the product or a faecal examination three to four weeks later should be used in a control program. For an appropriate study of immature stages efficacy, Jacobs *et al.*<sup>6</sup> (1994) recommended the knowledge of the

\* Granutest, Ind. Brasileira.

stage of development (in the case of natural infection) or the age of the parasite in days (in the case of artificial infections) at the time of treatment.

The efficacy of the product against adult worms increased consistently with the increasing of the dose rate. Jacobs *et al.*<sup>6</sup> (1994) considered high efficacy of a filaricidal drug a range of 90 to 96% of worms killed by the product and very high efficacy a range of 97 to 100%. Using the same range, the dose rate of 10 mg of pyrantel pamoate and oxantel pamoate and 5 mg of praziquantel/kg BW (group 3) and 20 mg of pyrantel pamoate and oxantel pamoate plus 10 mg of praziquantel/kg BW (group 4) were highly effective against *Ancylostoma* spp. and *Toxocara cati*. Robinson<sup>10</sup> (1979) also found the dosage of 20 mg of pyrantel pamoate/kg BW more effective than 5 mg base/kg, in a similar study with cats.

*A. braziliense* was the most prevalent species recovered from cats. However, in treated animals, 80% of those worms were *A. tubaeforme*, suggesting that this species is more resistant than *A. braziliense*.

*Toxocara cati* eggs were present in the eight cats of the control group prior to the beginning of the trial. However, at necropsy only six cats harboured the parasite. This spontaneous expulsion of *Toxocara cati* did not adversely affect the conclusion of the experiment as the amount of infected animals per group allowed the analysis of the results. Ridley *et al.*<sup>9</sup> (1991), in a similar

experiment, also observed *Toxocara cati* spontaneous expulsion.

In relation to *Dipylidium caninum*, it was difficult to determine the exact percentage of efficacy with the methodology used in this trial. Prior to necropsy the presence of scolex was observed only in three control cats. However, at necropsy, all the eight cats were positive. It is not possible to know if the same fact happened with the treated cats, since they were naturally infected, and the percentage of efficacy was not determined. However based in the results found, treatment showed good efficacy against *Dipylidium caninum*.

Some *Stroglyoides stercoralis* and *Physaloptera* spp. worms were found in a few animals at necropsy, however due to the very low occurrence of those worms, statistical analysis was not carried out. Kelly<sup>7</sup> (1975), in Australia, in an epidemiological survey in cats, found a high prevalence of *Toxocara cati* and *A. tubaeforme* while other intestinal nematodes presented an extremely low incidence.

In relation to *Physaloptera* spp. infection in cats, Santen *et al.*<sup>11</sup> (1993) found that a single oral dose of pyrantel pamoate (5 mg/kg body weight) was insufficient to remove the infection. Two doses, three weeks apart, were necessary to eliminate the parasitism.

Despite the high dose used in Group 4 cats, adverse reactions were not observed. Reinemeyer; De Novo<sup>8</sup> (1990) observed that no adverse reactions occurred with an overdosing five times the dosage of 20 mg/kg BW, which is the recommended dose for cats, in United States and Australia.

**Table 1**

Mean faecal egg counts pre and post treatment (on day 0 and 7) in the experimental groups and percentage of reduction in relation to the controls. (São Paulo – SP, 1995).

TREATMENT GROUP	<i>Ancylostoma</i> spp. (n = 6)			<i>Toxocara cati</i> (n = 8)		
	DAY AFTER TREATMENT		REDUCTION	DAY AFTER TREATMENT		REDUCTION
	0	7	%	0	7	%
1	1028 ± 1103 <sup>a</sup>	2608 ± 2527 <sup>a</sup>	-	1522 ± 2300 <sup>a</sup>	3286 ± 4528 <sup>a</sup>	-
2	3754 ± 5964 <sup>a</sup>	0 <sup>b</sup>	100.0	1719 ± 1499 <sup>a</sup>	64 ± 149 <sup>b</sup>	96.2
3	3508 ± 6474 <sup>a</sup>	0 <sup>b</sup>	100.0	1883 ± 1928 <sup>a</sup>	0 <sup>b</sup>	100.0
4	7118 ± 10998 <sup>a</sup>	8 ± 20.4 <sup>b</sup>	99.8	3738 ± 5517 <sup>a</sup>	0 <sup>b</sup>	100.0

n = number of cats infected.

Mean in each column and line with different letter superscript (a and b) differ significantly (p < 0.0001).

**Table 2**

Mean *Ancylostoma* spp. and *Toxocara cati* worm burdens (adult and immature forms) and anthelmintic efficacy (%) by treatment. (São Paulo – SP, 1995).

TREATMENT GROUP	<i>Ancylostoma</i> spp.			<i>Toxocara cati</i>			
	ADULT	IMMATURE	EFFICACY %	ADULT	IMMATURE	EFFICACY %	
	(m ± SD)	(m ± SD)		Adult	Immature	Adult	Immature
1	20.5 ± 20.2 <sup>a</sup> (6:6)	1.5 ± 2.5 <sup>a</sup> (3:6)	-	4.3 ± 3.6 <sup>a</sup> (6:8)	2.1 ± 2.3 <sup>a</sup> (5:8)	-	-
2	0.7 ± 0.8 <sup>b</sup> (3:6)	1.3 ± 3.3 <sup>a</sup> (1:6)	96.5	0.3 ± 0.4 <sup>b</sup> (2:8)	2.0 ± 2.6 <sup>a</sup> (5:8)	93.0	4.7
3	0.2 ± 0.4 <sup>b</sup> (1:6)	0.0 <sup>a</sup> (0:6)	99.0	0.1 ± 0.3 <sup>b</sup> (1:8)	0.3 ± 0.7 <sup>a</sup> (1:8)	97.6	85.7
4	0.0 <sup>b</sup> (0:6)	0.2 ± 0.4 <sup>a</sup> (1:6)	100.0	0.0 <sup>b</sup> (0:8)	1.0 ± 2.6 <sup>a</sup> (1:8)	100.0	52.3

( ) = number of positive cats: number of cats in the group.

Mean in each column with different letter superscripts (a and b) differ significantly (p < 0.0001).

## RESUMO

O presente trabalho teve por objetivo avaliar a atividade anti-helmíntica de três diferentes doses de uma associação de pamoato de pyrantel, pamoato de oxantel e praziquantel em dose única e via oral, em gatos naturalmente parasitados. Os animais foram obtidos no Centro de Controle de Zoonoses do Município de Diadema (SP) e divididos em quatro grupos de oito animais cada, baseados nos resultados de exames coproparasitológicos. Os gatos do Grupo 1 não receberam tratamento, os do Grupo 2 foram tratados com 5 mg de pamoato de pyrantel, 5 mg de pamoato de oxantel e 2,5 mg de praziquantel/kg de peso vivo (pv). Os gatos do Grupo 3 receberam 10 mg de pamoato de pyrantel, 10 mg de pamoato de oxantel e 5 mg de praziquantel/kg pv e aos animais do Grupo 4 foram ministrados 20 mg de pamoato de pyrantel, 20 mg de pamoato de oxantel e 10 mg de praziquantel/kg pv. Calculou-se a porcentagem de redução do número de ovos presentes nas fezes e a porcentagem de eficácia. As médias dos números de ovos tiveram um decréscimo significativo já no segundo dia pós-tratamento, independente da dose de medicamento utilizada. Houve decréscimo, não significativo, nos números de formas imaturas de *Toxocara cati* e de *Ancylostoma* spp. nos grupos tratados e significativo em relação às formas adultas. A porcentagem de eficácia contra *Toxocara cati* foi de 93,0%; 97,6% e 100,0% para os grupos 2, 3 e 4, respectivamente. Em relação ao *Ancylostoma* spp. a eficácia foi de 96,5%; 99,0% e 100,0%. O produto mostrou-se eficaz contra *Dipylidium caninum*, mas não atuou sobre *Physaloptera* spp. e *Strongyloides stercoralis*, no esquema de administração utilizado.

UNITERMOS: Gatos; Pamoato de pyrantel; Oxantel; Praziquantel; Helmintos.

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