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COMPARATIVE ACTIVITY OF VARIOUS ANTHELMINTICS IN RELATION TO THE TIME OF MUSCULAR INFECTION BY *TRICHINELLA PSEUDOSPIRALIS*

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Introduction

The treatment of experimental trichinosis has been based on the development of active compounds on *Trichinella spiralis* during the last few years. The absence of the cystic capsule in *T. pseudospiralis* may make its response to drugs different from that of *T. spiralis*. Its presumed circulation in nature [1, 2, 3] makes it advisable to test the effect of anthelmintics. The objective of the study was to compare the anthelmintic activity of eight compounds of diverse chemical structure on the following stages of muscular development: 1) muscular invasion - a period of uncertain limits because of the superposition in the time between the arrival of embryoes migrating to the skeletal muscle and their settlement in the muscular niche; 2) early muscular phase - definitive establishment of the larvae in the muscle; and 3) late muscular phase or "waiting" period for the eventual continuity of the life cycle of the parasite.

Material and methods

CRI-1 Swiss mice weighing 30 to 35 g were infected with 300 ± 50 larvae of GARKAVI's *T. pseudospiralis*, and treated with single and multiple oral doses (the latter doses were split up into three/day and administered at intervals of four hours), expressed in mg/kg/day, of the following drugs: Thiabendazole (250), Mebendazole (60), Parbendazole (100), Fenbendazole (300), Albendazole (100), Febantel (300), Levamisole (10) and Ivermectin (0.3). All were suspended in sodium carboxymethyl cellulose at 1%, except the Levamisole Hydrochloride - soluble

TABLE 1

Experimental schema

Phase under treatment	Period of treatment	Determination of effectiveness
Muscular invasion	13th, 14th and 15 th p.i. days	30th p.i. day
Early muscular phase	25th, 26th and 27th p.i. days	40th p.i. day
Late muscular phase	43rd, 44th and 45th p.i. days	48th and 57th p.i. days

(p.i.: post infection)

in distilled water - and Febantel - a commercial suspension of Bayer (Rintal) at 2.5% -, being based on the experimental schema indicated in Table 1. In the muscular invasion and prior to the anthelmintic treatment, the intestinal population, remaining up to the 9th and 11th post-infection (p.i.) days, was suppressed with Maretin (60 and 40 mg/kg, respectively) together with Atropine Sulfate (0.05 mg/kg).

The determination of the effectiveness of the treatment was carried out following the usual digestion techniques of the carcasses [4], followed by the count of live and dead larvae, in order to calculate the reduction percentages with regards to the corresponding control, as well as its statistical meaning by Student's "t" test. The percentages of dead larvae were also calculated for each group with respect to the total number of larvae isolated in the standard digestion.

Results

The results are indicated in Table 2; the effectiveness is expressed as a function of the reduction percentages (% R) and of dead larvae (% DL); the mean number of larvae and percentage of dead larvae in the control of each experiment are also expressed. Two determinations were undertaken in the late muscular phase up to the 3rd and 12th post-treatment days. This last one will be the subject of the discussion as it is comparable with those carried out in the two other stages.

Discussion

The effectiveness of the single Thiabendazole doses decreased as it advanced in the life cycle of the parasite — 47.4, 27.8 and 23% of reduction —, this behaviour being similar to the one obtained by Spaldonova et al. [5] on *T. spiralis* and *T. pseudospiralis*.

TABLE 2

Efficacy of anthelmintics, expressed in percentages of reduction (% R) and of dead larvae (% DL), against three muscular phases of *Trichinella pseudospiralis* S.D.: Single doses; M.D.: Multiple doses. $p < 0.01$ for all the % R, except those * $p < 0.05$ and ** $p > 0.05$ #: mean number of larvae and percentage of dead larvae (in brachets) in the controls

		Phase under treatment							
		Muscular invasion		Early muscular phase		Late muscular phase			
Efficacy determination, days p.i.		30		40		48		57	
DRUGS		S.D.	M.D.	S.D.	M.D.	S.D.	M.D.	S.D.	M.D.
Thiabendazole	% R	47.4	76.5	27.8	35.6	15.2**	21.0**	23.0	53.7
	% DL	43.4	59.9	24.5	36.3	10.3	26.3	10.0	15.9
	Control#	21,589	(14.8)	12,363	(6.4)	12,554	(8.3)	14,005	(7.9)
Mebendazole	% R	66.6	90.1	81.00	89.0	49.1	76.0	90.0	89.2
	% DL	62.5	65.3	100.0	100.0	100.0	100.0	100.0	100.0
	Control#	17,790	(25.2)	8,478	(10.6)	15,352	(31.2)	13,134	(16.3)
Parbendazole	% R	75.0	84.4	66.8	65.3	36.5	40.1	78.9	89.9
	% DL	25.8	22.0	56.3	61.6	74.3	81.8	48.4	67.1
	Control#	12,919	(6.7)	9,906	(5.2)	11,659	(15.3)	14,830	(4.7)
Fenbendazole	% R	72.1	60.9	37.9	67.9	43.3	61.1	63.9	77.5
	% DL	46.4	66.7	20.0	70.3	84.3	69.2	14.7	48.8
	Control#	17,790	(25.2)	8,478	(10.6)	11,659	(15.3)	14,830	(4.7)
Albendazole	% R	52.7	57.8	17.2*	78.4	10.8**	61.1	55.3	63.2
	% DL	52.4	45,8	21.7	71.8	16.9	64.3	13.0	29.7
	Control#	21,589	(14.8)	9,906	(5.2)	12,554	(8.3)	14,005	(7.9)
Febantel	% R	86,1	82.1	68.9	77.8	42.4**	55.9*	91.2	89.9
	% DL	56.2	67.3	100.0	100.0	99.5	98.7	100.0	100.0
	Control#	12,919	(6.7)	12,363	(6.4)	9,551	(11.7)	12,486	(6.5)
Levamisole	% R	28.6*	27.6*	24.3	26.4	23.8**	34.4**	57.7	39.2*
	% DL	24.2	30.2	14.1	15.3	20.8	17,0	6.9	12.0
	Control#	17,832	(14.8)	9,616	(4.6)	8,998	(9.9)	7,393	(11.3)
Ivermectin	% R	61.1	18.8**	34.6	20.3*	30.5**	23.6**	—	30.4*
	% DL	28.6	18.3	9.7	10.3	24.4	23.4	13.5	11.5
	Control#	17,832	(14.8)	9,616	(4.6)	8,998	(9.9)	7,393	(11.3)

On the contrary, the single administration of Mebendazole increased its effectiveness at the stage submitted to the treatment became older — until it reached 90% of reduction and 100% of dead larvae in the late muscular phase, as indicated previously [5, 6, 7]. Mebendazole maintained its high effectiveness in the multiple administration — 90% of reduction — during the three stages. This drug has been shown to be the most powerful benzimidazole carbamate for the treatment of *T. spiralis*, even with doses as low as 5 and 12.5 mg/kg [8, 9].

A slight infection can be noted with Parbendazole in the intermediate stage of the treatment for single and multiple doses, which is even

more marked with single doses of Albendazole - 52.7, 17.2 and 55.3% of reduction - and Fenbendazole - 72.1, 37.9 and 63.9%. When Spaldonova et al. [5] treated three successive stages of the *T. spiralis* infection with Parbendazole, they obtained effectiveness percentages which are similar to ours, although Spaldonova and Corba [10] obtained better results with Albendazole on early muscular larvae than on previous stages.

The application of multiple doses generally improves the efficacy of the benzimidazolic derivatives on muscular *T. pseudospiralis.*

The considerable effectiveness of Febantel, which had previously been indicated on *T. spiralis* [11, 12], on *T. pseudospiralis* is also shown with reduction percentages for single doses which vary from 68.9% (early muscular phase) to 91.2% (late muscular phase), reporting in both cases 100% of dead larvae.

The slight effectiveness of Levamisole was maintained throughout the three muscular phases, being outstanding (57.7%) only as a single dose on the late muscular phase. The maximum reduction obtained with Ivermactin was also similar - 61.1%, but on the earliar stage. Although some good results have been obtained on muscular *T. spiralis* subcutaneously [13], the oral administration does not seem to be appropriate.

The comparison of our results with the ones obtained previously by various authors on *T. spiralis* and *T. pseudospiralis* seems to indicate that the experimental treament of *T. pseudospiralis* is not substantially different from that of *T. spiralis.*

Summary

Studies were made on the effectiveness of single and multiple oral doses, expressed in mg/kg/day, of Thiabendazole (250), Mebendazole (60), Parbendazole (100), Fenbendazole (300), Albendazole (100), Febantel (300), Lavamisole (10) and Ivermectin (0.3) on the phases of muscular invasion, as well as early and late muscular phases of an experimental infection by *T. pseudospiralis* in mice. The effectiveness of single doses of Thiabendazole decreased with advancing stages in the life cycle of the parasite from 47.4 to 23.0% reduction, while the opposite circumstance happened with Mebendazole - 66.6% in the muscular invasion to 90.9% in the late muscular phase. A slight decrease can be noted in the intermediate stage of the treatment with Parbendazole, Fenbendazole, Albendazole and Febantel, while Levamisole and Ivermectin present a moderate effectiveness in the three stages (around 30%) being slightly increased in the late muscular phase for single doses of Levamisole (57.7%) and in the phase of muscular invasion for single doses of Ivermectin (61.1%).

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