

CLINICAL TRIALS OF BROAD SPECTRUM ANTHELMINTICS AGAINST SOIL-TRANSMITTED HELMINTHIASIS

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INTRODUCTION

Developing countries are still faced with health problems brought about by soil-transmitted helminthiasis. These problems are here to stay because of poor environmental sanitation, improper human waste disposal resulting in soil-pollution or contamination, lack of personal hygiene and low socio-economic status of the people.

With regards to the treatment and control of soil-transmitted helminths, there are very effective drugs against ascariasis currently available in the market. However, there seems to be no ideal drug as yet for the control and/or eradication of *Trichuris trichiura* and hookworm infections. Clinical field trials of flubendazole on hookworm, *Trichuris trichiura* and *Ascaris lumbricoides* infections by Bunnag *et al.*, (1979) in Thailand seem to indicate that flubendazole is relatively effective against the three soil-transmitted helminths with 100% cure rates for both ascariasis and trichuriasis and 81.5% for hookworm. Wershing *et al.*, (1979) also tried flubendazole in the Bahamas among children with ascariasis and trichuriasis and found that the egg reduction rates for trichuriasis ranged between 85.6% and 99.98% and cure rates between 82.8% and 88.9%. In ascariasis the cure rates ranged between 90.2% and 100%.

Clinical trial of oxantel-pyrantel by Cabrera *et al.*, (1978) at 15 mg/kg and 20 mg/kg then 15 mg/kg twice a day (12 hours interval) and 20 mg/kg daily for 2 days gave cure rates of

97% and 100% respectively for ascariasis; 53% and 41% respectively for trichuriasis. The 15 mg/kg twice a day and 20 mg/kg daily for 2 days gave cure rates of 100% in both schemes for ascariasis and 89.2% and 71.1% respectively for trichuriasis.

Further clinical trial of oxantel-pyrantel against trichuriasis by Cabrera *et al.*, (1979) using 20 mg/kg single dose and 15 mg/kg bid (12 hours interval) gave cure rates of 83.9% and 94.1% respectively and 96.9% and 98.6% egg reduction rate respectively.

The use of mebendazole (Antiox) as a single dose anthelmintic against soil transmitted helminthiasis has been tried previously in a few cases, by Cabrera *et al.*, in 1979 with cure rates of 100%, 100% and 50% for *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm infections respectively.

The primary purpose of this study is to compare the efficacy of flubendazole with oxantel-pyrantel in trichuriasis at their recommended doses and secondly to do further clinical trials of mebendazole used in a single dose.

MATERIALS AND METHODS

A helminthological survey was carried out at Barrio Bulusan, Irosin in Sorsogon Province in March 1980. A total of 283 stool specimens were collected, placed in clean screw-up plastic vials and sent by bus within the same day to the Institute of Public Health in Manila for processing.

In the laboratory, quantitation of eggs were done using the Kato-Katz technique. All those found positive for *Trichuris* eggs alone or in combination with *Ascaris* and/or hookworm were included in the study. Egg counts were made only for *Trichuris* and not for *Ascaris* and hookworm. Approximately one-third of the randomly selected patients received flubendazole tablets, 300 mg in one intake for two consecutive days while the other one-third received oxantel-pyrantel 10 mg/kg body weight in a single dose. The remaining subjects received 600 mg mebendazole in a single dose.

The intensity of *Trichuris* infection was classified into light (< 5,000 eggs/gram of stool), moderate (5,000-20,000 eggs/gm) and heavy (> 20,000 eggs/gm). Although the study was focused more on the effect of

treatment on trichuriasis, observations were likewise made on *Ascaris* and hookworm infections.

A second stool collection and examination was done 3-4 weeks after treatment. Quantitation of *Trichuris* eggs among those cases still with egg-positive stools were again performed to determine the egg reduction rate (ERR) before and after treatment. Post treatment cure rates for the three nematodes were also determined.

RESULTS

The results of treatment modalities for trichuriasis is shown in Table 1. Flubendazole gave an egg reduction rate (ERR) of 83.14% followed by oxantel-pyrantel 74.08% and mebendazole 71.96%. Table 2 shows the cure rates for trichuriasis using the same

Table 1
Results of treatment modalities for trichuriasis, Sorsogon, 1980.

Treatment	Egg per Gram (EPG)		Percent Egg Reduction (ERR)
	Before Rx	After Rx	
Flubendazole 300 mg daily for 2 days	543810	91681	83.14
Quantrel 10 mg/kg body wt. single dose	450105	116650	74.08
Antiox 600 mg single dose	31257	8763	71.96

Table 2
Cure rates for trichuriasis using three treatment modalities, Sorsogon, 1980.

Treatment	No. treated	Cured	
		No.	rate (%)
Flubendazole 300 mg daily for 2 days	53	7	13.2
Quantrel 10 mg/kg body weight single dose	65	5	7.7
Antiox 600 mg single dose	66*	30	45.5

* all cases were light infections (EPG < 5,000 eggs/gm.)

treatment modalities. It appears that flubendazole gave a cure rate of 13.2%, oxantel-pyrantel 7.7% and mebendazole 45.5%. One should take note however, that the 66 cases treated with a single dose of mebendazole were all light infections.

The distribution of study subjects by degree of *Trichuris* infection is shown in Table 3. Out of 53 cases treated with flubendazole, 19% were heavy infections, 32% were moderate and 49% were light. On the other hand, out of 65 cases treated with oxantel-pyrantel, 4.6% were heavy infections, 38.4% were moderate and 57% were light. All the 66 cases treated with mebendazole were light

infections with counts less than 5,000 eggs per gram of faeces.

The results of the three treatment modalities for ascariasis and hookworm infections are shown in Table 4. There were 48 ascariasis and 19 hookworm infections treated with flubendazole with cure rates of 89.6% and 42.1% respectively. There were 60 ascariasis and 22 hookworm infections treated with oxantel-pyrantel with cure rates of 95% and 72.7% respectively. Mebendazole as single dose was used in 51 ascariasis and 17 hookworm infections with cure rates of 94.1% and 88.2% respectively.

Table 3

Distribution of study subjects by degree of *Trichuris* infection, Sorsogon, 1980.

Degree of Infection	Group treated with Flubendazole		Group Treated with Quantrel		Group Treated with Antiox	
	No.	%	No.	%	No.	%
Heavy	10	19.0	3	4.6		
Moderate	17	32.0	25	38.4		
Light	26	49.0	37	57.0	66	100.0
Total	53	100.0	65	100.0	66	100.0

Table 4

Results of three treatment modalities for *Ascaris* and hookworm infections, Sorsogon, 1980.

Treatment	No. Treated		Cure Rate (%)	
	<i>Ascaris</i>	Hookworm	<i>Ascaris</i>	Hookworm
Flubendazole 300mg daily for 2 days	48	19	89.6	42.1
Quantrel 10mg/kg body wt. single dose	60	22	95.0	72.7
Antiox 600mg. single dose	51	17	94.1	88.2

In all of the subjects, side reactions, if any were practically nil and very transient. There were about two oxantel-pyrantel subjects treated who complained of nausea but with no actual vomiting. On the other hand, *Ascaris* erraticity, nausea and vomiting, were not observed in the flubendazole and mebendazole treated subjects.

DISCUSSION

Field workers evaluating a new drug particularly when mass treatment is contemplated, still prefer the single dose regimen. In the control and/or eradication of soil-transmitted helminthiasis, there seems to be a trend in the use of single dose regimens following a periodic treatment pattern of 3-4 times a year.

Of the three common soil-transmitted helminths, *Trichuris* appears to be the most difficult to eliminate, followed by hookworm with *Ascaris* as the easiest. Because of this existing problem, one has to rely on egg reduction rates rather than on cure rates, which can only be determined by egg quantitation or egg counting procedure.

In Table 1 are recommended dosages of flubendazole (Fluvermal) and oxantel-pyrantel (Quantrel) and a single dose of mebendazole (Antiox) on trichuriasis. Flubendazole given at a dose of 300 mg daily for 2 days gave the highest egg reduction rate (ERR) followed by oxantel-pyrantel and mebendazole. When comparing cure rate, mebendazole gave the highest, followed by flubendazole and oxantel-pyrantel. In both cure rates and egg reduction rates, one should take into account the degree of infection e.g. light, moderate and heavy. This could be the most reliable explanation of the high cure rate of a single dose of mebendazole since all the 66 subjects were with light infections.

From Table 4 it appears that oxantel-pyrantel gave the highest cure rate for

ascariasis followed by mebendazole and flubendazole. On the other hand for hookworm infection, mebendazole gave the highest cure rate followed by oxantel-pyrantel and then flubendazole.

SUMMARY

Clinical trials on the three broad spectrum anthelmintics against trichuriasis, ascariasis and hookworm infection were carried out in a rural community in Irosin, Sorsogon. Flubendazole (Fluvermal) appears to be a promising drug against trichuriasis particularly when periodic mass treatment of a community is carried out. Mebendazole (Antiox) also appears to be promising given as single dose during mass treatment of soil-transmitted helminthiasis. As shown in previous studies, oxantel-pyrantel (Quantrel) should be given at 15 mg/kg body weight at 12-hour intervals or 20 mg/kg body weight single dose rather than 10 mg/kg body weight in a single dose when treating trichuriasis.

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