

CLINICAL TRIAL OF PYRANTEL EMBONATE, LEVOTETRAMISOLE AND BEPHENIUM HYDROXYNAPHTHOATE AGAINST *NECATOR AMERICANUS*

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SYNOPSIS

A clinical trial was conducted to compare the efficacy of Pyrantel embonate, Levotetramisole and Bephenium hydroxynaphthoate for treatment of *Necator americanus* infection in Singapore. It was observed that 80% of the patients passing <5000 eggs per gram of faeces were cleared by a single dose of Pyrantel pamoate, in contrast to Levotetramisole which cleared 68.4% and Bephenium hydroxynaphthoate which cleared 43.7%. In addition to this Bephenium hydroxynaphthoate was not well tolerated giving greater side effects than both Levotetramisole and Pyrantel pamoate.

Studies by various authors have shown that *Necator americanus* is the predominant species of hookworm in Malaysia and Singapore (Lie Kian Joe, 1964). This information is relevant to the treatment of hookworm infestation as the drug activity differs according to the species of the worm involved.

Since Bephenium hydroxynaphthoate (Alcopar, Burroughs Wellcome) is widely used in Singapore and Malaysia for the treatment of "hookworm" infestation, we chose to compare its efficacy and side effects against two new wide spectrum anthelmintics, Pyrantel embonate (Combantrin, Pfizer) and Levotetramisole (Decaris, Johnson and Johnson).

MATERIAL AND METHODS

The trial was a single, blind, randomised and non-crossover comparison of Bephenium, Pyrantel and Levotetramisole given in a single dose for the treatment of patients with *Necator* infestation.

1000 patients attending Bukit Panjang Outpatient Dispensary were chosen at random for screening to produce 83 patients with *Necator* infestation. After excluding pregnant females and children under 3 because of anticipated difficulty in medication, 73 patients were allocated at random into one of the three treatment groups.

All agents were given on an empty stomach in a single dose and the dosage was calculated on body weight basis according to the recommended regime of the respective drug package insert.

A record of presenting symptoms and signs of infestation and of any side effects of treatment was maintained. Patients were seen again on 7th and 14th post-treatment days and stool specimens were collected for examination.

DIAGNOSIS OF HOOKWORM INFESTATION

Stool specimens were sent to the laboratory in the Department of Parasitology, Singapore Medical Faculty for examination, where the following tests were undertaken:

- (a) Faecal egg counts were done according to the method of Beaver (1950), using the direct smear technique.
- (b) Coprocultures were done according to the method of Harada and Mori (1955), using test-tubes.

Presence of other parasitic infestations were also noted.

The drugs were evaluated on the following points:

(a) Efficacy

The patients were considered cleared of *Necator* infestation when stool examination on post-treatment day 14 showed total clearance of hookworm eggs.

(b) Side Effects

All side effects both immediate and delayed were recorded.

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RESULTS

66 out of 73 patients completed the follow up and the efficacy of the drugs in this group is shown in Table I.

TABLE I

	Light Necator Infestation <5000 Eggs Per Gram			Heavy Necator Infestation 5000-15000 Eggs Per Gram.	
	No. Treated	No. Cleared	% Clear	No. Treated	No. Cleared
Pyrantel embonate	20	16	80 %	3	2
Levotetramisole	19	13	68.4%	2	0
Bephenium	16	7	43.7%	6	1

Multiple infestations with other intestinal nematodes were commonly seen and these were as following:

30% (20 out of 66) had associated ascariasis, 40% (26 out of 66) had associated trichuriasis, 21% (14 out of 66) had triple infestation with *Ascaris*, *Trichuris* and *Necator*.

All 3 drugs were observed to have good effect on *Ascaris* infestation but the number of cases studied were too small for a comparative evaluation. All the 3 drugs were ineffective against *Trichuris trichiura* infestation and not a single case showed complete disappearance of eggs from the stools.

The following side effects were noted:

Pyrantel Embonate—Mild abdominal pain was observed by 7 out of 23 patients which occurred mostly 24 hours after medication, usually lasting for 5 to 15 minutes and occasionally longer but required no treatment. Two of these patients had an associated episode of loose stool. No other side effects were seen.

Levotetramisole—Mild abdominal pain was observed by 6 out of 21 patients which occurred mostly at 2 to 3 hours after medication usually lasting for an average of 3 hours and occasionally longer, but required no treatment. Two patients had episodes of loose stool. One patient complained of nausea half an hour after medication.

Bephenium—21 out of 22 patients had side effects. Nine patients vomited, mostly half an hour after medication and all occurred within 2 hours of medication. Five patients complained of nausea

within 1 hour after medication and the symptom persisted for an average of 2 hours. Six patients had episode of loose stool within 1 hour of medication. Ten patients had diarrhoea, beginning mostly within 2 hours of medication, lasting usually between 2 to 8 hours but ranging from 1½ to 24 hours. One patient had abdominal pain.

DISCUSSION

Bephenium hydroxynaphthoate has been used for more than 12 years for the treatment of hookworm infestation all over the world. However, it is generally not appreciated that the drug is less effective against *Necator americanus* than *Ancylostoma duodenale*. Due to this reason repeated administration of this drug is required if a satisfactory response is to be obtained in *Necator americanus* infection (Botero and Castano, 1973). In addition to this disadvantage our observations have shown that Bephenium produced greater side effects than Levotetramisole and Pyrantel embonate. In this part of the world where *Necator americanus* is the dominant species, there is, therefore, little indication to use Bephenium salt for the treatment of hookworm infestation.

Polyparasitism (multiple infestation) consisting of *Necator*, *Ascaris*, *Enterobius* and *Trichuris* infestation are commonly seen in Singapore and Malaysia. A drug which will act against all these parasites will be very useful. Pyrantel embonate comes close to this, as it is effective against *Necator*, *Ascaris* and *Enterobius* and in this study was also found to be well tolerated. However, Pyrantel embonate was ineffective in curing infestation with *Trichuris*. We are, therefore, not recommending it for the treatment of this parasite.

ACKNOWLEDGEMENT

We are grateful to Dr. Ernest Lai for his assistance in conduction of this study.

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