# A TRIAL OF MEBENDAZOLE IN TRICHURIASIS (WHIPWORM) INFESTATION IN SINGAPORE CHILDREN

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#### SYNOPSIS

1. 10 cases of *Trichuris* infestation in children are described presenting with malaise, pica, diarrhoea, prolapse of the rectum, anaemia and infection.

2. All children suffered considerably in health by the infection aggravated by protein caloric malnutrition and anaemia.

3. Malay children were mainly affected living in the poor rural areas with poor sanitation.

4. Mebendazole has proved to be effective in the treatment of Trichuriasis in children. Administered orally in tablets it is well tolerated in doses of 100 mgm. daily for 3 days.

5. Pre ova count and post ova count of the stools while on the drug revealed a reduction rate of almost 100% in two weeks after administration.

6. No side effects were observed with the drug.

## **INTRODUCTION**

The most common intestinal helminth found in Singapore and Malaysia is *Trichuris trichiura* (Desowitz *et al*, 1961; Lie, 1964). In a recent survey done in the Outram Road General Hospital 38% of the cases were found to be infected with *Trichuris*. Infection was most prevalent in one to five-year age group. The prevalence and degree of infection was the highest amongst Malays, followed by Indians and the Chinese (Kan *et al*, 1971).

Until recently the most effective drug against this parasite was Dithiazanine iodide. This drug produced serious side effects and is no longer used. Recently, a new anthelminthic with a generic name of Mebendazole has been introduced in the market and the aim of this study was to try this drug in cases of severe Trichuriasis which also had protein-caloric malnutrition and nutritional anaemia, and were admitted into the children's ward, General Hospital, Singapore.

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## MATERIAL AND METHODS

The anthelminthic was administered in tablets containing 100 mg. of drug. In two children 50 mg.  $(\frac{1}{2}$  tablet) b.d. was given for three days. In the remaining eight children 100 mg. b.d. was given for three days.

Stool examination was conducted once before treatment and for four consecutive days post treatment. This was followed by one stool examination 2 weeks and 3 months later. The technique of examination was ordinary direct smear using 2 mg. of faeces according to Beaver's method (1950).

## RESULTS

# Case 1

M.K.B.S. was a 3-year old Malay boy admitted on 11.12.69 because of a left ear discharge and fever for one day. He was the 8th of 9 children and lived in a rural area with no modern sanitation. Physical examination revealed a malnourished child measuring only 31 inches in height (below-2 standard deviations for age) and weighing only 22 lbs (below-2 standard deviations for age). He was febrile because of a left otitis media. No abnormality could be detected clinically in the heart, lungs and abdomen. The following investigations were done:- Hb 10 gms. %. Total White Count 6,800 cm. P = 52% L = 4% M = 1% E = 5%. The peripheral blood film showed microcytic hypochromic cells while the bone-marrow revealed no iron stores. The serum folic acid was low being

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The child was sent to a convalescent home by the sea for a period of three months. He was sent back home after discharge to the same home environment but was followed up at monthly intervals should a re-infection occur.

# Case 2

N.B.R. was a 3-year old Malay female child who lived in a kampong and was admitted because of severe diarrhoea and fever for a week. She was very dehydrated and her height and weight were below the 3 percentils for her age. The liver was enlarged 2 cm. below the right costal margin. The haemoglobin was 6.9 gms.% and the peripheral blood film showed a marked hypochromic microcytic anaemia. A bone-marrow revealed eosinophil precursors and hardly any iron stores. The serum iron was also low being 23 µgms. %. The radiographs of the chest revealed a patchy broncopneumonia and examination of the stools revealed a heavy infestation with whipworm ova. The results of the ova count of the stools before and after Mebendazole treatment are shown in Table II.

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# Case 3

K.C.E. was a 3-year old Chinese girl admitted because of chronic diarrhoea for one month. The stools contained blood and mucus and on the day of admission the child was noted to have prolapse of the rectum. She was one of six siblings and lived in a rural area of Singapore where the stools were disposed of by the bucket system of latrine. On examination on 22.10.72 the child was pale and weighed 18 lbs. being well below the 3rd percentils for Chinese girls of the same age. The height was only 34 inches, again below median in height. A haemic systolic bruit was audible over the heart. The chest was clear. The abdomen was distended, and the liver was one cm. below the right costal margin. The rectum was prolapsed and the edges contained live Trichuris worms (Fig. 1). Proctoscopy revealed mucosal ulceration of the rectum with Trichuris worms on the ulcers. The stools were very foul smelling, profuse, watery and contained blood and mucus.

Laboratory investigations revealed a haemoglobin of 8.4 gms. % with a marked hypochromic microscytic anaemia. The bone marrow again showed marked eosinophil precursors. The serum iron was low being only 19 µgms. % and the serum folic acid was 2.8 % µgms. %. The results of the ova count and treatment with Mebendazole are shown in Table III.

This child was given blood transfusion initially on admission, and was treated with Folic

Pretreatment ova count	Pretreatment Day 1 ova count		Day 3	Day 4	2 wks	3 mths	
132/2mgm of stool	4/2mgm	0/2mgm	0/2mgm	0/2mgm		0/2mgm	
Mebendazole	50mgm b.d.	50mgm b.d.	50mgm b.d.	—			

TABLE I

TABLE II

Pretreatment ova count	reatment Day 1		Day 3	Day 4	2 wks	3 mths	
1289/2mgm of stool	99/2mgm	32/2mgm	16/2mgm		4/2mgm	2/2mgm	
Mebendazole	50mgm b.d.	50mgm b.d.	50mgm b.d.				



Fig. 1. Note *Trichuris* worms at the end of the prolapsed rectum.

acid and iron tablets and put on a high protein diet. Her prolapse of the rectum had to be reduced periodically but with the improvement of the diarrhoea the prolapse improved. She put on weight of four lbs. before going to the convalescent home in Changi. All members of the family showed *Trichuris* infestation and were given Mebendazole. The fifth sibling in the family showed a heavy infestation with *Trichuris* and required therapy too.

# Case 4

T.B.R. was a 4-year old male Malay child admitted because of pallor over a three-month period and diarrhoea over a three-week period. This child too lived in the rural area of Singapore. Physical examination revealed a stunted child measuring 32 inches (below the 3rd percentile in height) and measuring 22 lbs. (below the 3rd percentile in weight). There was a haemic bruit over the heart. The abdomen was protuberant and the liver was enlarged 2 cm. below the right costal margin. Investigations revealed that the haemoglobin was only 5 gms. % and the microcytic cells and the bonemarrow showed no iron stores with giant metamyelocytes. The child was treated with 100 cc. of packed cells and given a course of Mebendazole. As shown in Table IV.

The above child also suffered from protein caloric malnutrition with nutritional iron deficiency and Folic acid deficiency aggravated by whipworm infestation. He was given a good high protein diet with Mist Ferrous Sulphate mixture and Folic acid tablets. The haemoglobin rose to 10 gms.% and he was discharged home well after a month's stay in hospital.

Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths
132/2mgm of stool	204/2mgm	194/2mgm	61/2mgm	34/2mgm	14/2mgm	Negative
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.			

TABLE III

#### TABLE IV

Pretreatment ova count	Day 1 Day 2 Day 3		Day 4	2 wks	3 mths		
504/2mgm of stool	4/2mgm	Negative	Negative		Negative	Negative	
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.				

M.A.B.Z. was a 4-year old Malay child admitted because of constipation and pica for a period of 3 to 4 months. Physical examination revealed an extremely pale child with flat pale nails and a marked pot belly. There was a haemic murmur over the base of the heart and the liver was enlarged 2 cms. below the right costal margin. The haemoglobin was only 3.8 gms. % and the peripheral blood film showed a marked microcytic hypochromic anaemia. There were megaloblasts in the bone marrow. The serum iron was only 37 µgms. %. Examination of the stools revealed a light infestation with both

This child had a severe nutritional anaemia due to megaloblastic iron deficiency. It is remarkable how late these children arrive with only a haemoglobin of 3.8 gms. %. The child's habit of eating sand was probably to satisfy his hunger as the diet was very poor. The child was sent to the convalescent home where at the end of a three-month stay he put on 10 lbs. making him 30 lbs. at the 50th percentile for his age on discharge. He also grew taller by 2 inches making him 38 inches on discharge and at the 50th percentile for his height. In this child the *Trichuris* count was low and probably did not aggravate his nutritional state.

Ascaris and Trichuris ova. The results of the ova

count are shown in Table V.

# Case 6

M.F.B.M. was a 5-year old Malay boy, one of 5 children admitted because of fever and

cough for one week. He was one of five siblings and also lived in the rural area. This child was in a better physical condition compared to the cases described above but had a left pleural effusion, pyogenic in origin. The haemoglobin was 9.4 gms.%, and the peripheral blood film showed a microcytic hypochromic anaemia. The results of the ova count are shown in Table VI.

# Case 7

M.B.A. was a 7-year old Malay boy and was a known case of Thromboasthenia since the age of 3 years, characterised by tendency to bleed due to defective clot retraction of the blood. This time he was admitted because of progressive malaise and anorexia over a period of two months. Physical examination revealed a very pale child with no evidence of bruises. There was frontal bossing of the skull bones and a systolic and soft diastolic flow murmur was audible over the mitral area. The liver was 2 cms. below the right costal margin. The haemoglobin was only 1.6 gms. % and a bone-marrow puncture revealed both iron-deficiency and megaloblastic anaemia, and examination of the stools revealed whipworm ova. The results of the ova count are shown in Table VII.

This child was the tenth child in a family and lived in a small kampong village in Sembawang. Three months later the stools still showed whipworm ova due to re-infection in the same environment and he was given a second course of Mebendazole as an outpatient.

Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths	
10/2mgm of stool	1/2mgm	0/2mgm	1/2mgm		Negative	Negative	
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.				

TABLE V

TABLE VI

Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths
61/2mgm of stool	18/2mgm	3/2mgm	0/2mgm			
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.			

Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths
431/2mgm of stool	103/2mgm		91/2mgm	18/2mgm	Nil	Nil
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.			

#### TABLE VIII

Pretreatment ova count Day 1		Day 2	Day 3	Day 4	2 wks	3 mths	
472/2mgm of stool	367/2mgm	20/2mgm	17/2mgm		4/2mgm	Nil	
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.				

TABLE IX

Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths	
405/2mgm of stool	332/2mgm	42/2mgm	8/2mgm	0/2mgm	0/2mgm	0/2mgm	
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.				

# Case 8

A.B.L. was a 7-year old female and referred from the school health service because of anaemia and inability to cope with her lessons at school. Physical examination revealed a stunted child who was well below—2 standard deviations for her age in height and weight. She did not look ill except for pallor, the haemoglobin being 5.7 gms.%. The peripheral blood film showed hypochromic, microcytic cells and the bone marrow revealed eosinophil precursors. In addition to *Trichuris* ova, this child had hookworm and *Ascaris* ova in her stools. The results of the ova count are shown in Table VIII.

This child lived in the centre of the island at Botanical Gardens and one year later was admitted for joint pains due to rheumatoid arthritis. Examination of the stools did not reveal any whipworm ova on second admission. Her haemoglobin was satisfactory being 11.7 gms.%.

# Case 9

H.B.A. was an 8-year old female Malay school girl admitted because of fever and found to be extremely pale on admission. There was a past history of diarrhoea with blood and mucus in the stools. The patient lived in the kampong area of Geylang. On physical examination the child was pale; her weight was 44 lbs. which is at the 50th percentile using Hongkong standards. There was prolapse of the rectum on straining at stools and examination of the buttocks revealed a rash with little pin-point haemorrhages (Fig. 2). Examination of the stools revealed Trichuris ova, hookworm and a few amoebae. She was treated for all three infections. The results of the ova count are shown in Table IX.

This child had a severe iron-deficiency anaemia, as the bone marrow showed no evidence of iron stores.



Fig. 2. Note excoriation round the buttocks and vulva with prolapse of the rectum due to Trichuriasis.

## Case 10

K.B.B. aged 9 years old was referred from Ponggol Clinic because of fever for three days. On physical examination her nutritional status was poor and her height and weight were at the 10th percentile using Hongkong standards for children of that age. There was hepatosplenomegaly with the liver and spleen measuring 3 cms. This child frequently went to Johore but repeated films of the blood did not reveal any malarial parasite. The haemoglobin was 8.4 gms. % and the bone-marrow revealed eosinophil precursors. Examination of the stools revealed *Trichuris* ova, and the results of the ova count are shown in Table X. As reported by Wagner and Chavaria (1974) treatment with Mebendazole produced deformity of the *Trichuris* eggs. The deformed eggs were similar in appearance to that seen when Thiabendazole is administered. A normal *Trichuris* egg is barrel shaped with translucent plugs at either end (Fig. 3). The deformed eggs are irregular or oval in shape. The lateral plugs are indistinct and sometimes completely absent (Figs. 4, 5). The deformed eggs do not embryonate on incubation.

# DISCUSSION

The whipworm is cosmopolitan in distribution but occurs more commonly in warm



Fig. 3. A normal *Trichuris* egg which is barrel-shaped and shows distinct lateral plugs.



Fig. 4. A deformed egg after Mebendazole treatment. A single plug is still visible.

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Pretreatment ova count	Day 1	Day 2	Day 3	Day 4	2 wks	3 mths
41/2mgm of stool	31/2mgm	31/2mgm	0/2mgm	0/2mgm		
Mebendazole	100mgm b.d.	100mgm b.d.	100mgm b.d.			



Fig. 5. A deformed egg after Mebendazole treatment. The lateral plugs have disappeared.

humid climates. The adult worms are located in the caecum and upper parts of the colon. However, in heavy infection the whole large intestine may be involved. They attach themselves to the intestinal tissues by embedding their anterior end into the mucous membrane. Infection occurs by ingestion of eggs containing larvae which hatch in the lumen of the intestine and mature in about 12 weeks time without migrating through the lungs. In this respect they differ from hookworm and *Ascaris lumbricoides* both of which migrate through the lungs to complete their life cycle.

The clinical aspect of Trichuriasis has been described previously by Wong (1962) in Singapore and Kamath (1973) in Malaysia. The symptoms varied from dysentery and prolapse of the rectum to malaise and lassitude. Getz (1945) reported symptoms associated with *Trichuris* infection in the Panama region. In some of his cases the worms had entered the appendix giving rise to appendicitis. He also reported death in children due to heavy infestation. Those who survived had emaciation, cardiac dilatation and anaemia.

Chaia and Sales de Cunha (1971) were the first to report on the high efficacy of Mebendazole in Trichuriasis. This finding was further confirmed by Chavaria *et al* (1973) in Costa Rica. They also reported that this anthelminthic could be used safely and without significant side effects in persons with anaemia and malnutrition. No unfavourable drug induced changes were noted in the biochemical and helminthological parameters after the treatment. Mebendazole acts by interfering with the exogenous glucose uptake by the parasites. The consequent increased utilization of endogenous

		% Reduction	100 %	Almost $100\%$	100 %	100%	100%	100%	100%	100%	100%	100%
	nt	3 mths Later	0	2	0	0	0	0	0	0	0	0
OLE	ool Cou	2 wks Later	0	4	14	0	0	0	0	4	0	0
ENDAZ	St	3 Days Later	0	16	61	0		0	16	17	8	0
S ON MEB	Before Treatment	Ova Count	132	1289	1360	504	10	18	103	472	405	41
RIASI'		Days	ß	ω	ù	m	m	ω	m	ŝ	m	ω
WITH TRICHU	6	Dosage	50mgmsbd.	50mgmsbd.	100mgmsbd.							
N CHILDREN	Drue	(Mebenďazole)	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole	Mebendazole
IARY OF TEI	Haemoglobin	grams %	10 gms %	6-9gms %	8 ·4gms %	5gms%	3-8gms %	9.4gms %	5gms%	5.7gms%	5gms %	8-4gms %
6. SUMN		Касе	Malay	Malay	Chinese	Malay						
Fig.		· Sex	Male	Female	Female	Male	Female	Male	Male	Female	Female	Female
		aga	3 yrs	3 yrs	3 yrs	4 yrs	4 yrs	5 yrs	7 yrs	7 yrs	8 yrs	9 yrs
		Case	1	2	m	4	S	9	-	~	6	10

carbohydrate reserves lead to inadequate energy supply and death of the nematodes.

Our observations support the findings of these workers and we obtained almost 100% egg reduction in patients receiving Mebendazole (Fig. 6). This occurred in spite of the fact that two of our cases had extremely high worm burdens. The side effect profile of the drug is also good and we did not observe any side reactions attributable to the drug.

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#### REFERENCES

 Beaver, P.C.: "The standardization of faecal smears for estimating egg production and worm burden." J. Parasitol, 36, 451, 1950.

- 2. Chaia, G. and Sales da Cunha, A.: "Therapeutic action of mebendazole (R 17, 635) against human helminthiasis." A Folha Medica, 63, 843, 1971.
- Chavaria, A.P., Swartzwelder, J.C., Villarejos, V.M. and Zeledon, R.: "Mebendazole, an effective broad-spectrum!anthelmintic," Amer. J. Trop. Med. Hyg., 22(5), 592, 1973.
- 4. Desowitz, R.S., Zaman, V. and Ng, W.K.: "The incidence of intestinal parasites in various communities of Singapore island." Sing. Med. J., 2(3), 91, 1961.
- 5. Getz, L.: "Deaths due to Trichuriasis." Amer. J. Dis. Childhood, 70, 19, 1945.
- 6. Kamath, K.R.: "Severe infection with *Trichuris* trichiura in Malaysian children. A clinical study of 30 cases treated with Stillbazium iodide." Amer. J. Trop. Med. Hyg., 22(5), 600, 1973.
- Kan, S.P., Singh, M., Cheah, J.S. and Siak, C.L.: "Survey of helminthic infections in Singapore." Southeast Asian J. Trop. Med. Pub. Hlth., 2(2), 190, 1971.
- 8. Lie, K.J.: "Prevalence of intestinal helminths among patients of the General Hospital in Kuala Lumpur, Malaya. Trop. Geogr. Med., 16, 229, 1964.
- 9. Wagner, E.D. and Chavaria, A.P.: "Morphologically altered eggs of *Trichuris trichiura* following treatment with mebendazole." Amer. J. Trop. Med. Hyg., 23(2), 154, 1974.
- 10. Wong, H.B. and Tan, K.H.: "Severe whipworm infestation in children." Sing. Med. J., 2, 34, 1962.