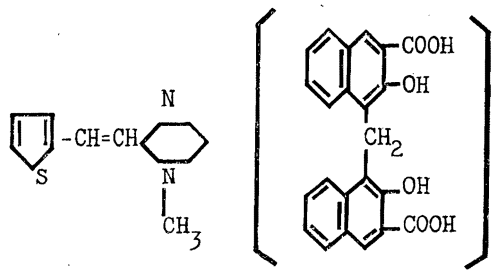
TREATMENT OF *ASCARIS*, HOOKWORM AND *TRICHURIS* INFECTIONS WITH A SINGLE DOSE OF PYRANTEL PAMOATE (COMBANTRIN)

HSIEN-CHEN HSIEH and ENG-RIN CHEN

Department of Parasitology, Kaohsiung Medical College, Taiwan, Republic of China.

INTRODUCTION

Pyrantel pamoate (Combantrin) is a new chemical discovered and developed by Pfizer Research. It is a yellowish crystalline and water-insoluble, tasteless pamoic acid salt of pyrantel. It is trans-1, 4, 5, 6-tetrahydro-1-methyl-2-[2-(d-thienyl)-vinyl] pyrimidine pamoate. The structural formula of pyrantel pamoate is as follows:



Pyrantel pamoate

Pyrantel suspension contains the equivalent of 50 mg pyrantel base per ml and the pyrantel tablet contains the equivalent of 125 mg pyrantel base. The drug requires neither purging nor dietary restriction before or after therapy. It has been reported to be highly effective against *Ascaris lumbricoides* (Desowitz *et al.*, 1970; Kobayashi *et al.*, 1970; Hsieh and Chen, 1970, 1971; Villarejos *et al.*, 1971; Bell and Nassif, 1971; Cervoni and Oliver-González, 1971; Rim *et al.*, 1972), *Necator americanus* (Desowitz *et al.*, 1970; Yokogawa *et al.*, 1970; Suzuki *et al.*, 1971; Villarejos *et al.*, 1971; Cervoni and Oliver-González, 1971), *Ancylostoma duodenale* (Hsieh and Chen, 1970; Hori, 1971; Pandey *et al.*, 1971), *Enterobius vermicularis* (Bumbalo *et al.*, 1969; Burriel *et al.*, 1969; Yokogawa *et al.*, 1970; Hori, 1971; Baranski *et al.*, 1971; Hsieh *et al.*, 1971; Yamamoto *et al.*, 1971; Rim and Lim, 1972), *Trichostrongylus orientalis* (Rim and Lim, 1972), *Trichuris trichiura* (Cervoni and Oliver-González, 1971; Villarejos *et al.*, 1971) and *Ternidens deminutus* (Goldsmid and Saunders, 1972).

In a continued search for a minimal effective dose of pyrantel pamoate for periodic mass treatment of *A. lumbricoides*, *A. duodenale*, *N. americanus*, *T. trichiura*, and *E. vermicularis*, which often occur as mixed infections in Taiwan, the authors have conducted a series of field trials in South Taiwan.

Previous studies on the treatment of *A. lumbricoides* with a small dose (2.5 mg/kg) of pyrantel pamoate (Hsieh and Chen, 1971) and of *E. vermicularis* with different dosage regimens (Hsieh *et al.*, 1971) have been published. This paper presents the result of treatment of these nematodes other than *E. vermicularis* with doses ranging from 2.5 mg to 10 mg/kg body weight.

MATERIALS AND METHODS

The subjects of the trial were children attending two neighbouring rural primary schools in South Taiwan, just outside Kaohsiung City. After a series of parasitological surveys, more than 700 children were found to be concurrently infected with *A.*

lumbricoides, *A. duodenale*, and *N. americanus*. They were randomly divided into four groups according to four dosage regimens of pyrantel pamoate, i.e. each child received one dose of either 2.5 mg, 5 mg, 7.5 mg or 10 mg per kg of the drug. A total of 630 children were accepted for the trial. The age distribution of the four groups was similar and ranged from 6 to 13 years. The effect of different doses of pyrantel pamoate against *T. trichiura* was in addition evaluated on 307 out of the 630 children.

The tablet form of pyrantel pamoate (Combantrin) with a base activity of 125 mg or 50 mg was used.

Before and after therapy, stools of the children were examined on 3 consecutive days by Stoll dilution egg counting method (Stoll, 1962) and the flotation method with saturated-brine magnesium-sulfate solution (450 gm of sodium chloride, 675 gm of magnesium sulfate in 1,500 ml of distilled water). For the flotation method (with approximately 0.3 gm of stool for each tube), one test-tube examination was made on the daily stool sample of each subject. The 24-hour stool of each was collected in a plastic bag at the subject's home and brought to the laboratory for microscopic examination. Modified test-tube filter-paper culture method (MTFC) (Hsieh, 1971) was also employed for specific analysis of hookworm infection.

If the post-treatment stool (4 weeks after therapy) is free of eggs by the Stoll and flotation methods, the child was considered to be negative except for hookworm infection. The negative conversion rate (NCR) for hookworm species was determined by MTFC and the Stoll and flotation methods. The negative conversion rate was the ratio of negative case to all cases evaluated for each nematode species. The egg reduction rate was the ratio of the egg-count per gram faeces (EPG) reduced from the pre-treatment level to the post-treatment EPG.

A single dose of pyrantel pamoate (2.5 mg, 5 mg, 7.5 mg or 10 mg/kg) was administered to each child with a glass of pre-boiled cool water. The drug was given on an empty stomach in the authors' presence about 2 hours before lunch or supper at their schools. Young children were advised to chew the tablets and then swallow them with several mouthfuls of water as pyrantel tablets are tasteless and harmless to the buccal mucosa.

Within 24 hours after medication the children were revisited by the authors for recording side effects. No special inquiry was made to the 630 children by the authors about any symptom or side effect due to the drug. If no complaint was reported the drug was considered to be acceptable.

RESULTS

Table 1 shows the egg reduction rates(ERR) and negative conversion rates (NCR) of *A. lumbricoides*, *A. duodenale*, *N. americanus*, and *T. trichiura* which resulted from the four dosage regimens (2.5 mg, 5 mg, 7.5 mg, 10 mg/kg) of pyrantel pamoate.

For *A. lumbricoides*, a single dose of 2.5 mg/kg of pyrantel pamoate was found to be highly effective (ERR of 93% and NCR of 85%). The ERR and NCR of the higher doses reached 100% and 99% respectively after a dose of 10 mg/kg.

For *A. duodenale*, both ERR and NCR of all 4 dosage regimens were remarkably high, over 95%, except NCR of 79% with a dose of 5.0 mg/kg body weight.

Pyrantel pamoate was found to be less effective against *N. americanus* than against *A. duodenale*. The highest dose (10.0 mg/kg weight) in this series of trials yielded ERR of 87% and NCR of 84%. This indicates

Table 1

Efficacy of pyrantel pamaote against *A. lumbricoides*, *A. duodenale*, *N. americanus* and *T. trichiura*.

	Dosage (mg/kg)	No. cases evaluated	Average EPG before therapy	ERR (%)	NCR (%)
A. lumbricoides	2.5	162	38,400	93	85
	5.0	144	36,200	98	91
	7.5	156	34,700	99	97
	10.0	168	45,700	100	99
A. duodenale	2.5	162	3,200	98	79
	5.0	144	3,400	99	95
	7.5	156	3,000	99	96
	10.0	168	3,200	99	98
N. americanus	2.5	162	1,200	77	53
	5.0	144	1,200	81	68
	7.5	156	1,400	82	79
	10.0	168	1,300	87	84
T. trichiura	2.5	58	1,800	56	7
	5.0	59	1,600	40	7
	7.5	64	1,600	45	35
	10.0	126	1,800	56	41

ERR: Egg reduction rate.
NCR: Negative conversion rate.

substantial efficacy but less than that against *A. duodenale*.

Pyrantel pamoate showed some effect against *T. trichiura*. The average egg-count per gram faeces (EPG) of this nematode infection in our series was very light ranging from 1,600 to 1,800. The highest dose (10.0 mg/kg body weight) yielded only ERR of 56% and NCR of 41%. The lower the dose of pyrantel pamoate the lower ERR and NCR were observed. The NCR produced with a smaller dose (2.5 mg/kg or 5.0 mg/kg) of pyrantel pamoate was only 7%.

Pyrantel pamoate was extremely well tolerated. Presumptive side effects from a single dose (2.5-10.0 mg/kg) of pyrantel were abdominal discomfort, abdominal pain, diarrhoea, headache and vomiting. As shown in Table 2, these were very infrequent in all dosage regimens and were noted in only 8 of 630 children.

DISCUSSION

These studies have confirmed that pyrantel pamoate in a single dose of 10 mg/kg is very effective against *A. lumbricoides* and *A. duodenale*, effective but less so against *N. americanus*, and has moderate effect against light infection of *T. trichiura*.

When a reduced dose of 5.0 mg or 7.5 mg/kg was administered, therapeutic efficacy remained high against *A. lumbricoides* and *A. duodenale*. The effect on *N. americanus*

Table 2

Side effects in children with different doses of pyrantel pamoate.

Dosage (mg/kg)	No. cases evaluated	Per cent of symptoms				
		Abdominal discomfort	Abdominal pain	Diarrhoea	Headache	Vomiting
2.5	162	1	0	1	0	0
5.0	144	0	1	0	0	0
7.5	156	0	0	0	0	0
10.0	168	0	2	1	1	1

was less with a single dose. In treating *N. americanus* infection with pyrantel pamoate, Ishizaki *et al.* (1971) reported that 3 consecutive daily doses of pyrantel pamoate (10 mg/kg) produced NCR of 89% among 28 cases with *N. americanus*. Villarejos *et al.* (1971) also reported that a 3-day regimen of pyrantel pamoate (10 mg/kg) was much more efficacious for *N. americanus* than a single dose. From the result of our trials and these reports, more doses of pyrantel pamoate (10 mg/kg) should be recommended against *N. americanus*, especially when infections are heavy.

In periodic treatment of *Ascaris lumbricoides* infection alone, the dosage of pyrantel pamoate can be reduced to 2.5 mg/kg. The single small dose could produce ERR of 93% and NCR of 85% in our series of trials.

The advantages of pyrantel pamoate are its multiple activity with a single oral dose, tastelessness, and acceptability to children and adults, and the side effects due to this drug, if any, have been observed to be mild and transient.

SUMMARY

A single oral dose (10 mg/kg) of pyrantel pamoate, a new synthetic anthelmintic, was found to be highly effective against *Ascaris lumbricoides* and *Ancylostoma duodenale*, effective but less so against *Necator americanus*, and moderately effective against light infection with *Trichuris trichiura*. A smaller dose (5.0 mg or 7.5 mg/kg) was highly effective against *A. lumbricoides* and *A. duodenale*. In treating *A. lumbricoides* alone, even a dose of 2.5 mg/kg could produce egg reduction rate (ERR) of 93% and negative conversion rate (NCR) of 85%. Side effects from pyrantel pamoate were infrequent, mild and transient.

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REFERENCES

BARANSKI, M.C., CARNEIRO, FILHO, M., GUSSO, J.F. and TARRAN, A.F., (1971). Treatment of enterobiasis with pyrantel pamoate. Comparative study with pyrvinium pamoate. *Revta Inst. Med. Trop. S. Paulo, 13*: 422.

BELL, W.J. and NASSIF, S., (1971). Comparison of pyrantel pamoate and piperazine phosphate in the treatment of ascariasis. *Amer. J. Trop. Med. Hyg., 20*: 584.

BUMBALO, T.S., FUGAZZOTO, D.J. and WYCZALEK, J.V., (1969). Treatment of enterobiasis with pyrantel pamoate. *Amer. J. Trop. Med. Hyg., 18*: 50.

BURRIEL, L.M., FERNANDEZ-AGNADO, P., HERNANDEZ, O.G. and BACHILLER, L., (1969). Preliminary clinical trial with a new drug (Pyrantel) in the treatment of intestinal parasitism by *Oxyuris. Med. Klin.* (Spanish Edition), *96*: 63.

CERVONI, W.A. and OLIVER-GONZÁLEZ, J., (1971). Clinical evaluation of pyrantel pamoate in helminthiasis. *Amer. J. Trop. Med. Hyg., 205*: 89.

DESOWITZ, R.S., BELL, T., WILLIAMS, J., CARDINES, R. and TAMURA, M., (1970). Anthelmintic activity of pyrantel pamoate. *Amer. J. Trop. Med. Hyg., 19*: 775.

FORBES, L.S., (1972). Toxicological and pharmacological relations between levamisole, pyrantel and diethylcarbamazine and their significance in helminth chemotherapy. *Southeast Asian J. Trop. Med. Pub. Hlth., 3*: 235.

GOLDSMID, J.M. and SAUNDERS, C.R., (1972). Preliminary trial using pyrantel pamoate for the treatment of human infections with *Ternidens deminutus. Trans. Roy. Soc. Trop. Med. Hyg., 66*: 375.

HORI, E., (1971). Anthelmintic effect of pyrantel pamoate (combantrin) against enterobiasis. *Jap. J. Parasit., 20*: 142.

HSIEH, H.C., (1971). Combining MTFC and Stoll dilution egg counting for species analysis of hookworm in man. *Chinese J. Microbiol., 4*: 25.

HSIEH, H.C., (1972). Chemotherapy of intestinal nematode infections in man. *Proc. 10th SEAMEO TROPMED Seminar: Symposium on Chemotherapy in Tropical Medicine of Southeast Asia and the Far East*, Bangkok, 26-30 October 1971, P. 12-52.

HSIEH, H.C. and CHEN, E.R., (1970). Evaluation of anthelmintic activity of pyrantel pamoate (combantrin) against *Ascaris* and hookworm. *Chinese J. Microbiol., 3*: 126.

HSIEH, H.C. and CHEN, E.R., (1971). Treatment of *A. lumbricoides* with a small dose of pyrantel pamoate (combantrin). *Southeast Asian J. Trop. Med. Pub. Hlth., 2*: 362.

HSIEH, H.C., CHEN, E.R. and SHIH, C.C., (1971). Treatment of *Enterobius vermicularis* infections with pyrantel pamoate in Taiwan. *Chinese J. Microbiol., 4*: 247.

KOBAYASHI, A., KUMADA, M., KUTSUMI, H., ITO, Y., IMAI, K., ISHIZAKI, T., KATO, K. and KATO, K., (1970). Anthelmintic effect of pyrantel pamoate (combantrin) against ascariasis. *Jap. J. Parasit., 19*: 296.

PANDEY, K.N., SHARATCHANDRA, S.G., SARIN, G.S., AJMANI, N.K. and CHUTTANI, H.K., (1971). Pyrantel embonate in treatment of hookworm infestation. *Brit. Med. J., 4*: 399.

RIM, H.J. and LIM, J.K., (1972). Treatment of enterobiasis and ascariasis with combantrin (pyrantel pamoate). *Trans. Roy. Soc. Trop. Med. Hyg., 66*: 170.

STOLL, N.R., (1962). For hookworm diagnosis : is finding an egg enough? *Ann. N.Y. Acad. Sci., 98*: 712.

SUZUKI, N., ISHIZAKI, T., ENDO, T., KOBAYAKAWA, T., KANNO, T., HANEDA, M., KUDO, H. and HARA, T., (1971). The anthelmintic effect of pyrantel pamoate upon *Necator americanus. Jap. J. Parasit., 20*: 285.

VILLAREJOS, V.M., ARGUEDAS-GAMBOA, J.A., EDUARTE, E. and SWARTZWELDER, J.C., (1971). Experiences with the anthelmintic pyrantel pamoate. *Amer. J. Trop. Med. Hyg., 20*: 842.

YAMAMOTO, H., HAYASHI, S., MOTOYOSHI, K. and MORI, Y., (1971). Anthelmintic effect of pyrantel pamoate against

enterobiasis vermicularis. *Jap. J. Parasit.*, *20*: 359.

YOKOGAWA, M., ARAKI, K., KOJIMA, S., NIIMURA, M., OGAWA, K., KAGEI, N., KIHATA, M., TSUJI, M., SAITO, S. and IWANAGA, Y., (1970). Clinical evaluation of a new anthelmintic, pyrantel pamoate in hookworm infection. *Jap. J. Parasit.*, *19*: 301.

YOKOGAWA, M., KOJIMA, S., ARAKI, K., OGAWA, K., NIIMURA, M., KAGEI, N. and KIHATA, M., (1970). Mass-treatment for enterobiasis vermicularis with pyrantel pamoate. *Jap. J. Parasit.*, *19*: 593.