made, the more it will be influenced by organic binding. This means that a fall in the 20-minute uptake during treatment with carbimazole is due partly to impairment of organic binding, and this effect must be taken into account if conclusions on thyroid suppression are based on this measurement. Of interest in this context are some recent observations by Shimmins *et al.* (1971), who found that the 20-minute uptake of ^{131}I fell by about 20% as soon as treatment with carbimazole was started.

Attempts to predict the outcome of antithyroid drug treatment on the basis of thyroid suppressibility have met with limited success (Alexander *et al.*, 1970; Goolden *et al.*, 1971; Lowry *et al.*, 1971). Suppression is not necessarily indicative of long-term remission, and patients who fail to suppress do not always relapse when treatment is discontinued. Despite these limitations the examination of thyroid function during treatment may sometimes be helpful, and for this purpose $^{99}\text{Tc}^{\text{m}}$ uptake would seem to be the most appropriate method.

In our experience $^{99}\text{Tc}^{\text{m}}$ uptake measurements have proved very satisfactory for the routine assessment of thyroid function. In the absence of a direct comparison it cannot be said that they are any more efficient than early radioiodine uptake tests in differentiating between euthyroid and hyperthyroid individuals, but we think it unlikely that such a comparison would show any great difference. Points in favour of $^{99}\text{Tc}^{\text{m}}$ are that it gives a small radiation dose to the thyroid and that tests can be repeated at short time intervals. Furthermore, techniques for measuring the uptake of this radioisotope allow accurate correction for extrathyroidal activity, an essential requirement for any early thyroid uptake measurement. The reproducibility of the method described is such that suppression tests can be used when necessary even when thyroid uptake is within the normal

range. Finally, $^{99}\text{Tc}^{\text{m}}$ is particularly well suited for the assessment of thyroid function in patients being treated with an antithyroid drug.

This work was supported in part by a grant from the Medical Research Council.

References

- Alexander, W. D., Harden, R. McG., and Shimmins, J. (1966). *Lancet*, **2**, 1041.
 Alexander, W. D., Harden, R. McG., Shimmins, J., McLarty, D., and McGill, P. (1967). *Journal of Clinical Endocrinology*, **27**, 1682.
 Alexander, W. D., *et al.* (1970). *Journal of Clinical Endocrinology*, **30**, 540.
 Andros, G., Harper, P. V., Lathrop, K. A., and McCardle, R. J. (1965). *Journal of Clinical Endocrinology*, **25**, 1067.
 Atkins, H. L., and Richards, P. (1968). *Journal of Nuclear Medicine*, **9**, 7.
 Berson, S. A., and Yalow, R. S. (1955). *Journal of Clinical Investigation*, **34**, 186.
 de Garreta, A. C., Glass, H. I., and Goolden, A. W. G. (1968). *British Journal of Radiology*, **41**, 896.
 Goolden, A. W. G., Glass, H. I., and Silvester, D. J. (1968). *British Journal of Radiology*, **41**, 20.
 Goolden, A. W. G., Brown, M., and Williams, E. D. (1971). In *Further Advances in Thyroid Research*, ed. K. Fellinger and R. Höfer. Vienna, Wiener Medizinischen Akademie.
 Ibbertson, H. K., Hunton, R. B., White, B. McL., and Gluckman, P. D. (1971). In *Further Advances in Thyroid Research*, ed. K. Fellinger and R. Höfer. Vienna, Wiener Medizinischen Akademie.
 Koutras, D. A., and Sfontouris, J. (1966). *Journal of Endocrinology*, **35**, 135.
 Lowry, R. C., Lowe, D., Hadden, D. R., Montgomery, D. A. D., and Weaver, J. A. (1971). *British Medical Journal*, **2**, 19.
 Shimmins, J., Hilditch, T., Harden, R. McG., and Alexander, W. D. (1968). *Journal of Clinical Endocrinology*, **28**, 575.
 Shimmins, J., Alexander, W. D., McLarty, D. G., Robertson, J. W. K., and Sloane, D. J. P. (1971). *Journal of Nuclear Medicine*, **12**, 51.
 Thomas, I. D., Oddie, T. H., and Myhill, J. (1960). *Journal of Clinical Endocrinology*, **20**, 1601.
 Williams, E. D., Glass, H. I., Goolden, A. W. G., and Satyavanich, S. (1971). *Journal of Nuclear Medicine*. In Press.

Pyrantel Embonate in Treatment of Hookworm Infestation

K. N. PANDEY, S. G. SHARATHCHANDRA, G. S. SARIN, N. K. AJMANI, H. K. CHUTTANI

British Medical Journal, 1971, **4**, 399-400

Summary

The efficacy of pyrantel embonate (1,4,5,6-tetrahydro-1-methyl-2-(*trans*-2-(2-thienyl)-vinyl)-pyrimidine embonic acid salt; Combantrin) was evaluated in 60 cases of hookworm infestation. They were divided into six groups of 10 cases. Pyrantel embonate was administered orally, in dosage schedules (randomized) of 100, 75, 50, 20, 15, and 10 mg/kg of body weight. The stool examination for hookworm ova and coproculture were positive in each case. The predominant species was *Ancylostoma duodenale* (in 58 patients). After treatment with pyrantel embonate the stool examination for hookworm ova and coproculture were negative on the 10th and 15th days in each group. The blood levels of the drug were significantly higher in patients receiving 100 and 75 mg/kg body weight. In groups A and B one patient experienced nausea and vomiting on the day of administration of drug. There were no abnormal changes in liver function

tests or blood urea levels in any of the groups. Hence the optimum single dose of the drug effective against hookworm infestation is 10 mg/kg body weight, and further studies are required to evaluate the minimum effective dose of pyrantel embonate.

Introduction

Pyrantel embonate (Pamoate, Combantrin) is a 1,4,5,6-tetrahydro-1-methyl-2-(*trans*-2-(2-thienyl)-vinyl)-pyrimidine embonic acid salt. It is a yellow crystalline solid, with a molecular weight of 594.7. It has the molecular formula $\text{C}_{24}\text{H}_{30}\text{O}_6\text{N}_2$ and the structural formula shown in the Diagram. It has been shown

to be very effective against pinworm, roundworm, and hookworm of animals (Austin *et al.*, 1966; Cornwell and Hones, 1968; Howes and Lynch, 1967). The present study was under-

Maulana Azad Medical College, New Delhi 1, India
 K. N. PANDEY, M.B., B.S., Senior Resident in Medicine
 S. G. SHARATHCHANDRA, M.D., Registrar in Medicine
 G. S. SARIN, B.Sc., Assistant Research Officer
 N. K. AJMANI, M.D., Lecturer in Medicine
 H. K. CHUTTANI, M.D., Professor of Medicine

taken to determine its efficacy in eradicating the hookworm infestation, and to evaluate its optimum dosage and safety in human beings.

Patients and Methods

The study was carried out in the departments of gastroenterology and medicine of Maulana Azad Medical College, New Delhi, from early 1969 to early 1970. Sixty patients (45 males and 15 females) with a positive stool for hookworm ova were submitted to this study. Their ages ranged from 16 to 70 years and their mean body weight was 42.67 ± 7.17 kg, with a range of 25 to 55 kg. Detailed clinical features were recorded.

Routine haematological studies and liver function tests—namely, serum bilirubin, alkaline phosphatase, serum aspartate aminotransferase, serum alanine aminotransferase, and blood urea estimation—were undertaken before treatment and on the third and tenth days after treatment, standard methods being used (Varley, 1967).

Twenty-four-hour sample of stool was examined for faecal egg load by the Stoll and Hausheer (1926) technique on three consecutive days before therapy and on the 10th, 11th, 12th, 18th, 19th, and 20th days after administration of the drug. No patients with an ova count below 3,000/g of faeces was included in this trial. The 24-hour sample of stool was sieved for identification of adult worms on the 1st, 2nd, and 3rd days of treatment. Coproculture was performed according to the method of Belding (1965) before treatment and on the 10th, 15th, and 20th days after treatment.

Dosage Schedule.—Six dosage schedules were used: group A, 100 mg/kg body weight, group B, 75 mg/kg, group C, 50 mg/kg, group D, 20 mg/kg, group E, 15 mg/kg, and group F, 10 mg/kg. The drug was supplied in tablet form of 50-, 125-, and 250-mg strength. It was administered orally in a single dose, on an empty stomach, and food was withheld for two hours. The allocation was randomized on the basis of a preplanned schedule. There were 10 patients in each group. The blood level of pyrantel embonate was estimated at 4 and 12 hours after administration of the drug. Patients were kept in the ward for over 20 days and a careful daily record of any symptoms developing during this period was noted. The blood level of pyrantel embonate was estimated colorimetrically (method provided by the Research Laboratories of Pfizer Limited).

Observations and Comments

The results of therapy are summarized in Table I. The coproculture was positive in all cases before treatment, and identification of species showed *Ancylostoma duodenale* in 57 patients and *Necator americanus* in two. Species identification after deworming by examination of adult worms in stool gave similar results, and there was a direct correlation between hookworm ova count and worms expelled. The stool was free from ova on the 10th, 12th, 15th, 18th, 19th, and 20th days. The coproculture was negative on the 10th, 15th, and 20th days in all six groups (Table I). Hookworm ova were not found by the concentration method between the 10th and 20th posttreatment days. Hence complete eradication (100%) of hookworm ova was achieved in each group.

There was no evidence of hepatocellular or renal toxicity as indicated by serum bilirubin, alkaline phosphatase, transaminase

TABLE I—Summary of Results of Drug Therapy in Different Groups

Group	Mean Dosage (mg)	Pretreatment Hookworm Ova Load (Mean of 3 days) (eggs per g of faeces)	Copro-culture before Treatment	Posttreatment Hookworm Ova Count on Day 10, 11, 12, 18, 19 and 20	Copro-culture after Treatment on Day 10, 15, and 20
A	4,180 $\pm$ 666.0	6,166 $\pm$ 2,831	Positive	Nil	Negative
B	3,345 $\pm$ 428.4	4,389 $\pm$ 1,584	Positive	Nil	Negative
C	2,005 $\pm$ 439.5	4,436 $\pm$ 1,843	Positive	Nil	Negative
D	780 $\pm$ 152.9	5,119 $\pm$ 1,547	Positive	Nil	Negative
E	660 $\pm$ 105.2	4,859 $\pm$ 1,375	Positive	Nil	Negative
F	430 $\pm$ 55.7	5,726 $\pm$ 3,391	Positive	Nil	Negative

levels, and blood urea on the 3rd and 10th post-treatment days in any group. The differences in blood drug levels at 4 and 12 hours after administration of the drug were not significant in groups C, D, E, and F (Table II). In groups A and B the 12-hour blood level was significantly higher than at four hours (Table II). This shows a higher rate of absorption of the drug at 100- and 75-mg/kg dosage. Though these dosage schedules seemed very effective, side effects like nausea and vomiting were noted in one patient each in groups A and B. Otherwise the drug was well tolerated.

TABLE II—Blood Levels of Pyrantel Embonate (P.E.) in Different Dosage Groups

Group	No. of Cases	Blood Level of P.E. (μ g/ml)		Mean Diff.	t	D.F.	P
		At 4 Hours	At 12 Hours				
A	7	2.01 $\pm$ 1.23	2.47 $\pm$ 1.33	+0.46	2.72	6	<0.05
B	6	1.87 $\pm$ 1.25	2.33 $\pm$ 1.47	+0.46	4.70	5	<0.01
C	7	1.47 $\pm$ 1.07	1.34 $\pm$ 0.82	-0.13	1.07	6	>0.05
D	10	0.80 $\pm$ 0.26	0.86 $\pm$ 0.40	+0.06	0.62	9	>0.05
E	10	0.81 $\pm$ 0.44	0.78 $\pm$ 0.50	-0.03	0.43	9	>0.05
F	10	0.75 $\pm$ 0.28	0.61 $\pm$ 0.41	-0.04	0.49	9	>0.05

In this trial the drug was found to be effective in the eradication of hookworm infection even at the lowest dosage schedule of 10 mg/kg. It is necessary to extend further trials of the drug at still lower dosage to find out the minimum effective dose against hookworm.

We are grateful to Dr. S. Padmavati, Director-Principal, Maulana Azad Medical College, New Delhi, for permission to publish this work. We are thankful to Dr. R. D. Mann, Medical Director of Pfizer Ltd., New York, and Dr. V. V. Apte, Medical Director of Pfizer Ltd., India, for providing the drug and a liberal grant for this study. We are also thankful to Mr. D. S. Ahluwalia, Deputy Director, Indian Standards Institution, New Delhi, for statistical analysis of the data.

Requests for reprints should be sent to Professor H. K. Chuttani.

References

- Austin, W. C., et al. (1966). *Nature*, 212, 1273.
- Belding, D. L. (1965). *Text Book of Parasitology*, 3rd edn. New York, Appleton-Century-Crofts.
- Cornwell, R. L., and Hones, R. M. (1968). *Journal of Tropical Medicine and Hygiene*, 71, 165.
- Howes, H. L., and Lynch, J. E. (1967). *Journal of Parasitology*, 53, 1085.
- Stoll, N. R., and Hausheer, W. C. (1926). *American Journal of Hygiene*, 6, Suppl. p. 134.
- Varley, H. (1967). *Practical Clinical Biochemistry*, 4th edn. New York, Heinemann-Medical Books and Interscience Books.