

Preliminary Report

AMBILHAR, A NITROTHIAZOLE DERIVATIVE, IN URINARY TRACT BILHARZIA

S. J. POWELL, M.D., F.R.C.P. (EDIN.) AND I. N. MACLEOD, M.D., F.C.P. (S.A.), M.R.C.P., *Amoebiasis Research Unit and Department of Medicine, University of Natal, Durban*

Despite wide usage, reports of the efficacy of antimony preparations and of the thioxanthenes in bilharzia vary in different regions. The consensus of opinion is, however, that neither group of drugs provides entirely satisfactory therapy. Recently the nitrothiazole derivative, Ambilhar—5-(nitrothiazolyl-[2]-2-oxo-tetrahydro-imidazole)—has been introduced with encouraging preliminary results.¹ Clarke and Blair² have found it to be effective in Southern Rhodesia and we now report our findings in an outpatient trial in Durban.

MATERIAL AND METHODS

One hundred and fifty African and Indian outpatients attending King Edward VIII Hospital, Durban, with urinary tract bilharzia, were studied. All complained of haematuria for periods varying from a few days to several years. Their ages ranged from 5 to 28 years, although the majority were in their second decade. Urine specimens were obtained between 11 a.m. and 1 p.m. and viable ova of *Schistosoma haematobium* were identified before commencing treatment. Quantitative determinations of egg output were done according to the method of Bell³ adapted for *S. haematobium*.

All patients were given Ambilhar orally in the dosage of 25 mg./kg. daily in divided doses for 7 days and were instructed to reattend 1 and 2 months after completing treatment.

RESULTS

Cure was assessed as the absence of ova or the presence of scanty non-viable ova only. Complete follow-up at 2 months could not be obtained as only 90 of the original 150 patients could be traced. At 1 month follow-up 147 patients and at 2 months 87 of the 90 patients, appeared cured. In all instances the patients stated that their haematuria had ceased or was markedly reduced.

Forty-six percent of the patients were found to be excreting moderate to heavy loads of ova on initial examination according to Jordan's criteria,⁴ but response to treatment was unrelated to the load of eggs being excreted.

Apart from 2 patients who complained of abdominal pain and headache, no intolerance or toxicity was encountered.

DISCUSSION

Although to ensure permanent cure of bilharzia it is desirable to observe patients for 3 months following treatment, this is rarely possible among Indian and African outpatients. The follow-up attendance of 60% at 2 months in the present trial is relatively high in our experience. Our past attempts to assess the efficacy of antimony preparations and of the thioxanthenes have failed owing to reluctance to reattend hospital because of toxicity, poor tolerance or failure to relieve symptoms. By contrast, Ambilhar produced rapid symptomatic relief and was

both easily administered and well tolerated. There were only two minor instances of intolerance and none of significant toxicity. The extremely high cure rate of 97% at 2 months which we report is similar to that found in preliminary trials elsewhere¹ and by Clarke and Blair,² and the results were as satisfactory in patients excreting heavy loads of eggs as in those with minimal infections.

Ambilhar goes far to meet the need for an effective, cheap, oral, outpatient remedy for urinary tract bilharzia. However, caution regarding possible toxicity is still indicated. When a 10-day course of the drug was used in adult hospital patients with invasive amoebiasis, minor electrocardiographic changes were frequent, and, in some instances, confusional mental states, necessitating prompt cessation of treatment, were of concern.⁵ Although we have not encountered other evidence of significant cardiotoxicity with Ambilhar alone, when it was given in combination with dehydroemetine, the electrocardiographic changes were markedly accentuated.⁵ Since antimony preparations are well known to produce similar alterations in the electrocardiograms, we do not consider that they should be given simultaneously with Ambilhar and, until further experience has been gained, it is advisable to allow some weeks to elapse before administering Ambilhar to patients who have received antimony compounds. In Natal bilharzia is predominantly a disease of African and Indian children and it is probable that among them, provided care is taken and the correct dosage is adhered to, side-effects will not be a major problem. Nevertheless, Ambilhar is a potent drug and wide usage may result in some instances of toxicity similar to that encountered in amoebiasis, so that plans for indiscriminate and unsupervised mass treatment should only be approached with caution.

SUMMARY

The results of a trial of Ambilhar in 150 African and Indian outpatients with urinary tract bilharzia are reported. All but 3 patients appeared cured 1 month after completing treatment and cure was maintained in all who could be traced at 2 months. Tolerance was good and no toxicity was encountered. Ambilhar is a most effective outpatient remedy, but some caution regarding toxicity is still advisable.

We wish to thank the Director of Medical Services, Natal Provincial Administration, Pietermaritzburg, and Dr. H. Wannenburg, Medical Superintendent, King Edward VIII Hospital, Durban, for facilities; and Mr. M. Mason for technical assistance. The Amoebiasis Research Unit is sponsored by the Council for Scientific and Industrial Research, the Natal Provincial Administration, the University of Natal and the US Public Health Service Grant AI-01592.

REFERENCES

1. Symposium: Thérapeutique Nouvelle de la Bilharziase et de l'Amoebiasis (1966): Acta trop. (Basel), suppl. 9.
2. Clarke, V. de V. and Blair, D. M. (1966): Cent. Afr. J. Med., 12, 64.
3. Bell, D. R. (1963): Bull. Wild Hlth Org., 29, 525.
4. Jordan, P. (1965): *Ibid.*, 33, 553.
5. Powell, S. J., MacLeod, I. N., Wilmot, A. J. and Elsdon-Dew, R. (1966): Lancet, 2, 20.