Tinidazole in treatment of acute amoebic dysentery in children

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Scragg, J. N., Rubidge, C. J., and Proctor, E. M. (1976). Archives of Disease in Childhood, 51, 385. Tinidazole in treatment of acute amoebic dysentery in children. The excellent results obtained in this trial indicate that tinidazole is a drug worthy of extensive evaluation in the treatment of amoebiasis, as three single daily doses is a simple form of treatment. The drug was well tolerated and free from any toxic effects.

A combination of emetine hydrochloride or dehydroemetine with tetracycline and a 'luminal' amoebicide such as diloxanide furoate was for several years regarded as the treatment of choice for severe cases of amoebic dysentery in adults (Wilmot, 1966; Powell, 1967, 1969a, b). In African children, who are frequently malnourished and suffering from additional diseases, amoebic dysentery is a serious condition. The onset is often acute and should complications occur the prognosis is worse than in adults (Scragg, 1960; Wilmot, 1962; Scragg and Powell, 1966, 1970). Thus in the past it was our practice to use the combined regimen in all children with amoebic dysentery. The introduction of metronidazole was one of the most significant advances in the treatment of amoebiasis in recent years (World Health Organization, 1969). It has been shown (Powell, Wilmot, and Elsdon-Dew, 1967; Powell, 1972) to be outstandingly effective in the treatment of invasive amoebiasis and, since it combines both intestinal and systemic activity, it has until now been regarded as the single drug of choice in this disease. Our studies have shown that metronidazole alone, given orally in divided daily doses for 5–7 days, is as effective as the previously favoured combined regimen of amoebicides in children with amoebic dysentery (Rubidge, Scragg, and Powell, 1970; Powell, Rubidge, and Elsdon-Dew, 1973). We have further established (Scragg and Powell, 1973) that metronidazole in a dose of 50 mg/kg in divided daily doses for 5 days in the absence of any other drug therapy is effective in curing the majority of children with the complication of amoebic liver abscess. It is a safe and simple form of treatment.

Since these studies there is evidence (Welling and Monroe, 1972; Taylor, Migliardi, and Schach von Wittenau, 1970; Howes, Lynch, and Kvlin, 1970) that tinidazole, the most recent derivative of the nitroimidazole group of compounds, at a lower dose achieves significantly higher peak serum concentrations than metronidazole, and that serum levels of tinidazole immediately before a subsequent dose are approximately threefold higher than those of metronidazole. Thus tinidazole appears to be particularly well suited for the treatment of systemic amoebiasis. The drug has been shown to be very effective in amoebiasis in adults, and in the absence of a luminal amoebicide tinidazole, as a single drug, has given excellent results in the treatment of amoebic dysentery and amoebic liver abscess (Powell, 1975; Zuberi and Ibrahim, 1973; Misra and Laiq, 1974; Lewis, Cook, and Adeleye, 1974; Nava, Metlich, and Marti, 1974; de Esesarte, 1974; Prakash, Bansal, and Bansal, 1974; Gaber et al., 1975). The drug has been well tolerated and free from toxic effects. On the basis of this information the present trial was designed to determine the efficacy of tinidazole in treatment of children in Durban with acute amoebic dysentery.

Material and methods
Thirty African children, aged 7 months to 11 years (mean age 3 years), were treated in hospital. All had
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acute amoebic dysentery with haematophagous Ent. histolytica in their stools. All were kept in hospital for a minimum of 28 days after starting treatment. Repeated stools were examined by direct smear and zinc sulphate flotation after completion of therapy. Before the start of therapy full blood counts, liver function tests, blood ureas, and urine examinations were done in all and were repeated on days 7, 14, 21, and 28. Based on the adult dose of 2 g tinidazole daily, the dose was adjusted according to the percentage method of Catzel (1974) and was given in a single dose in the morning for 3 consecutive days. However, the body weight of all were recorded and on a weight basis the mean dose was 63 mg/kg per day. Final assessment was made at 28 days. However, only 3 cases remained under observation for as short a period as this. In the remainder stools were examined over periods extending up to many months (Table I).

| TABLE I |
| Stool follow-up after treatment |
| --- | --- | --- |
| Case no. | No. of stools examined | Period of follow-up (d) |
| 1 | 9 | 115 |
| 2 | 5 | 34 |
| 3 | 20 | 414 |
| 4 | 6 | 28 |
| 5 | 15 | 250 |
| 6 | 6 | 35 |
| 7 | 7 | 53 |
| 8 | 7 | 82 |
| 9* | 4 | 28 |
| 10 | 5 | 63 |
| 11 | 6 | 34 |
| 12* | 5 | 35 |
| 13 | 4 | 31 |
| 14 | 5 | 49 |
| 15 | 4 | 28 |
| 16 | 8 | 64 |
| 17 | 6 | 36 |
| 18 | 5 | 36 |
| 19 | 5 | 31 |
| 20 | 5 | 123 |
| 21 | 4 | 39 |
| 22 | 4 | 38 |
| 23 | 6 | 34 |
| 24 | 7 | 33 |
| 25 | 14 | 72 |
| 26 | 11 | 65 |
| 27 | 8 | 32 |
| 28 | 7 | 32 |
| 29 | 9 | 64 |
| 30 | 13 | 112 |

*Parasitic failure.

Results (Table II)

The results were classified into the following categories. Cure: symptom-free and Ent. histolytica absent. Parasitic failure: persistence or recurrence of either trophozoites or cysts of Ent. histolytica after completion of therapy. Cure was obtained in all but 2 cases. These 2 rapidly became symptom free but began to pass cysts of Ent. histolytica during follow-up in hospital. One of them subsequently relapsed after 35 days. Tolerance was excellent. Full blood counts did not show any adverse effects on the bone marrow. No toxic effects were shown from the liver function tests, blood urea, and urine.

| TABLE II |
| Results of treatment |
| --- | --- | --- |
| No. of patients | No. of cures | Parasitic failure |
| 30 | 28 (93%) | 2 |

Discussion

Our results establish that for the treatment of amoebic dysentery in children tinidazole in a single daily dose (adjusted according to the percentage method) for 3 days is as efficient (cure 93%) as metronidazole, where the cure rate was 85% in children with amoebic dysentery using a divided dose based on weight for 5-7 days (Rubidge et al., 1970; Watson, Leary, and Hartley, 1970). In adults with amoebic dysentery (Powell, Wilmot, and Elsdon-Dew 1969) and Powell (1972), using a single daily dose of metronidazole for 2-3 days, reported cure in 90-95%. We have not undertaken a trial of single daily doses of metronidazole in children with amoebic dysentery or amoebic liver abscess. However, in view of the results in adults it is likely that the same favourable result would be obtained. Such a trial is now underway.

As the exact ages of our African children are often in doubt and as many are much below the normal weight for age, it is preferable to recommend a dosage based on weight rather than age. It seems reasonable therefore to undertake further trials with tinidazole in order to establish the optimum dose based on actual body weight.

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