

# Single-Dose Tinidazole for the Treatment of Giardiasis

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Sixty-three expatriate residents and travellers in Bangladesh, infected with *Giardia lamblia*, participated in two studies to compare the therapeutic efficacy of tinidazole and metronidazole. In the first trial 33 randomly selected patients were treated with tinidazole (50 mg/kg of body weight to a maximum of 2 g) or metronidazole (60 mg/kg of body weight to a maximum of 2.4 g) in a single oral dose. Patients were followed for 4 weeks after the end of therapy for the presence of *G. lamblia* in their stools. Sixteen (94%) of 17 patients receiving tinidazole were free of *G. lamblia* during that period, compared to only 9 (56%) of 16 patients who had received metronidazole ( $P < 0.02$ ). In the second trial patients were randomly allocated to a treatment schedule of either metronidazole as a single dose on 3 successive days (50 mg/kg of body weight to a maximum of 2 g daily) or tinidazole as a single oral dose (50 mg/kg of body weight to a maximum of 2 g). All 15 patients treated with tinidazole and 14 (93%) of 15 patients treated with metronidazole were free of *G. lamblia* during the 4-week follow-up period. A single oral dose of tinidazole is a highly effective treatment for giardiasis and is equal in efficacy to a 3-day therapy with metronidazole.

*Giardia lamblia*, a protozoan parasite with worldwide distribution, is hyperendemic in Bangladesh (9, 10). The spectrum of *Giardia* sp. disease ranges from asymptomatic infection and mild diarrhea to chronic diarrhea with malabsorption (2, 5, 7). Currently recommended regimens for therapy of giardiasis include quinacrine hydrochloride or metronidazole for a duration of 5 to 10 days (3, 6, 15, 17, 22). In developing countries drug regimens of this duration are problematic, as medicines are frequently purchased in quantities which represent less than a single day's dose and effective therapies of short duration are preferable (8). In an attempt to evaluate the efficacy of a shorter duration of therapy in giardiasis we conducted two studies: single-dose tinidazole versus single-dose metronidazole and single-dose tinidazole versus a 3-day course of metronidazole.

## MATERIALS AND METHODS

**Patient selection and therapy.** (i) **First trial: single-dose tinidazole versus single-dose metronidazole.** The 33 patients in the first trial were expatriate residents in Bangladesh, who were enrolled in an ongoing prospective study of enteric protozoal infections. Expatriates enrolled in this study had stool examinations at once every three months and at the time of a diarrheal illness. From March 1981 until September 1982 patients who had giardia cysts or trophozoites or both on stool microscopic examination were eligible for entry into the treatment study. Both symptomatic and asymptomatic patients were enrolled. Duration of symptoms was less than 1 week in all patients. Treatment was randomized between single-dose metronidazole (60 mg/kg of body weight to a maximum dose of 2.4 g) or single-dose tinidazole (50 mg/kg of body weights to a maximum dose of 2 g). Randomization was done for each patient by drawing a slip labeled either "M" or "T" from an envelope, initially filled with 20 M's and 20 T's.

(ii) **Second trial: single-dose tinidazole versus a 3-day course of metronidazole.** Patients participating in the second trial

were selected from both symptomatic and asymptomatic travellers and expatriates bringing in fecal specimens for microscopic examination and culture. Two patients had complaints originating more than 3 weeks previously. In this trial tinidazole was again given as a single dose of 50 mg/kg of body weight to a maximum dose of 2 g, and metronidazole was given as a single daily dose of 50 mg/kg of body weight to a maximum dose of 2 g for 3 consecutive days. Randomization of patients was performed in the same way as in the first trial.

**Evaluation of efficacy and side effects.** Patients were followed for 4 weeks after the end of therapy. During this period patients were requested to bring in two fresh stool specimens weekly for microscopic examination. Only those patients who brought at least one specimen weekly were included in the data analysis. Fecal specimens were examined by a technician unaware of the treatment regimen. Stools were initially examined at  $\times 400$ , using a wet preparation. If no *Giardia* sp. cysts or trophozoites were found, stools were reexamined by using a formal-ether concentration technique (1). Patients were considered a treatment failure when one or more of the fecal specimens brought to the laboratory 1 to 4 weeks after the end of therapy were positive for either cysts or trophozoites of *G. lamblia*. In the second trial patients were asked to fill out a questionnaire daily for 7 days after the initiation of therapy. The questionnaire included questions about nausea, vomiting, headache, dizziness, metallic taste, diarrhea, constipation, fever, skin rash, loss of appetite, abdominal pain, and excessive gas formation.

## RESULTS

**First trial: single-dose tinidazole versus single-dose metronidazole.** Thirty-five patients were initially entered into this trial, 18 in the tinidazole group and 17 in the metronidazole group. Two patients, one in each group, were ultimately excluded from analysis because they did not bring in the required number of stool samples. The age distribution, sex, and clinical status of the 33 patients who comprised the final study population are shown in Table 1. Age distribution,

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TABLE 1. Clinical features and therapeutic results of patients in the first trial, comparing single-dose treatments of tinidazole and metronidazole

Drug treatment	Dosage		No. of patients			Age distribution (yr)						No. (%) of patients:			
	Adults (g)	Children (mg/kg of body wt)	Total	Male	Female	0-4	5-9	10-19	20-29	30-39	40	Symptomatic	Asymptomatic	Success	Failure
Tinidazole	2.0	50	17	10	7	7 <sup>a</sup>	2	0	3	4	1	9	8	16 (94) <sup>b</sup>	1 (6)
Metronidazole	2.4	60	16	10	6	6	6	0	3	1	0	8	8	9 (56) <sup>b</sup>	7 (44)

<sup>a</sup> Number of patients.<sup>b</sup>  $P < 0.02$  by Fisher's exact test.

sex, and clinical status (symptomatic versus asymptomatic) were similar for both treatment groups. Seven (44%) of the 16 patients treated with metronidazole were treatment failures compared with 1 (6%) of the 17 patients treated with tinidazole ( $P < 0.01$ ; Fisher's exact test). In this patient who remained symptomatic, parasites initially disappeared from the stool but were present again 2 weeks after start of therapy. Of the seven patients who were treatment failures on metronidazole, one patient had persistently positive stool examinations, two relapsed 2 weeks after treatment, three relapsed after 3 weeks, and one relapsed after 4 weeks. Three symptomatic patients who failed metronidazole treatment reported recurrence of symptoms. Symptoms subsided in all symptomatic patients who were parasitologically cured.

**Second trial: single-dose tinidazole versus 3-day course of metronidazole.** Thirty-five patients were enrolled in the second trial, 18 in the tinidazole group and 17 in the metronidazole group. Five subjects did not bring in the required number of samples and were excluded. Age distribution, sex, and clinical status for the two groups are shown in Table 2. There were no significant differences for these characteristics between the two groups. One patient in the metronidazole group relapsed 2 weeks after the start of treatment, but had no recurrence of symptoms. None of the tinidazole patients failed treatment. All symptomatic patients, including two persons with complaints of more than 3 weeks in duration, responded well in the first week after start of treatment.

**Side effects.** Thirteen of 15 patients in the tinidazole group and 14 of 15 patients in the metronidazole group returned the side effects questionnaire. No serious side effects were encountered in either group. Eight children were treated with tinidazole syrup. The mothers of five of these children reported problems with administration of the syrup due to a highly unpleasant taste, whereas similar problems were not reported by the mothers of the six children treated with metronidazole syrup ( $P < 0.03$ ; Fisher's exact test). Although patients in the metronidazole-treated group more

frequently complained of a metallic taste, nausea, and dizziness, these differences were not statistically significant (Table 3).

## DISCUSSION

For many years either metronidazole or quinacrine hydrochloride for 5 to 10 days has been recommended as the treatment of choice for giardiasis (3, 6, 15, 17, 22). The long duration of treatment and the side effects of metronidazole (metallic taste, anorexia, headache, nausea, vomiting) and of quinacrine (dizziness, headache, vomiting, toxic psychosis, yellow staining of skin and sclera, exfoliative dermatitis) have been important disadvantages to their use (3, 14, 21). With the appearance of newer imidazole derivatives, which are effective when given as a single dose and are associated with fewer side effects, the routine use of metronidazole and quinacrine has been challenged. Several authors have recommended tinidazole as the drug of choice for treatment of giardiasis (11, 13, 20).

In our study we have shown that tinidazole, given as a single oral dose, is more effective than metronidazole as a treatment for giardiasis. We have also demonstrated that a single dose of tinidazole is as effective as a 3-day course of metronidazole. The high failure rate of single-dose metronidazole was previously demonstrated by Jokipii and Jokipii, who reported that 13 of 26 patients relapsed 1 to 8 weeks after the therapy (12). Metronidazole (2 g for adults), as a single daily dose on 3 successive days, has been tested earlier by Wright et al., who observed a cure rate of 91%, similar to our cure rate of 93% (23). Tinidazole as a single oral dose was highly effective in adults and children in both treatment trials, with cure rates of 94 and 100%, respectively. These data confirm those of previous investigations (4, 11, 16).

Side effects were reported by both treatment groups. Complaints of a metallic taste, nausea, and dizziness were more common in the metronidazole-treated group, but these

TABLE 2. Clinical features and therapeutic results of patients in the second trial, comparing single-dose tinidazole and 3-day-course metronidazole

Drug treatment	Dosage		No. of patients			Age distribution (yr)						No. (%) of patients:			
	Adults (g)	Children (mg/kg of body wt)	Total	Male	Female	0-4	5-9	10-19	20-29	30-39	≥40	Symptomatic	Asymptomatic	Success	Failure
Tinidazole	2.0	50	15	10	5	6 <sup>a</sup>	4	0	2	3	0	10	5	15 (100)	0 (0)
Metronidazole	2.0	50	15	9	6	4	2	1	3	3	2	11	4	14 (93)	1 (7)

<sup>a</sup> Number of patients.

TABLE 3. Side effects reported by patients participating in a trial, comparing single-dose tinidazole and a 3-day course of metronidazole for treatment of giardiasis

Side effect	No. of patients	
	Tinidazole group (n = 13)	Metronidazole group (n = 14)
Metallic taste	0	4
Nausea	1	3
Vomiting	1	1
Headache	1	2
Dizziness	1	3
Anorexia	2	1
None	5	8
Problems with administration of syrup	5 <sup>a,b</sup>	0 <sup>b,c</sup>

<sup>a</sup> n = 8.

<sup>b</sup> P < 0.05 (Fisher's exact test).

<sup>c</sup> n = 6.

differences were not statistically significant. Problems with the administration of the syrup to children, because of an unpleasant taste, were only reported in the tinidazole group ( $P < 0.05$ ). The current syrup preparation therefore precludes therapy of infants and children, the most commonly affected group.

Tinidazole as a single oral dose is highly effective and has no substantial side effects. It may, therefore, be regarded as the drug of choice for adults with giardiasis. Because of problems with acceptability in infants and children, treatment with a 3-day course of metronidazole syrup is the preferred option in this age group.

The conclusions of this study, carried out among expatriate residents and travellers in Bangladesh, can only apply to this group at present. A study in Bangladeshi patients with different nutritional and infectious status, which could influence the therapeutic outcome, should be considered.

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