

# LOW DOSE TINIDAZOLE IN THE TREATMENT OF AMOEBIC LIVER ABSCESS

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## INTRODUCTION

Amoebic liver abscess is a severe and potentially life-threatening disease in many tropical countries. Therapeutic efficacy of metronidazole in the treatment of liver abscess is well known (Powell *et al.*, 1969; Aswapokee *et al.* 1974; Bunnag *et al.*, 1975). New drugs such as tinidazole and ornidazole have been tried in amoebiasis. In Bangladesh, Quaderi *et al.*, (1978) used tinidazole and obtained a cure rate of 100% in 35 patients with amoebic liver abscess while in Thailand, Lasserre *et al.*, (1982) achieved a cure rate of 94.3%. In Southeast Asia, constraints in health budgets have been strong incentives to develop low cost drug regimens. A clinical trial was thus carried out to evaluate the efficacy of low dose tinidazole in the treatment of amoebic liver abscess.

## MATERIALS AND METHODS

Thirty-six patients with uncomplicated amoebic liver abscess admitted to the Bangkok Hospital for Tropical Diseases, Bangkok from 1973 to 1984 were selected for the study (Table 1). There were 31 males and 5 females with age ranging from 19 to 67 years. Their weights ranged from 40 kg to 83.5 kg. The diagnosis of amoebic liver abscess was based on enlarged tender liver, fever, leucocytosis with slight impairment of liver function tests and radiological evidence of raised right dome of the diaphragm. A serologic test for *Entamoeba histolytica* by counter current immuno-

electrophoresis was performed in every case. 22 patients had cold area on liver scanning or abscess by sonogram. All patients had characteristic sterile pus with or without *Entamoeba histolytica* trophozoites in the pus. The clinical features and laboratory findings of the patients are summarized in Table 2 and Table 3.

Table 1

Age-sex distribution of patients with amoebic liver abscess.

No. of patients	36
males	31
females	5
Age (yrs)	
average	42.3
range	19-67
Weight (kg)	
average	51.3
range	40-83.5

Table 2

Clinical features of patients with amoebic liver abscess.

Clinical	No. of patients (%)
Hepatomegaly	36 (100)
Fever	31 (86)
Pain and tenderness	27 (75)
Rt. Hypochondrium	22 (81.5)
Epigastric	5 (18.5)

Table 3

Laboratory findings in 36 patients.	
Laboratory findings	No. of patients (%)
Leucocytosis	32 (88.9)
<i>E. hist.</i> trophozoite in stool + ve	8 (22.2)
<i>E. hist.</i> trophozoite in pus + ve	15 (41.7)
Immunodiagnosis by IEP	
IEP + ve	29 (80.6)
IEP - ve	7 (19.4)
Liver Scanning/Sonogram	
Positive	22 (61.1)
Negative	1 (2.7)
Not done	13 (36.1)

All patients were carefully examined by the attending physician. Daily observation and records were done. Various biochemical investigations were done weekly including estimations of the liver function tests, serum glutamic oxaloacetic and pyruvic transaminases, blood urea, serum creatinine. Patients had an electrocardiogram and X-ray examination of the chest including a postero-anterior view and a lateral view. To enhance contrast, Potter-Bucky film of the liver region, antero-posterior and right lateral views were also done. A diagnostic liver aspiration using a large bore needle at the point of maximum tenderness or at a site corresponding to the cold area on liver scan in those patients who had no definite point of tenderness. After successful diagnostic aspiration, 5 ml of dense radiopaque iodised oil was instilled to visualise the bottom of the abscess and about 50 ml of air was also injected into the abscess to line the top of the cavity. The approximate size of the abscess cavity was calculated from the maximum vertical, horizontal and antero-posterior diameters. After treatment with tinidazole, needle aspirations of pus were repeated at intervals depending on the size of the abscess.

Table 4

Treatment schedule for amoebic liver abscess.		
Group	No. of patients	Dosage of Tinidazole
I	16	1.2 g single dose
II	4	1.2 g in 3 divided doses
III	1	1.2 g in 2 divided doses
IV	8	1.25 g single dose
V	7	1.5 g single dose

The dosage schedule of tinidazole given to the patients is shown in Table 4. Patients were considered cured when defervescence occurred, the pain subsided and hepatomegaly regressed with normal biochemical studies. Treatment was considered to have failed when there was persistent fever, pain, hepatomegaly, impairment of the biochemical tests, or when there were recurrence of symptoms at follow up. All cases were followed up for a period of at least 6 months. Healing of the abscess cavity was determined by the presence of droplets or a compact shadow of opaque medium at the site of the cavity as opposed to a horizontal level when the cavity was still open.

## RESULTS

The results of the clinical trial are summarized in Table 5. All patients responded well. Thirty one patients had fever before treatment ranging from 37.6°C to 40.2°C, the fever subsided in 1-16 days (average 3.6 days). Five patients had no fever during the course of treatment. Pain was present in 27 patients (average 75%) and subsided in 3 to 9 days (average 6.09 days). The size of the abscess cavities ranged from 3 × 4 × 4.5 cm (28.3 ml) to 15 × 24.5 × 9.8 cm (1886.5 ml). These healed in 2 to 15 weeks (average 6.2 weeks). Delayed healing of the abscess cavities in 7 and 10 months was observed in two patients with large cavities of 12 × 16.5 × 13.5 cm (1400 ml) and 8.5 × 14.2 × 11.5 cm (727.06 ml) and who received tinidazole 1.25 g.

Table 5

Results of treatment with tinidazole in 36 patients with amoebic liver abscess.

	I	II	III	IV	V
No. of Pt.	16	4	1	8	7
Temperature subside (days)	1-7 (3.07)	1-14 (9)	8 (8)	3-16 (3.3)	2-12 (7.1)
No. of aspirations	3-7 (4.75)	3-7 (4.75)	2 (2)	1-10 (3.37)	2-7 (3.8)
Pus aspirated (ml)	40-950 (273.75)	268-1505 (663.75)	55 -	50-4430 (758.4)	110-1400 (404.3)
Average size of cavity (c.cm)	221.29	249.34	179.66		
Healed (wks)	2-8 (4.1)	2-5 (3.25)	3	3-10+m* 15	4-12 (6.07)
Overall cure rate (%)	100	100	100	100	100

Mean values shown in parenthesis.

Remarks :- \*Delayed healing of the abscess cavity in 7 and 10 months was observed in two patients in group IV because of huge cavities.

Side-effects:- No serious side-effects were observed.

No relapse or failure of treatment was observed. No drug related toxicity was noted with tinidazole. The clinical response as well as the rate of healing were similar in all groups.

## DISCUSSIONS

Since the introduction of tinidazole for amoebiasis various dosage schedules for long or short term treatment have been used. Powell *et al.*, (1972) reported that tinidazole in a dosage of 800 mg thrice daily for 5 days in 10 patients was inferior to metronidazole 800 mg thrice daily for the same period. On the other hand in a short term trial for the treatment of amoebic liver abscess, Bunnag *et al.*, (1973) obtained excellent results with 2,400 mg of tinidazole given in 3 divided doses in one day in patients followed up to 7 months. No relapse was observed. Treatment of amoebic liver abscess with 2 g of tinidazole in two divided doses in one day also showed satisfactory results (Lasserre *et al.*, 1983).

In the present study the dose of tinidazole was lower than has been used previously but the results were still excellent. No relapse or treatment failure was observed. The clinical response and the rate of healing were similar in all groups. Therefore, a single dose of 1.2 g to 1.5 g tinidazole appears adequate for the treatment of amoebic liver abscess.

Low dose therapy will be particularly useful in developing countries since treatment costs are reduced, side effects are few and the duration of hospitalization can be significantly reduced.

## SUMMARY

Thirty-six patients with uncomplicated amoebic liver abscess were treated with low dose tinidazole 1.2 g to 1.5 g in a single or divided doses, and aspiration of the abscess. No drug related toxicity was noted. All patients responded well and there was no relapse or treatment failure.

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