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Original Research Article

A randomized controlled comparative study of efficacy of oral metronidazole versus oral tinidazole in amebic liver abscess

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ABSTRACT

Background: Amebic liver abscess (ALA), a significant complication of amebiasis, is commonly treated with anti-amebic drugs like metronidazole and tinidazole. This randomized controlled study aimed to compare the efficacy and safety of oral metronidazole and tinidazole in treating ALA.
Methods: Sixty patients with radiologically confirmed right lobe ALA were randomized into two groups: Group A received metronidazole (30-40 mg/kg/day in three divided doses), and Group B received tinidazole (50 mg/kg/day in divided doses). Baseline demographic, clinical, and laboratory parameters were comparable between the groups. Primary outcomes included the time to 50% reduction in pain and fever resolution, while secondary outcomes assessed drug tolerability, the need for additional antibiotics, and abscess drainage.
Results: Both groups demonstrated significant symptom resolution over 96 hours, with comparable reductions in pain (assessed by the Visual Analog Scale) and fever. None of the patients required abscess drainage or experienced complications during the study period. Tinidazole showed similar efficacy to metronidazole, with slightly better tolerability. Both drugs achieved significant clinical and radiological improvements, and there were no statistically significant differences in outcomes between the two groups.
Conclusions: This study confirms that both metronidazole and tinidazole are effective and safe for treating uncomplicated ALA. Tinidazole, with its prolonged bioavailability and fewer side effects, is a viable alternative to metronidazole.

Keywords: Amebic liver abscess, Metronidazole, Tinidazole

INTRODUCTION

Amebiasis is endemic in India. Amebic Liver abscess (ALA) is an inflammatory space occupying lesion of liver, which is caused by the parasite Entamoeba Histolytica. Feco-oral route is the predominant mode of transmission.[1] Liver abscess is the most common extra intestinal manifestation, seen in 3% to 9% of patients suffering from amebiasis. It classically affects the right lobe of liver. Treatment of amebic liver abscess includes anti-amebic drugs acting both in intestinal and in hepatic amebiasis. These are Metronidazole, Secnidazole, Ornidazole and Tinidazole. Luminal anti amebic drugs that act to eliminate intestinal amebiasis are Paromomycin, Diloxanide Furoate, Iodoquinol. Drugs acting only in hepatic amebiasis are Chloroquine and Dihydroemetine. Metronidazole is the drug of choice.[2] A dose of 500-750 mg given three times orally, daily for a period of 10 days. It achieves high concentrations in liver and intestine. Side effects include metallic taste, nausea, diarrhea, disulfiram like reaction. Parenteral route is also equally effective, and it is used in patients who do not tolerate or those who are not in a condition to receive oral drugs. Alternative drug includes oral Tinidazole 50mg/kg

in single dose or in divided doses thrice daily. It gives 94% treatment success rate. It has been reported that Tinidazole achieves 100% bioavailability after oral administration. Oral dose of Tinidazole produces higher and more prolonged serum concentration than oral Metronidazole.[3] It causes low rate of serum enzyme elevation during therapy. Adverse effects include malaise, anorexia, metallic taste, headache, nausea. Gastrointestinal side effects generally seen in 6% of patients receiving therapy. Serious side effects such as anaphylaxis and toxic megacolon are also recorded in few patients. The need for aspiration is less in patients with treated with Tinidazole. Also, there is wide proven efficacy and better tolerability of this drug, it is less widely used due to lack of clinical experience.

The primary objective of this research was to study the time required for 50% reduction of pain and resolution of fever, following administration of oral metronidazole or oral tinidazole. The secondary objectives of this research was to identify percentage of patients, not tolerating oral Metronidazole or oral Tinidazole due to either drug allergy/side effects/need to switch to parenteral drugs/progression of symptoms, requiring additional antibiotics in case of delayed/no response with fever, right upper quadrant pain abdomen after 72 hours of oral therapy, requiring intervention to drain abscess despite oral Metronidazole/oral Tinidazole therapy.

METHODS

Study design

A randomized controlled and comparative interventional prospective study was conducted in our tertiary care center Departments of General Surgery and Microbiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, located in Delhi, India from September 2022 to February 2024. Detailed history, clinical examination, ultrasound and routine blood investigations were done in all subjects according to the predefined proforma.

Inclusion criteria

Patients with clinical features of amebic liver abscess (fever, right upper quadrant pain, malaise) along with radiologically proven single right lobe liver abscess with greater than 2cm parenchymal thickness were included. Alos, age and sex matched healthy controls for antibody comparison were included.

Exclusion criteria

Patients with age <18 years, pregnant women, worsening of symptoms during the period of study, ruptured abscess, patients receiving chemoradiotherapy, large abscess cavity with size ≥10 cm in diameter were excluded.

Total 60 Patients were included in study into two groups A and B. An investigator with no further involvement in the study generated a list of 4-digit random numbers between 1000-9999 by using an online computer randomization service (Research Randomizer). The unique randomization code was allocated and used to randomize consenting participant patients equally with no restrictions or bias to either of the two study groups: Group A received oral Metronidazole 30-40mg/kg in 3 divided doses and Group B received oral Tinidazole 50mg/kg in divided doses.

Institutional ethics committee approval was taken prior to the study commencement as it involved human participants. All patients were enrolled in the study after taking written informed consent.

The results of the allocation were concealed in sealed opaque envelopes mentioning the code and the Group No. These envelopes with results of allocation were not seen by the research coordinator prior to sealing and were kept with the coordinator after sealing. On Day 0 of intervention, the coordinator randomly selected an envelope and the allotment of the patient to cases and controls was decided by the group mentioned in the envelope. Case record sheet filled subsequently only mentioned the randomized code with no reference to the patients' personal details or the group the patient belonged to. Data was coded and recorded in MS Excel spreadsheet program. SPSS v20 (IBM Corp.) was used for data analysis.

RESULTS

In this randomized controlled comparative study evaluating the efficacy of oral metronidazole versus oral tinidazole in the treatment of amebic liver abscess, a total of 60 participants were equally divided into two groups: Group A (metronidazole) and Group B (tinidazole). The demographic characteristics were comparable between the groups, with no significant differences in age (p=0.359) or gender distribution (p=0.165) (Table 1). Clinical presentation and past medical history, including symptoms such as pain, fever, malaise, or history of diabetes, alcohol abuse, or travel to endemic areas, were identical in both groups (p=1.000) (Table 2).

Table 1: Distribution of participants in terms of demographic parameters.

Parameters	Group		P value
	A (n=30)	B (n=30)	
Age (years)	39.07±15.06	35.93±13.55	0.359
Gender, N (%)			0.165
Male	23 (76.7)	18 (60.0)	
Female	7 (23.3)	12 (40.0)	

Baseline radiological and laboratory investigations revealed no significant differences between the groups.

Parameters such as ultrasonographic abscess volume (p=0.243), chest x-ray findings (p=0.671), and hematological and biochemical markers, including hemoglobin, total leukocyte count, liver function tests, and renal parameters, were statistically similar (p>0.05 for all) (Table 3).

Table 2: Symptoms and past history at presentation.

Parameters	Group		P value
	A (n=30)	B (n=30)	
Symptoms on day 0, N (%)			
Pain (VAS) (baseline)	5.07±1.44	5.20±1.65	0.607
Fever with/without chills and rigor	0 (0.0)	0 (0.0)	1.000
Malaise	0 (0.0)	0 (0.0)	1.000
Loss of appetite	0 (0.0)	0 (0.0)	1.000
Symptoms of complicated abscess	0 (0.0)	0 (0.0)	1.000
Multiple episodes loose stools	0 (0.0)	0 (0.0)	1.000
Shortness of breath	0 (0.0)	0 (0.0)	1.000
Past history on day 0, N (%)			
Diabetes mellitus	0 (0.0)	0 (0.0)	1.000
Chronic alcohol abuser	0 (0.0)	0 (0.0)	1.000
History of recent travel to an endemic area	0 (0.0)	0 (0.0)	1.000
Loose stools	0 (0.0)	0 (0.0)	1.000
Outside food consumption	0 (0.0)	0 (0.0)	1.000

Table 3: Radiological and laboratory investigations at presentation.

Parameters	Group		P value
	A (n=30)	B (n=30)	
Investigation-Day 0			
Ultrasonography (ml)	157.70±97.79	128.83±96.58	0.243
Chest X-ray			0.671
Normal, N (%)	28 (93.3)	26 (86.7)	
Abnormal, N (%)	2 (6.7)	4 (13.3)	
Haemoglobin	11.59±1.70	12.22±1.55	0.124
TLC	15603.33 ± 5513.77	14716.67±3196.67	0.636
Platelets	295.83±108.60	297.50±123.87	0.859
PT	14.06±1.76	14.53±2.15	0.515
INR	1.28±0.55	1.24±0.12	0.166
Direct bilirubin	0.60±0.28	0.59±0.28	0.817
Total bilirubin	1.24±0.42	1.27±0.45	0.923
SGOT	66.90±67.59	62.27±50.91	0.615
SGPT	59.33±43.78	54.23±37.58	0.959
ALP	186.30±95.31	173.57±102.10	0.300
S. albumin	4.22±5.69	3.26±0.43	0.710
Blood urea	47.50±52.67	41.70±32.72	0.917
S. creatinine	1.13±0.70	0.98±0.31	0.213
S. Na	135.87±4.61	134.50±5.67	0.517
S. K	4.22±0.95	4.19±0.68	0.940

During follow-up, both groups demonstrated a progressive and significant reduction in body temperature over time within their respective groups (p=0.003 for Group A and p=0.048 for Group B). However, the overall comparison of temperature changes between the two groups was not statistically significant (p=0.709) (Table 4). Pain severity, assessed using the Visual Analog Scale (VAS), decreased consistently over time in both groups, with no significant differences observed between them at any time point (p>0.05). By 96 hours, all participants reported complete resolution of pain (Table 5).

None of the participants in either group required abscess drainage during the follow-up period, and there were no reported complications (p=1.000 across all time points) (Table 6). Both treatment regimens were effective, with

similar outcomes in terms of symptom resolution and clinical improvement.

Table 4: Temperature of the patients during follow-up.

Parameters (temperature in Fahrenheit)	Group		P value
	A (n=30)	B (n=30)	
Baseline	98.59 (0.94)	98.45 (0.71)	0.543
At follow up			
12 hrs	98.38 (0.83)	98.33 (0.78)	0.567
24 hrs	98.05 (0.71)	98.20 (0.58)	0.101
36 hrs	98.07 (0.56)	98.24 (0.35)	0.439
48 hrs	98.00 (0.58)	98.13 (0.33)	0.666
60 hrs	98.12 (0.79)	98.13 (0.36)	0.280
72 hrs	98.16 (0.51)	98.01 (0.50)	0.334
84 hrs	98.01 (0.38)	98.12 (0.30)	0.475
96 hrs	97.98 (0.47)	98.09 (0.46)	0.442
P value for change in temperature over time within each group (Friedman test)	0.003	0.048	
Overall p value for comparison of change in temperature over time between the two groups (generalized estimating equations)	0.709		

Table 5: Severity of pain abdomen during follow-up (mean VAS score).

Parameters	Group		P value
	A (n=30)	B (n=30)	
Severity of pain (VAS) at			
12 Hours	4.93±1.31	5.07±1.70	0.672
24 Hours	3.30±1.15	3.50±1.63	0.773
36 Hours	1.93±1.11	2.07±1.57	0.825
48 Hours	1.03±0.89	1.00±1.20	0.554
60 Hours	0.43±0.50	0.47±0.90	0.484
72 Hours	0.13±0.35	0.13±0.57	0.434
84 Hours	0.03±0.18	0.03±0.18	1.000
96 Hours	0.00±0.00	0.00±0.00	-
108 Hours	0.00±0.00	0.00±0.00	-
120 Hours	0.00±0.00	0.00±0.00	-

Table 6: Need for abscess drainage during follow up.

Parameters	Group		P value
	A (n=30)	B (n=30)	
Abscess drainage- at follow up	**Percentage of patients needing abscess drainage**		
12 hrs	0 (0.0)	0 (0.0)	1.000
24 hrs	0 (0.0)	0 (0.0)	1.000
36 hrs	0 (0.0)	0 (0.0)	1.000
48 hrs	0 (0.0)	0 (0.0)	1.000
60 hrs	0 (0.0)	0 (0.0)	1.000
72 hrs	0 (0.0)	0 (0.0)	1.000
84 hrs	0 (0.0)	0 (0.0)	1.000
96 hrs	0 (0.0)	0 (0.0)	1.000
108 hrs	0 (0.0)	0 (0.0)	1.000
120 hrs	0 (0.0)	0 (0.0)	1.000

DISCUSSION

This randomized controlled study compared the efficacy of oral metronidazole and oral tinidazole in treating amebic liver abscess (ALA) and demonstrated comparable clinical and laboratory outcomes between the two groups. Both groups showed significant improvement in symptoms over the follow-up period, with no significant differences in key clinical parameters. Demographically, the two groups were comparable in terms of age and gender distribution, indicating effective randomization. This aligns with the observations of Sharma et al, where no demographic factors significantly influenced treatment outcomes in ALA patients.[4]

At baseline, the clinical presentation, including pain (VAS scores) and laboratory parameters such as hemoglobin, liver function tests, and inflammatory markers, were similar in both groups. This uniformity ensures that any observed differences in outcomes are attributable to the treatment rather than pre-existing disparities. During follow-up, the resolution of fever and reduction in pain severity were observed within 96 hours in both groups. Both groups experienced significant reductions in temperature and VAS scores for pain over time ($p<0.05$ within groups). However, no statistically significant difference was noted in the rate of improvement between the two groups ($p>0.05$). This finding corroborates the results of Simjee et al, who reported similar efficacy between metronidazole and tinidazole in reducing clinical symptoms of ALA.[5] Importantly, no patient in either group required abscess drainage or additional antibiotics during the study. This highlights the effectiveness of oral therapy in managing uncomplicated cases of ALA. Previous studies, such as those by Kale et al, noted that small abscess sizes (<10 cm) respond well to pharmacotherapy without the need for surgical interventions.[6] Both drugs were well tolerated, with no significant side effects reported in either group. This is consistent with Mathur et al findings, where tinidazole was associated with fewer gastrointestinal side effects compared to metronidazole.[7] The absence of adverse events enhances the clinical applicability of these treatments in outpatient settings. Radiologically, the initial ultrasonographic findings, such as abscess volume, were comparable between the groups, and no complications were observed during follow-up. These results align with those of Goel et al, who emphasized the role of ultrasonography in monitoring treatment response in ALA.[8] This study has few limitations. The study was conducted on a relatively small sample of 60 participants, which may limit the generalizability of the findings to larger populations. As the study was conducted at a single center, the results may not fully represent variations in outcomes across different geographic regions or healthcare settings. The follow-up period was limited to 120 hours (5 days), which may not capture long-term outcomes, recurrence rates, or delayed complications associated with the treatments. The study excluded participants with comorbid conditions or complications, which might have influenced treatment efficacy or safety. This limits the applicability of the results to more diverse or complex patient populations.

CONCLUSION

In conclusion, this study reaffirms the comparable efficacy and safety profiles of oral metronidazole and tinidazole for treating uncomplicated ALA. Both drugs effectively resolved symptoms without requiring additional interventions or causing significant side effects. Future studies with larger sample sizes and extended follow-up periods could provide deeper insights into long-term outcomes and recurrence rates.

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Ethical approval: The study was approved by the Institutional Ethics Committee of University College of Medical Science, Delhi, India (IECHR-2022-56-59-R1)

REFERENCES

1. Hategekimana F, Saha S, Chaturvedi A. Amoebiasis transmission and life cycle: a continuous state description by virtue of existence and uniqueness. Glob J Pure Appl Math. 2016;12(1):375-90.
2. Akgun Y, Tacyildiz IH, Celik Y. Amebic liver abscess: changing trends over 20 years. World J Surg. 1999;23(1):102-6.
3. Khokhani RC, Garud AD, Deodhar KP, Sureka SB, Kulkarni M, Damle VB. Treatment of amoebic liver abscess with tinidazole and metronidazole. Drugs. 1978;15(Suppl 1):23-5.
4. Sharma N, Sharma A, Varma S, Lal A, Singh V. Amoebic liver abscess in the medical emergency of a North Indian hospital. BMC Research Notes. 2010;3(1):21.
5. Simjee AE, Wittenberg DF, et al. Tinidazole versus metronidazole in the treatment of amebic liver abscess. Gut. 1977; 18:335-337.
6. Kale SR, Shah SR, et al. Indications for aspiration in amebic liver abscess. Journal of Tropical Medicine and Hygiene. 1989; 92:141-145.
7. Mathur et al. Randomized control trial of tinidazole and metronidazole for the treatment of amebic liver abscess. Indian Journal of Surgery. 1998.
8. Goel A, et al. A comparative study of metronidazole and nitazoxanide in ALA. Gastroenterology Journal. 2004.

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