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Comparative study of various modalities of treatment in uncomplicated amoebic liver abscess

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Abstract

Background: Amoebic liver abscess is the most frequent extra-intestinal manifestation of *Entamoeba histolytica* infection.

Aims and Objectives: To compare the various modalities of treatment in uncomplicated amoebic liver abscess.

Materials & Methods: This prospective and randomized trial was carried out in the Surgery Department of M.L.N. Medical College, Allahabad, from 1st August, 2016 to 30th July, 2018. Total 96 patients with history and clinical examination suggestive of amoebic liver abscess attending surgical opd and those coming for follow up in outpatient department at regular intervals were included in the study.

Results: Patients subjected to percutaneous needle aspiration had a higher success rate of 62.5% then those with conservative treatment. But this was lower than those who were percutaneously drained (100%).

Conclusion: Interventional therapy with chemotherapy is more effective than conservative management alone. In interventional therapy, percutaneous drainage is best option for treatment of amoebic liver abscess.

Keywords: *Entamoeba histolytica*, amoebic liver abscess, percutaneous drainage, conservative management.

Introduction

Amoebic liver abscess is the most frequent extra-intestinal manifestation of infection by the protozoan *Entamoeba histolytica*. This is an important cause of inflammatory space-occupying lesions of the liver, mainly in developing countries. The prevalence of infection is higher than 5-10% in endemic areas and sometimes as high as 55%.² the highest prevalence is found in developing countries in the tropics, particularly in Mexico, India, Central and South America, and tropical Africa.

Amoebic liver abscess is endemic in India. Infections with *E. histolytica* rank second worldwide among parasitic causes of death, following malaria. Amoebic liver abscess is marked by a 7-12 times higher incidence in males than in females despite an equal sex distribution of noninvasive colonic amoebic disease among adults.⁴ However, no sexual preponderance exists among children. Peak incidence is seen in third, fourth and fifth decades.

Surgical Care considerations

1. Therapeutic aspiration of amoebic liver abscess is considered in the following situations:
 - a. High risk of abscess rupture, as defined by cavity size greater than 5 cm.
 - b. Left lobe liver abscess, which is associated with higher mortality and frequency of peritoneal leak or rupture into the pericardium.
 - c. Failure to observe a clinical medical response to therapy within 5-7 days.
 - d. Cannot differentiate from a pyogenic liver abscess.

2. The following are predictive of the need for aspiration:^[25]
 - a. Age older than 55 years
 - b. Abscess greater than 5 cm in diameter
 - c. Failure of medical therapy after 7 days.

3. Imaging-guided needle aspiration and catheter drainage are the procedures of choice.

Material and Methods

The present study titled "Comparative study of various modalities of treatment in uncomplicated amoebic liver abscess" was a prospective and randomized trial, carried out in the Surgery Department of M.L.N. Medical College, Allahabad, from 1st August, 2016 to 30th July, 2018. Total 96 patients with history and clinical examination suggestive of amoebic liver abscess attending surgical opd and those coming for follow up in outpatient department at regular intervals were included in the study.

Inclusion Criteria

- Patients suggestive of clinical presentation
- USG findings in all cases
- All non-complicated abscesses.
- No features of rupture
- No feature of impending rupture (liver tissue rim <1cm)
- No compression effects
- Abscess size >3 cm
- IgM ELISA +ve

Exclusion Criteria

- Complicated abscess
- Multiple abscess cavities
- Ruptured/impending rupture – peritonitis.
- Abscess < 3 cm.
- Pregnancy
- Treatment with amoebicidal drugs before hospital admission

USG Criteria for Diagnosis

For any space occupying lesion to diagnose as amoebic liver abscess:

- Wall – echo poor, fine echogenic, or thick echogenic
- Content – hyper and hypo echoic mixed pattern, homogenous hypo echogenic pattern, hypo echoic and anechoic pattern
- Associated right pleural effusion as evidence of rupture
- Aspiration of typical anchovy sauce pus under ultrasound guidance

After selection of patients, they were randomly allocated into three groups. Randomization was done using computer software, according to a standardized previously reported protocol [Urbaniak G C, Plous S. Research Randomizer (version 3.0) {computer software}. The three sets of random numbers generated were assigned to the two intervention groups and sealed numbered envelopes were made with the serial number mentioned on the outside and intervention mentioned inside by a non-participating individual.

Treatment Modalities

Three groups of different treatment modalities were formed:

- Group A - Drug therapy only
- Group B - USG guided aspiration (PCA) + Drug.
- Group C - Percutaneous Catheter Drainage (PCD) + Drug

Informed consent was taken from all patients undergoing the above therapy. Amoebicidal therapy in the form of metronidazole (i.e. 40 mg/kg body weight / day) in three divided

doses given to all patients for 10 days. In 32 patients, ultrasound guided percutaneous intervention was done along with anti-amoebic therapy.

The percutaneous treatment procedure was performed under local anesthesia (2% lignocaine) with IV analgesia and sedation when required within 24 hours after hospital admission. The procedure was performed under continuous real time sonographic guidance using freehand technique.

In the patient assigned to needle aspiration group, a 16-gauge needle was advanced into the abscess cavity and the content was aspirated completely to evacuate the cavity.

For percutaneous catheter drainage appropriately sized catheters (8-12 Fr pigtail) were introduced into an abscess cavity using the Seldinger technique. The catheter was connected to a completely closed collecting system and routine catheter care was instituted. A daily estimate of the amount, color and consistency of drainage fluid was recorded. Irrigation of the catheter with sterile saline water was done daily to avoid catheter blockage. Catheter was removed when catheter output dropped to <10 ml/24 hrs for 2 consecutive days, the patient showed clinical improvement (i.e. defervescence and relief from local symptom and normalization of elevated leucocyte count) and follow up sonography showed negligible residual cavity.

All patients were followed up to assess the time needed for clinical improvement, length of hospital stay and development of any complications. Patients were followed as inpatients during therapy for 10 days and re-examined weekly for a month after discharge. Body temperature, pain, and tenderness of the right upper abdomen were followed daily from day 1 to 10. WBC and hemoglobin were measured on day 1, 4,7, 10 and 28 days after discharge; ESR on day 1, 10 and after 28 days of discharge. Periodic sonography was done every 4th day to assess the cavity size until the patients were hospitalized.

Patients in group A who did not improve clinically after 96 hours or whose sonographic finding showed increase in cavity size or feature of impending rupture were subjected to percutaneous modalities. These were considered as failure of therapy, and these patients were subjected to percutaneous needle aspiration and were excluded from the study.

Patients in percutaneous needle aspiration group who did not improve clinically after first aspiration and continued to have leukocytosis or showed refilling of the abscess cavity on follow up sonography were subjected to second aspiration on 4th day. Failure of the patients to improve after a second aspiration was considered as failure of aspiration therapy at the 3rd USG done on 7th day, and these patients were given catheter drainage (however, these patients were not included in the catheter drainage group).

After discharge all patients were followed up with periodic clinical and sonographic examinations to assess for any reoccurrence of disease and to monitor the size of the abscess cavity. The patients were examined weekly for one month, monthly for the next three month and at two monthly thereafter until complete resolution of the abscess was achieved.

Treatment was considered successful if all of the following criteria were met.

1. The patient improved clinically (i.e. subsidence of fever and local sign and symptom)
2. Elevated leucocyte counts were normalized
3. Follow up imaging showed resolution of the abscess (total resolution or reduction in size to <3 cm).

Observations

Table 1: Age Incidence of Liver abscess

Age group (Years)	No. of patients
<20	4
21-30	34
31-40	28
41-50	20
51-60	8
61-70	2
Total	96

The incidence was maximum (34) in the age group 21-30 years. This was followed by 28, 20, 8, 4 and 2 patients each in 31-40, 41-50, 51-60, 0-20 and 61-70 years age groups, respectively. (Table 1)

Table 2: Sex incidence of liver abscess

	number of patients (total n = 96)
Male	82(85.41%)
Female	14(14.59%)

Among 96 cases of amoebic liver abscess, 82 (85.41%) were male and 14 (14.58%) were females, with M: F= 5.9:

Table 3: Outcome in different group's therapy.

Parameters	Treatment groups						P value (on way ANOVA- 5% level of significant 95% CI)
	Conservative management[n=32]		Needle aspiration[n=32]		Catheter drainage[n=32]		
	No. of patients	Value	No. of patients	Value	No. of patients	Value	
Success rate	12	36%	20	62.5%	32	100%	0.0008
Clinical improvement	12	6-12 8.5± 2.42 days	20	4-8 5.6± 1.35 days	32	3-8 4.63± 1.63 days	Fc-37.66 P<0.05
Time needed for 50% reduction	12	7-28 16.0± 7.56 days	20	5-25 9.4± 5.67 days	32	4-12 6.94± 2.79 days	Fc-21.704 P<0.05
Time needed for Total reduction	12	15-27 20.33± 6.91 weeks	20	7-17 10.5± 3.66 weeks	32	5-24 9.88± 5.5 weeks	Fc-36.102 P<0.05
Hospital stay	12	14-25 20.33± 4.67 days	20	6-21 12.3± 4.57 days	32	5-22 9.94± 4.45 days	Fc-47.014 P<0.05

Table 4: Success rate in different groups

Parameter	Treatment groups						P value (by chi-square test)
	Conservative management [n=32]		Needle aspiration [n=32]		Catheter drainage [n=32]		
	No. of patients	Value	No. of patients	Value	No. of patients	Value	
Success rate	12	36%	20	62.5%	32	100%	0.0008

Among 96 patient, 32 patients treated conservatively with success rate of 36% (12 out of 32), patient treated with needle aspiration and metronidazole therapy with success rate 62.5% (20 out of 32) and patient treated with catheter drainage with metronidazole therapy with success rate of 100%.

Table 5: Time needed for clinical improvement in different groups

	Group A	Group B	Group C
No. of days Mean ± SD	8.50±2.42	5.60±1.35	4.63±1.63

It took 8.50±2.42 days for clinical improvement in patients treated conservatively, 5.60±1.35 days for patient treatment with percutaneous needle aspiration and metronidazole therapy and 4.63±1.63 days for patient treated with catheter drainage and metronidazole therapy.

Table 6: Time needed for 50% reduction in cavity size

No. of days	Group A	Group B	Group C
Mean ± SD	16.0±7.56	9.4±5.67	6.94±2.79

Table 7: Time needed for total reduction in cavity size

	Group A	Group B	Group C
No. of weeks	20.33±6.91	10.5±3.66	9.88±5.5

Time needed for total reduction of cavity in patients treated conservatively with metronidazole are 20.33±6.91 weeks, treated with percutaneous needle aspiration and metronidazole therapy 10.5±3.66 weeks and when treated with catheter drainage 9.88±5.5.

Table 8: Hospital stay

	Group A	Group B	Group C
No. of days	20.33±4.67	12.3±4.57	9.94±4.45

- Out of 96 patients, 32 conservatively managed given metronidazole therapy- for 10 days with serial ultrasound done every 4th day. Success rate was 36%(12 patients) i.e. out of 32 patients; 12 were improved clinically and radiologically, among these 12 patients (Improved in 1-10 days) pain subsided in 1-3 days, tenderness subsided in 3-10 days. All patients had 50% reduction in size of cavity (average vol-300ml) within 10-30. Total reduction in cavity in 8-3 weeks. Failure rate- 64% i.e. 20 patients (among 32), which were subjected to ultrasound, 8 were improved, 12 developed re-accumulation. Aspiration done among these 12 patients, 8 were improved and 4 didn't, these 4 were went for percutaneous drainage.
- Group b- percutaneous needle aspiration (PNA): done in 32 patients and given metronidazole therapy along with PNA from 1st day. They were subjected on serial USG every 4th day and reaspiration if required.out of 32- 20 were improved radiologically and clinically. Pain and fever subsided within 72 hrs, success rate of 62.5%. 50% reduction in size of abscess cavity found in 1-30 days and total reduction was seen in 8-30 wks (avg cavity size-510 ml). 12 were excluded due to failure of study- four patients did not improve and out of these four, 4 developed signs of rupture (cavity size 1000 and 1200 ml respectively), they were managed surgically and excluded from study. Patients were discharged and followed with serial usg. Total reduction in size of abscess cavity was found in 6-26 wks.

- Group c- percutaneous drainage (PCD): USG guided PCD done in 32 patients along with metronidazole therapy, with success rate of 100%. Total clinical improvement was seen in 3-8 days. Regular monitoring on 4th and 7th day. 50% reduction in cavity seen in 4-12 days. Duration of stay in hospital-5-22 days.

Discussion

Although infection with *Entamoeba histolytica* occurs worldwide, yet liver abscess is the most common extra intestinal complication in 3% to 9% of patients [Petri (2000), Hughes *et al.* (2000), Ravdin (1995), WHO group (1980)]^[4, 5, 14], Mehta *et al.* found that ALA is widely prevalent in the Indian subcontinent. The WHO estimates *E. histolytica* case 50 million cases and 10,000 deaths annually.

Patients generally belong to middle age group. Mean age in our study was 35, which is consistent with Stanley SL (2003)² study. According to Sepulveda B (1986)⁶⁶ male dominated 3-10 times more than females. In our study male are predominant to female as in all studies.

In our study patient presented with most common symptoms of abdominal pain which is consistent with Mehta *et al.* (1970)^[15], Basil *et al.* (1983)^[17] and S. Singh *et al.* (2013)^[12] common sign was fever (88%). In our study fever was present in 93.73%, abdominal tenderness in 83.33% and hepatomegaly present in 66.66% and jaundice was present in 8.33%.

Incidence of Jaundice varied from 1% to 17% according to various studies [Hai *et al.* (1971)^[20], Abuabara *et al.* (1982)^[18] and Thompson *et al.* (1986)^[21].

Treatment

Our study was based to compare the clinical outcome of three most widely used regimen in the treatment of ALA. This comprised ALA patient treated either only with metronidazole or with a combination of metronidazole with aspiration or metronidazole with catheter drainage. Patient treated conservatively had a success rate of 36%. Rest patients were treated surgically or aspirated or drained.

In patients who had undergone percutaneous aspiration, the success rate was 62.5%. In first aspiration it was 50% which increased to 62.5% in second aspiration. The success rate in other various reported literature varies from 79% to 100% [Baek *et al.* (1993) Giorgio *et al.* (1995), Dietrick *et al.* (1984)]^[10, 22, 23] Study conducted by Rajak *et al.* (1998)^[7], the success rate was 60% as per our study. He conducted that in the above studies repeated aspiration were done 3-4 times. But in his study a repeat aspiration was done only in case of no response to the first aspiration.

We preferred to subject the patient to percutaneous catheter drainage after failure by second aspiration.

One important reason for failure of needle aspiration was inability to completely evacuate the thick viscous pus that may be present in some of the abscess [Singh JP (1989), Giorgio *et al.* (1995)]^[8, 12]. Rapid re-accumulation of abscess after needle aspiration is another problem described by Dietrick *et al.* (1984)^[23].

In contrast to percutaneous needle aspiration, percutaneous placement of an indwelling catheter provides a continuous drainage. Hence incomplete evacuation and re-accumulation are not associated with catheter drainage [Attar B *et al.* (1986)⁷³, Singh *et al.* (1989), Saraswat *et al.* (1992), Rajak *et al.* (1998)]^[24, 9, 7].

In our study percutaneous drainage had a success rate of 100% and p value < 0.008.

Joerge Blessmann *et al.* (2003)^[6] did a comparative study on metronidazole alone as in combination with USG guided aspiration in which resolution pattern for the various laboratory and clinical parameter revealed no difference except for liver tenderness which disappeared faster in aspiration group during the first 3 days (p < 0.001) which was consistent with our study.

The average hospital stay when compared was greater in patient treated conservatively because of the tenderness and time taken for reduction in cavity size. In percutaneous needle aspiration group average hospital stay was 12 days and percutaneous drainage it was 10 days.

Singh and Kashyap (1989)^[8] noted much faster and complete resolution of abscess cavity after percutaneous drainage than after percutaneous aspiration.

Complications have been reported with both catheter drainage (12% in the series of Lambiasi *et al.*)^[25] and needle aspiration (4%) in the series of Baek *et al.* Rajak *et al.* (1998)^[7] suggested that both procedure if properly performed are essentially safe procedure with minimal complication.

Reason of failure in percutaneous drainage in other studies (Rajak *et al.*)^[7] was thick pus. It was overcome by use of 14F catheters for percutaneous drainage as in Shilpi *et al.* (2011) study.

Conclusion

- In our study a clear male predominance of cases were seen in comparison to female with a ratio of 5.9:1.
- Age range in our study was 18-65 years. Most patients were between age group of 25- 45 years.
- Most common symptom being abdominal pain and most common sign being fever.
- Serological marker and ultrasonographic finding were used as a diagnostic tool and exclusion of cases were done according to its finding.
- Right lobe of liver is affected more than the left lobe of liver.
- Interventional treatment is more effective than conservative treatment as patients discomfort is relived earlier, less duration in reduction of cavity size, less complication and less hospital stay.
- In conservative treatment defervescence is almost equal to those with interventional treatment except for liver tenderness. But the average hospital stay in this group was greater due to time taken for reduction in cavity size.
- Patients subjected to percutaneous needle aspiration had a higher success rate of 62.5% then those with conservative treatment. But this was lower than those who were percutaneously drained (100%).
- Complication such as re-accumulation and increase in cavity size was seen in percutaneously needle aspirated group.
- Percutaneous drainage appears better in quickening clinical improvement, decreased duration of chemotherapy, and quicker resolution of cavity size.
- To conclude interventional therapy with chemotherapy is more effective than conservative management alone. And in interventional therapy percutaneous drainage is best option for treatment of amoebic liver abscess.

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