

# Role of Albendazole in the Management of Hydatid Cyst Liver

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## ABSTRACT

**Background/Aim:** Hydatidosis has a worldwide distribution and the liver is the most common organ involved. Hydatid cysts of the liver can be managed either by nonoperative or operative methods. Nonoperative methods include chemotherapy and percutaneous treatment. The study aimed at understanding the effect of albendazole therapy on the viability of protoscolecids and recurrence rate of hydatid disease of the liver. **Patients and Methods:** The study was conducted at Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir, India, over a period of 2 years from January 2002 to December 2003, with further follow-up of 5 years. The study included 72 cases in the age group of 17-66 years, comprising 39 males and 33 females. The patients were randomized into two groups of 36 patients each. In group A, patients were directly subjected to surgery, while in group B, patients were administered albendazole for 12 weeks preoperatively, followed by a further postoperative course for 12 weeks. **Results:** Of patients who received albendazole therapy, no patient had viable cysts at the time of surgery, as compared to 94.45% of the patients who did not receive any preoperative albendazole ( $P < 0.01$ ). In patients who did not receive any albendazole therapy, recurrence rate was 16.66%, while no recurrence was seen in patients who received albendazole therapy ( $P \leq 0.05$ ). **Conclusion:** We conclude that albendazole is an effective adjuvant therapy in the treatment of hydatid liver disease.

**Key Words:** Albendazole, hydatid, recurrence, viability

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Hydatidosis is the most frequent cause of liver cysts worldwide.<sup>[1]</sup> The disease is more prevalent in rural areas with poor sanitation facilities and poor living conditions, where human beings, dogs, and cattle exist in close proximity.<sup>[2]</sup> More than 70% of cases present with an abdominal mass.<sup>[2,3]</sup> Pain in the right upper quadrant is the most common complaint in symptomatic patients. Acute, severe abdominal pain indicates rupture, biliary complications, or secondary bacterial infection.<sup>[2,4]</sup> Ultrasonography is the best diagnostic tool as it can detect cysts as small as 1 cm in diameter.<sup>[1]</sup> On the basis of ultrasonographic findings, Gharby *et al.*<sup>[5]</sup> have classified hydatid cysts of liver into five types. Type 1- pure fluid collection with well-defined borders, Type

11- pure fluid collection with a split wall, Type 111- fluid collection with multiple septa (honeycomb appearance), Type IV- heterogenous appearance, and Type V- cyst with reflecting thick walls (calcified cyst). Computed tomography (CT) of the abdomen has a sensitivity of 100% in detecting liver cyst and helps in accurate anatomic localization of cysts.<sup>[3]</sup> Various serological tests have been used for diagnosis of hydatid disease, including complement fixation test, immunoelectrophoresis, and enzyme-linked immunosorbent assay (ELISA). Among these tests, ELISA is the most widely used.<sup>[3,6]</sup>

Hydatid cyst of the liver can be managed either by nonoperative or operative methods. Operative methods may be conservative or radical. Nonoperative methods include chemotherapy and percutaneous treatment.<sup>[7]</sup> Chemotherapy can be used as an adjuvant to surgical treatment preoperatively or postoperatively, or both. A preoperative course of chemotherapy sterilizes the cysts and reduces their tension, making surgery easier. A short course of chemotherapy after surgery reduces the risk of recurrence. Bekhti *et al.* were the first to report successful

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results of chemotherapy of hydatid disease by using mebendazole.<sup>[8]</sup> Albendazole is another benzimidazole carbamate with better absorption properties. It has been noted that its metabolite, albendazole sulfoxide, is active against protoscolec of *Echinococcus granulosus* in *in vitro* cultures, and can penetrate the hydatid cysts.<sup>[7,8]</sup> When the therapeutic results of the two drugs are compared, albendazole has been found to be better than mebendazole.

The aim of our study was to assess the effect of preoperative albendazole therapy on the viability of protoscolec at the time of surgery and the effect of preoperative and postoperative use of albendazole on the recurrence rate of hydatid disease of the liver. The confirmation was made by demonstrating hydatid material—sand, hooklets, protoscolec, or daughter cysts—at the time of surgery.

## PATIENTS AND METHODS

This study was conducted in the Department of General Surgery at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, on the patients admitted with diagnosis of hydatid liver from January 2002 to December 2003, with further follow-up for another 5 years. Patients were included in the study after a proper informed written consent was taken. The infected cysts, ruptured cysts, densely calcified cysts (type V cyst), liver cyst with associated extrahepatic cysts, patients with multiple cysts, and female patients who were pregnant or intended to conceive during the study period were excluded from the study.

A total of 72 patients were studied. These patients were randomized into two groups of 36 patients each by systematic random sampling. In group A ( $n=36$ ), the patients were directly taken for surgery, while in group B ( $n=36$ ), patients were put on preoperative albendazole therapy for 12 weeks with subsequent surgery, followed by postoperative course of albendazole for another 12 weeks.

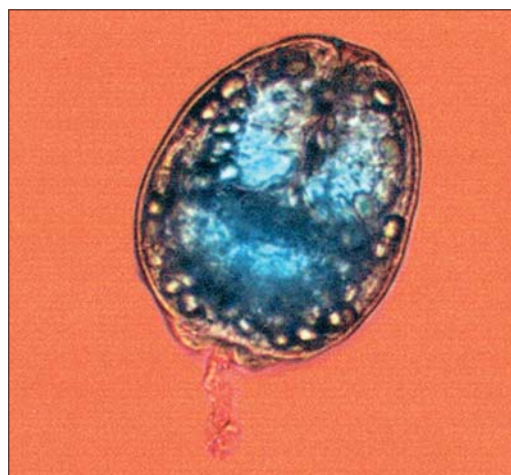
All patients were subjected to detailed history taking, physical, and systemic examination. All patients underwent various investigations such as hemogram, kidney function test, liver function test, coagulogram, electrocardiography, and X-ray of chest. Ultrasonography was the major tool for diagnosis. All patients were subjected to ELISA for hydatidosis. Computed tomography (CT) abdomen was performed in cases in which results of ultrasonography were equivocal. Patients were administered albendazole at a dose of 10 mg/kg/day in divided doses. All patients put on chemotherapy were initially monitored weekly, and thereafter monthly by liver function test, kidney function tests, white cell and platelet counts, and urine analysis.

A right subcostal approach was used in all patients for surgical

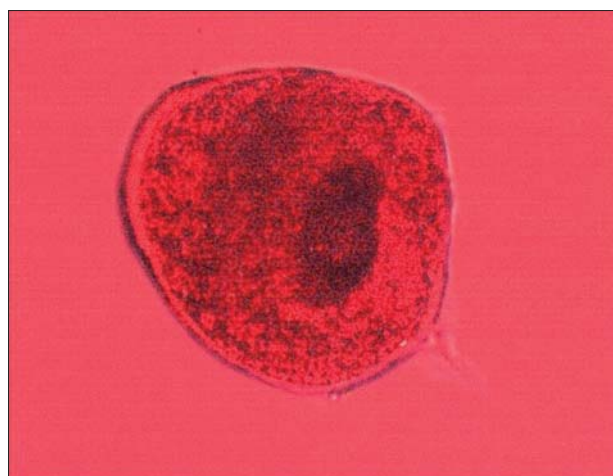
intervention. The principles of operative management include adequate exposure of the cyst, safe decompression and prevention of intraoperative contamination by use of active scolicidal agents. We used 1% povidone iodine as the scolicidal agent. Cyst contents were collected in all cases for cytological and bacteriological examination. The cyst fluid was centrifuged and examined for the fragments of laminated membrane, hooklets, and scolices. Viability assessment of the cysts was performed by observing the motility of the scolices and their ability to exclude 5% eosin, under immediate microscopy. Scolices that were motile and did not stain with eosin were considered live [Figure 1], while scolices that were immotile and stained with 5% eosin were considered dead [Figure 2]. All operative and postoperative complications were recorded.

## Follow up

All patients were followed up initially every 2 weeks for 3 months, and thereafter every month for 1 year, and,



**Figure 1:** Photomicrograph (high power) of cyst aspirate showing live protoscolex – able to exclude 5% eosin



**Figure 2:** Photomicrograph (high power) of cyst aspirate showing dead protoscolex – stained with 5% eosin

subsequently, every 3-6 months. Ultrasonography was done at every visit and cyst diameter, volume, and cyst pattern were recorded. During ultrasonographic examination, other abdominal organs were examined to exclude recurrent cyst formation. In case of any doubt, CT abdomen was done. Radiograph of chest was done at 6-month intervals to look for any hydatid disease in the lung. Hydatid serology IgG and IgM by Enzyme-Linked Immunosorbent Assay (ELISA) was done every 6 months.

### Statistical analysis

In addition to descriptive statistics, standard statistical methods were used for data analysis. These included the Student's *t* test and Chi-square test. A *P* value of <0.05 was taken as the criterion for statistical significance.

## RESULTS

Total number of patients studied was 72, which included 39 (57%) males and 33 (43%) females, and the male to female ratio was 1.3:1 [Table 1]. A majority of patients were in the age group of 26-45 years, with a mean age of  $36.77 \pm 11.45$ . Fifty-two (72%) patients belonged to rural areas, while the remaining 20 (28%) belonged to urban areas. Group A included 19 males and 17 females, while Group B had 20 males and 16 females. Abdominal pain was the most common presenting symptom (87%), followed by abdominal mass in 60% patients. About 11% patients were asymptomatic. All patients had a hemoglobin of more than 12 g, with normal kidney and liver functions. ELISA for hydatid serology was positive in all 72 patients. Coagulogram was done in all patients, with normal result in all. The right lobe of liver was the most common site of hydatid cyst in 57.81%, followed by left lobe in 32.52%, and bilobar cyst in 9.67% patients.

Of the 72 cases included in our study, 33 (45.83%) patients had type-I hydatid cyst, 18 (25%) had Type-II hydatid cyst, followed by type-III in 16 (22.22%) patients, and type-IV in 5 (6.9%) patients [Table 2]. All patients in Group A, ie, surgery only group, and 5.55% of patients in Group B (albendazole group) had viable protoscoleces at the time of surgery [Table 3]. All patients in Group B with viable cyst had multiple daughter cysts in the main cyst. Patients who had received preoperative albendazole therapy had significantly lower percentage of viable cysts at the time of surgery ( $P < 0.01$ ). In our series of 72 operated patients, 6 (16.66%) patients in Group A developed postoperative recurrence, while none of the patients from Group B developed any recurrence in the mean follow-up period of 5 years [Table 4].

All patients treated with albendazole tolerated the drug without any severe side effects. Gastrointestinal symptoms

**Table 1: Age and sex distribution of the study population (n=72)**

	Group A (n=36)	Group B (n=36)
No. males	19	20
No. females	17	16
Age (yrs)		
Mean	36.75	36.78
+SD	11.34	11.79
Range	16-64	17-62

**Table 2: Types of hydatid cysts in different groups (n=72)**

Type (n=72)	Total (%)	Group A (n=36) (%)	Group B (n=36) (%)
Type I	33 (45.83)	12 (33.33)	11 (30.55)
Type II	18 (25)	10 (27.25)	11 (30.55)
Type III	16 (22.22)	8 (22.22)	10 (27.77)
Type IV	5 (6.9)	6 (16.66)	4 (11.11)

**Table 3: Comparison of cyst viability in two study groups as determined by scolices motility and ability to exclude 5% eosin**

Study groups	Viable no. (%)	Non-viable no. (%)
Group A (n=36)	36 (100)	0 (0)
Group B (n=36)	2 (5.55)	34 (94.45)

$\chi^2 df_3 = 49.44; P < 0.01$

**Table 4: Comparison of recurrence in the two study groups**

Study groups	Follow-up (yrs)	Recurrence no.	%
A (n=36)	5	6	16.66
B (n=36)	5	nil	nil

$P \leq 0.05$

(mild abdominal pain, nausea, vomiting) were observed in 4.16% of patients. Reversible alopecia was observed in 2% of the patients. There was no derangement in liver function tests in any of the patients.

## DISCUSSION

Liver is the most common site of hydatidosis.<sup>[1]</sup> The mainstay of treatment of hepatic hydatid disease is surgery.<sup>[1]</sup> Mebendazole was the first drug to be used for hydatid disease.<sup>[9]</sup> Later, Albendazole was introduced as it has better absorption properties. Both these drugs belong to benzimidazole carbamate group of antibiotics.<sup>[10,11]</sup> Albendazole given preoperatively in a dose of 10 mg/kg/day for 1 month kills most of the protoscoleces within the hepatic hydatid cyst.<sup>[11]</sup> However, better results have been reported after 3 months of uninterrupted treatment with albendazole.<sup>[10-14]</sup> The usual dosage scheme for albendazole, suggested by Horton (1989) and endorsed by World Health Organization

(WHO) is, three 28-day courses of 10 mg/kg/day in divided doses separated by 2-week intervals.<sup>[15]</sup> These benzimidazole carbamate groups of drugs act by blocking glucose uptake in the parasite and depletion of its glycogen stores.

Praziquantel is another drug used against hydatid cyst liver disease in the dose of 40-60 mg/kg/day in divided doses.<sup>[15,16]</sup> It is the most active and rapid scolicidal agent. It is highly effective against protoscolices.<sup>[13]</sup> Praziquantel is probably an ideal agent for prophylaxis in the preoperative and postoperative setting to prevent implantation of protoscoleces and subsequent recurrence.<sup>[15,16]</sup> It is unlikely to be as effective as albendazole in treating whole cyst, as it is less active against germinal layer of the hydatid cyst.<sup>[15]</sup>

Chemotherapy is effective in small cysts with diameter less than 4 cm, those with thin walls; this is also effective in younger patients.<sup>[6,7,13]</sup> It is indicated in patients who are at high risk for surgery, in patients with multiple peritoneal cysts, cysts in multiple organs, bone cysts, cyst in brain, to prevent secondary echinococcosis after spillage during surgery and as a concomitant therapy with percutaneous drainage.<sup>[7,13]</sup> Recently, percutaneous drainage of hydatid cysts, popularly known as the puncture, aspiration, installation of scolicidal agent and reaspiration (PAIR) technique, has been used.<sup>[7,13]</sup>

A prospective study was carried out to determine the role of albendazole in the management of hydatid disease of the liver. Albendazole used in the dose of 10 mg/kg/day in divided doses as an adjuvant therapy to surgical treatment significantly improved the results in our patients. Cyst viability at the time of surgery was significantly decreased in patients in whom albendazole was used preoperatively, as was demonstrated by the motility of the scolices and their ability to exclude 5% eosin under immediate microscopy. Of the patients who received preoperative albendazole for 3 months, only 2 (5.55%) patients had viable cysts at the time of surgery as compared to 94.55% of patients who did not receive any preoperative albendazole therapy. This decrease in cyst viability was statistically significant ( $P < 0.01$ ) and indicates that 3 months of preoperative course of albendazole kills most of protoscoleces within hydatid cysts.

In our study, only two patients had viable cysts and in both patients, cysts contained multiple daughter cysts. Protoscoleces in the main cyst were dead, while in daughter cysts, these were viable. It is because preoperative albendazole while being successful in killing the parasites within the mother cyst is not fully effective in eradicating the scolices in the daughter cysts. This may be due to poor penetration of the drug into the daughter cysts enclosed within the mother cyst.

Our results and observations are in agreement with several

previous studies. Sajad Hussain Arif *et al.*<sup>[16]</sup> conducted a study involving 64 patients. Of these, 32 patients were directly taken for surgery, while another 32 patients were put on preoperative albendazole for 8 weeks at the dose of 10 mg/kg/day. Of those patients who received preoperative albendazole, only 9.37% patients had viable cysts at the time of surgery as compared to 96.87% patients who did not receive any preoperative albendazole. In patients who did not receive any albendazole therapy, the recurrence rate was 16.66%, while no recurrence was seen in patients who received albendazole therapy. Morris<sup>[14]</sup> managed 16 patients with preoperative albendazole at the dose of 10 mg/kg/day for a variable period of 1 week to 1 month. Of the 14 patients who received albendazole for 1 month or more before operation, only one had viable protoscoleces. In contrast, each of the two remaining patients who received therapy for only one and three weeks had liver disease at the time of operation. Horton<sup>[15]</sup> treated 500 patients with 800 mg of albendazole daily in cycles of 28 days with a drug-free interval of 2 weeks between the cycles for a mean duration of 2.5 cycles. A recurrence rate of 18.75% was noticed over a follow-up period of 5-6 months in patients who did not receive any albendazole, while preoperative use of albendazole was found to significantly reduce the risk of recurrence to 4.16%.

During a follow-up period of 5 years, there was no recurrence in any of our patients treated with albendazole therapy. This is in agreement with observations made by Evangelos *et al.*<sup>[17]</sup> who treated 67 patients having liver hydatidosis with preoperative mebendazole at the dose of 40 mg/kg/day (18 patients) or albendazole at the dose of 10 mg/kg/day in 49 patients for 5 days before surgery. This was followed by a 1-month course of the same benzimidazole in patients with viable protoscoleces at the time of surgery. None of these patients had any recurrence of disease after a follow-up of 15-67 months (average, 41 months).<sup>[17]</sup> Mottaghlan and Saidi<sup>[18]</sup> observed a recurrence of 11.3% over a period of 6 months to 3 years in a study comprising 106 patients. Little *et al.* observed a recurrence rate of 22% in his study.<sup>[19]</sup> Morris in 1989 observed no recurrence in patients treated with preoperative albendazole for 1 month, with a median postoperative follow-up of 28 months.<sup>[20]</sup>

## CONCLUSION

Preoperative and postoperative use of albendazole decreases the viability of cysts at the time of surgery and significantly reduces the chances of cyst recurrence. Thus, we conclude that albendazole is an effective adjuvant therapy in the management of hepatic hydatid cyst.



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