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ALBENDAZOLE THERAPY FOR HEPATIC HYDATID DISEASE

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Khayitov Ilkhom Bakhodirovich
The chair of Surgical diseases in family medicine
Tashkent State Medical University
Tashkent, Uzbekistan
ilhom.med.1979@mail.ru
Jabbarov Elyor Normuminovich
Surgical department of "Dusel" private clinic
Tashkent, Uzbekistan
Shukurov Abdurasul Abdurakhmonovich
Surgical department of "Dusel" private clinic
Tashkent, Uzbekistan
Babajonov Akhmadjon Bakhodirovich
The chair of Surgical diseases in family medicine
Tashkent State Medical University
Tashkent, Uzbekistan
babadjan.md@gmail.com
https://orcid.org/0000-0001-8921-0028

Background: Echinococcosis is one of the most common parasitic diseases in humans. The disease is more frequently encountered in rural areas of Southern Europe, North Africa, South America, Australia, and Central Asia, where it represents a social problem. The liver is most commonly affected in humans, followed by the lungs in frequency of involvement, with other organs being significantly less affected [7]. Today, treatment of echinococcal cysts is predominantly surgical in nature. To avoid recurrence, viable scolices in the echinococcal cyst must be removed before surgical evacuation. The liver is the most common site of echinococcus occurrence [14]. The effectiveness of various preventive and treatment methods with anti-recurrence focus in echinococcosis is traditionally evaluated by the recurrence rate of the disease in operated patients. Meanwhile, clinical practice and analysis of literature sources [2,13]. The basis of hepatic echinococcosis treatment is surgical intervention [14,16]. Mebendazole was the first drug used in hepatic echinococcosis [4]. Albendazole was later introduced due to its better absorption properties. Albendazole administered before surgery at a dose of 10 mg/kg/day for 1 month kills most protoscolices in hepatic hydatid cysts [9]. However, better results were reported after 1.5 months of continuous

albendazole treatment [5,6]. The standard albendazole dosing regimen proposed by Horton (1989) and approved by the World Health Organization (WHO) consists of three 28-day courses of 10 mg/kg/day in divided doses, separated by 2-week intervals [11]. These benzimidazole carbamate drug groups act by blocking glucose uptake by the parasite and depleting its glycogen stores.

Biltricide is an anthelmintic agent used against hepatic echinococcal cysts at a dose of 40-60 mg/kg/day in divided doses. It is the most active and rapid scolicidal agent. It is very effective against protoscolices [10]. Biltricide is probably the ideal agent for prophylaxis in preoperative and postoperative settings to prevent protoscolex implantation and subsequent recurrence [1,11]. It is unlikely to be as effective as albendazole in treating the whole cyst, as it is less active against the germinal layer of the echinococcal cyst [11].

Chemotherapy is effective for small cysts less than 5 cm in diameter with thin walls; it is also effective in younger patients [3,10,12]. Albendazole therapy is indicated in patients at high surgical risk as adjunctive therapy with percutaneous drainage [10,12]. Recently, percutaneous drainage of echinococcal cysts has been used, widely known as the puncture, aspiration, injection of scolicidal agent, and reaspiration (PAIR) method [10,12]. PAIR is indicated for small cysts, and PAIR for large cysts in combination with medical therapy is an effective treatment method for hepatic echinococcosis [8]. The action of albendazole on echinococcal cysts remains controversial. Albendazole is the drug of choice against this disease because its degree of systemic absorption and penetration into cysts is higher than other anthelmintic drugs.

Thus, some questions regarding immediate and long-term postoperative results remain open.

The aim of our study was to evaluate albendazole therapy on scolex viability during surgery and the effect of postoperative albendazole use on recurrence rates in hepatic echinococcosis.

Materials and methods. A total of 92 patients were studied, including 47 men (51%) and 45 women (49%), with a male to female ratio of 1.1:1. Most patients were in the age group of 26-45 years, with a mean age of 36.77. 62 (%) patients belonged to rural areas, while the remaining 20 (%) belonged to urban areas. All patients were divided into two groups of 46 patients each by systematic random sampling. In group A (n = 46), patients were taken directly for surgery, while in group B (n = 46), patients underwent preoperative albendazole therapy for 6 weeks followed by surgery, after which a postoperative course of albendazole followed for another 6 weeks. Group A included 24 men and 22 women, while group B had 23 men and 23 women. Abdominal pain was the most common symptom (87%), followed by

abdominal mass in 60% of patients. About 11% of patients were asymptomatic. All patients had hemoglobin above 11 g/L with normal kidney and liver function. ELISA for echinococcal serology was positive in all 92 patients. The right lobe of the liver was the most common site of echinococcal cysts in 57.81%, left lobe in 32.52%, and bilobar cysts in 9.67% of patients.

All patients underwent various investigations such as hemogram, kidney function tests, liver function tests, coagulogram, electrocardiography, and chest X-ray. Ultrasound was the main diagnostic tool. Abdominal computed tomography (CT) was performed in cases where ultrasound results were ambiguous. Patients were administered albendazole at a dose of 10 mg/kg/day in divided doses. All patients undergoing chemotherapy were initially monitored weekly and then monthly with liver function tests, kidney tests, white blood cell and platelet counts, and urinalysis.

All patients were followed up initially every 2 weeks for 3 months, then monthly for 1 year, and then every 3-6 months. Ultrasound was performed at each visit, recording the diameter, volume, and nature of the cyst. During ultrasound, other abdominal organs were examined to exclude cyst recurrence. In case of any doubts, abdominal CT was performed. Chest X-ray was taken at 6-month intervals to detect any lung cysts. Serological testing of IgG and IgM by enzyme-linked immunosorbent assay (ELISA) was performed every 6 months.

Results and discussion. A retrospective study was conducted to determine the role of albendazole in the treatment of hepatic echinococcosis. The use of albendazole at a dose of 10 mg/kg/day in divided doses as adjunctive therapy to surgical treatment significantly improved outcomes in our patients. Cyst viability during surgery was significantly reduced in patients who used albendazole before surgery. Of patients who received preoperative albendazole for 3 months, only 2 (5.55%) patients had viable cysts during surgery compared to 94.55% of patients who did not receive preoperative albendazole therapy. This reduction in cyst viability was statistically significant ($P < 0.01$) and indicates that albendazole kills most protoscolices in echinococcal cysts 3 months before surgery.

In our study, only two patients had viable cysts, and both patients' cysts contained multiple daughter cysts. Protoscolices in the main cyst died, while in the daughter cysts they were viable. This is because preoperative albendazole, while successful in destroying parasites in the mother cyst, is not completely effective in eradicating scolices in daughter cysts. This may be due to poor drug penetration into daughter cysts enclosed within the mother cyst.

Of these, 32 patients were taken directly for surgery, while another 32 patients underwent preoperative albendazole treatment for 8 weeks at a dose of 10

mg/kg/day. Of those patients who received preoperative albendazole, only 9.37% of patients had viable cysts during surgery compared to 96.87% of patients who did not receive preoperative albendazole. In patients who did not receive any albendazole therapy, the recurrence rate was 16.6%, while in patients who received albendazole therapy, no recurrences were observed. Morris [14,15] treated 16 patients with preoperative albendazole at a dose of 10 mg/kg/day for a variable period from 1 week to 1 month. Of 14 patients who received albendazole for 1 month or more before surgery, only one had viable protoscolices. In contrast, each of the two remaining patients who received therapy for only one and three weeks had liver disease during surgery. Horton treated 500 patients with 800 mg of albendazole daily in 28-day cycles with a 2-week drug-free interval between cycles for a mean duration of 2.5 cycles. The recurrence rate was 18.75% during the 5-6 month follow-up period in patients who did not receive albendazole, while preoperative use of albendazole was found to significantly reduce the risk of recurrence to 4.16%.

During the 3-year follow-up period, there were no recurrences in any of our patients who received albendazole therapy. This is consistent with observations made by leading specialists in hepatology.

Conclusion:

1. Preoperative and postoperative use of albendazole reduces cyst viability during surgery and significantly reduces the likelihood of cyst recurrence.
2. Chemotherapy in combination with percutaneous aspiration or PAIR therapy can lead to cyst size reduction and in our study, it improved the effectiveness of hepatic echinococcosis treatment.
3. When surgery cannot be avoided, preoperative use of albendazole in echinococcal invasion reduces the risk of recurrence and facilitates surgical intervention by reducing intracystic pressure.

Thus, we conclude that albendazole is an effective therapy in the treatment and prevention of hepatic echinococcal cyst recurrence.

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