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Short Communication

A 20 Years Retrospective Descriptive Study of Human Cystic Echinococcosis and the Role of Albendazole Concurrent with Surgical Treatment: 2001-2021

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Abstract

Background: Hydatid cyst, caused by the larvae of *Echinococcus granulosus*, is one of the most severe cestode infections occurring in Iran. The liver is the most commonly involved organ. The present study was carried out to review the demographic of 20 years surgically treated hydatic cysts.

Methods: Ninety-eight patients were enrolled in the study. Demographic features, time of surgery, cyst size, and albendazole usage have been reviewed from the medical records of patients in Loghman Hakim Hospital, Tehran, Iran, from 2001 to 2021. Statistical analysis was performed to find any correlation between the uses of concurrent albendazole with surgical procedure.

Results: Of 98 patients with hydatid cyst, 57 (58.2%) were female. The mean age of patients was 39.4 ±18.7 yrs, and the mean surgery time was 217.5 ± 81.4 minutes. Regarding the infection site, the liver (60.2%) and lungs (22.4%) were the most affected organs, respectively. 56.1% of patients had one cyst, and 42.9 % had two or more cysts. 20.4% of them had taken albendazole before surgery, but 86.7 % took it after the operation. No recurrent cysts were seen among 91.8% of them, but 8.2% mentioned suffering from a recurrent cyst. 85.7% of those recurrent cases did not receive albendazole before surgery, and 75% of recurrent cases after surgery did not take albendazole ($P<0.05$).

Conclusion: Administration of albendazole before and after the operation was significantly related to reduced recurrence, bleeding, morbidity, and even the time of surgery.

Introduction

Iran in the is one of the hydatid cyst endemic regions of the world reported by the WHO (1). In Iran, echinococcosis is actively transmitted, with an estimated annual incidence of 0.61 per 100,00 (2) .The positive effects of Albendazole on hydatidosis in the preoperative period have been described in the literature (3, 4). Although the mandatory step in the treatment of hydatidosis has remained surgical intervention, perioperative administration of benzimidazole carbamates (e.g., mebendazole) can improve outcomes (5).

Some studies have been conducted to date about the preoperative and postoperative effects of albendazole as an adjuvant antibiotic alongside the primary surgical intervention (6). In general, it seems that administration of albendazole in the perioperative era leads to reduced cysts viability and the risk of recurrence (7). Also, in the cysts with lower diameters, taking albendazole can be used as the only treatment (8).

Considering new surgical and nonsurgical methods have been introduced to treat hydatid cysts; still, traditional open surgery is the mainstay of treatment (2). On the other hand, other therapies like laparoscopy and percutaneous treatment (PAIR) have their own limitations and disadvantages. They cannot be used in every case (9).

Nevertheless, the open surgical procedure has its own complications like prolonged operation time. Since previous studies reported that the usage of albendazole in the preoperative period could reduce the time of surgery (6), we decided to review our experience in this context. We aimed to present the experience of our institution in the surgical management of liver hydatid disease over a period of 20 years and to assess the effect of preoperative usage of albendazole concurrent with surgical treatment on operation duration and postoperative complications including recurrence rate, morbidity and mortality.

Methods

We reviewed all the medical records with echinococcosis diagnosis based on the International Statistical Classification of Diseases (ICD-10:B67) (10).The study was conducted at Loghman Hakim Hospital, Tehran, Iran, a referral center for infectious diseases and admits patients from all around the country. We included the medical records available in electronic formats from September 2001 to August 2021. In addition, we searched the files manually in known cases with no electronic data available and extracted the data.

All the data collection and study process was under supervision of Ethical Committee of Shahid Beheshti University of Medical Sciences numbered: IR.SBMU.MSP.REC.1400. 697.

For each confirmed case, demographic information like age, gender, occupation, number of cysts, location and size of the cysts, utilizing albendazole, recurrence, and residence status (rural/urban) were entered into an electronic spreadsheet. Reviewing and entering the data was performed by a trained general surgery resident (PGY-4) and rechecked by the authors.

The surgical procedure was open surgery with midline or subcostal laparotomy. After entrance to the abdomen and exploring the intraabdominal space, the pericystic area was filled with laparotomy pads soaked with scolocidal agents like Silver nitrate or hypertonic saline (20%). Then the cysts were drained after injection of about 20 cc of scolocidal agents (11). In every case, the surgeons placed two draining tubes: one inside the cavity of the cysts and another in the subhepatic region to find the bile leakage. Our study described morbidity after surgery was prolonged bile leak, treated with sphincterotomy (12). So, the variable morbidity" in the text can be considered as

prolonged bile leakage after the surgery. In addition, the dosage of albendazole in both preoperative and postoperative periods was 400 mg twice a day. Patients were categorized as full dosage preoperative treatment with albendazole if they took it for 4 weeks before surgery. Patients were also considered in group treated with albendazole after surgery if they took it for 6 months afterwards.

We did not define any age restriction for including the study. However, in cases of very young infants, we excluded the records. Very young children were referred to a children's hospital. Also, medical records that had important missing data (e.g., surgery reports) were not entered in the study. On the other hand, we just enrolled the cases with Iranian nationality. We came across some records from adjacent countries (Afghanistan and Pakistan) during the review process and excluded them. In addition, we omitted the records from the final dataset in the cases of surgical interventions other than laparotomy, e.g., Laparoscopy or Percutaneous treatment of the hydatid cyst (PAIR).

The final dataset was imported to IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA). We used descriptive analysis for quantitative variables. In addition, for qualitative variables, frequencies were used. The comparable parameters were analyzed by one-way ANOVA and chi-square (Fisher exact test) tests, and $P < 0.05$ was accepted to be statistically significant.

Results

Nighty eight patients (58.2% female) were included in the study. The majority of the cases (57.1%) had a single cyst. The liver was the most common organ involved (60.2%), and in 11.2% of cases, both liver lobes were affected. The cysts were frequent in the lungs, abdomen, brain, skeletal muscles, and spinal cord, respectively Most of the patients lived in urban areas, and 36 (36.7 %) were from rural areas. (Table 1).

Information about perioperative variables like operation time, length of stay, and the diameter of the cyst has been mentioned in Table 2.

Table 1: Demographics and distribution pattern of cysts

Variable				
Age (yr)	2-77		39.76 ± 18.43	
Sex	Male		41(41.8%)	
	Female		57 (58.2%)	
Location of cyst	Liver	Right lobe	59 (60.2%)	30 (39.7%)
		Left lobe		8 (8.1%)
		Bilobar		11 (11.2%)
	Lung		22 (22.4%)	
	Brain		6 (6.1%)	
	Skeletal muscles		2 (2%)	
	Abdomen		8 (8.2%)	
	Spine		1 (1%)	
Number of cysts	1 cyst		56 (57.1%)	
	2 or more cysts		42 (42.9%)	

Table 2: Clinical and Radiological data

Variable	*Min-Max*	*Mean ± SD*
Surgery time (minutes)	90-480	217.55 ± 81.41
Hospital stay (days)	1-42	9.13 ± 7.03
Cysts diameter (millimeter)	8.41 – 300	89.30 ± 47.42

Preoperative systemic albendazole was used as tablets for an average of 5.37 ±2.42 days (0-18 days). Most of the patients took albendazole for less than two weeks. In addition, the patients were treated with albendazole in the postoperative period for 0-20 months (6.98 ± 4.53 months). Only 20 cases (20.4%) have taken albendazole before surgery, but 86.7 % of them took albendazole after surgery. No recurrent cysts were seen among 91.8 % of whole cases, but 8.2 % developed recurrent cysts. Among recurrent cases, 85.7% of them had not received albendazole before surgery, and 75 % of them did not take albendazole after surgery (P<0.05) (Table 3).

Table 3: Correlation between taking albendazole before and after surgery and recurrence of cysts

Variable N (%)		*No recurrence N (% of recurrence)*	*Recurrence N (% of recurrence)*	*Chi-square*	*95 % CI*	*P-value*
Albendazole before	Yes 20 (20.4)	19 (21.1)	1 (12.5)	80.81	0.007 – 0.39	0.004
	No 78 (79.6)	71 (78.9)	7 (87.5)			
Albendazole after	Yes 79(80.6)	77 (85.6)	2 (25)	93.50	0.006 – 0.10	0.00
	No 19(19.4)	13 (14.4)	6 (75)			

No morbidity was seen among 87 (88%) of whole cases but 11 cases (11.2 %) presented with some degrees of prolonged bile leakage after the surgery. Of cases with morbidity after surgery, 81.8% of them had not taken albendazole before surgery, and 45.5 % of them did not take albendazole after surgery. Taking albendazole before and after surgery was significantly related to occurring morbidity after surgery (P<0.05) (Table 4).

Table 4: Correlation between taking albendazole before and after surgery and morbidity after hydatid cyst

Variable N (%)		*Without morbidity N (% of morbidity)*	*With morbidity N (% of morbidity)*	*Chi-square*	*95 % CI*	*P-value*
Albendazole before	Yes 20 (20.4)	18 (20.7)	2 (18.2)	67.06	0.02 – 0.47	0.003
	No 78 (79.6)	69 (79.3%)	9 (81.8)			
Albendazole after	Yes 79(80.6)	73 (83.9)	6 (54.5)	71.49	0.12 – 0.99	0.04
	No 19(19.4)	14 (16.1)	5 (45.5)			

As you can see the details in Tables 5 and 6, we compared the effects of using albendazole in the preoperative period on the variables such as blood loss during the surgery and the time of operation. There were no significant correlations between taking albendazole and these variables.

Table 5: Correlation between taking albendazole before surgery and time of operation

Variable N (%)		*Operation time≥200minutes N (%)*	*Operation time<200minutes N (%)*	*Chi-square*	*P-value*
Albendazole before	Yes 20 (20.4)	11 (55)	9 (45)	49.04	0.83
	No 78 (79.6)	50 (64.1)	28 (35.9)		

Table 6: Correlation between taking albendazole before surgery and blood loss during surgery

Variable N (%)		*Blood loss during operation ≥500milimiteres N (%)*	*Blood loss during operation <500milimiteres N (%)*	*Chi-square*	*P-value*
Albendazole before	Yes 20 (20.4)	13 (65)	7 (25)	29.03	0.69
	No 78 (79.6)	46 (58.97)	32 (41.03)		

Discussion

Human infection with *E. granulosus* in different areas of Iran is common (2, 13). In Iran, this disease is responsible for 4% of hospital admissions in the general surgery ward (13-15). Nevertheless, the accurate prevalence of the disease is not estimated yet in Iran. Due to the vast differences in the geographical features of Iran's provinces, the incidence rate of infections may differ for each region (16). A myriad of descriptive studies is available about the incidence of hydatidosis in many areas of Iran. However, their validity and methodology are not clear enough. But some reported that the incidence of hydatidosis is about 0.6-12 per 100000 (17). However, we assume that due to public education and warnings from the Ministry of Health and greater control over the slaughter of livestock, this rate has declined in recent years.

Clinical signs depend on the size and the site of the involved organ. Most patients are asymptomatic. However, patients may be symptomatic if the cysts become infected or abscesses formed (18). Nevertheless, some patients may have even multiple asymptomatic cysts inside their bodies.

The liver was the most common location of hydatid cysts in our study (2, 14, 19). Our research found that the lung, brain, skeletal muscles, abdomen, and spine were other infected organs. However, the echinococcal infection can involve any organ, and many clinical cases have been reported so far. Females were more affected than males (58.2% vs. 41.8%), similar to other reports in Iran (17, 20). Maybe the main reason the echinococcal infection is more prevalent among women in Iran is that many household chores, such as

cleaning the house and caring for animals, are done by women.

The treatment of echinococcosis is based on size, location, and complications. The most common site of infection is the liver, followed by the lungs and brain, but it can affect all parts of the body (18). Surgical treatment is chosen except when the hydatid cyst is small, asymptomatic, and isolated, or with radiological evidence of cyst inactivation (21, 22). Various surgical approaches have been described. Traditionally open surgery is used widely around the world. In addition, minimally invasive methods are reported by some surgeons. The laparoscopic approach, for example, can be a safe alternative method in selected patients. Although randomized clinical trials in this context are not done correctly, many descriptive studies have been performed about the advantages of this method (23). All patients of this study were operated with open surgery with midline or subcostal laparotomy.

Albendazole and mebendazole are two antiparasitic agents from the benzimidazole family, and its anthelminthic action is known well. The use of albendazole perioperatively (before and after surgery) has been identified as an influential factor in reducing postoperative recurrence. The preventive dose of albendazole varies in different studies, but we concluded that the administration of 400 mg twice a day is more prevalent among clinicians (16, 24). The effects of this medicine on various variables have been investigated. For example, several valid studies confirmed the lower recurrence rate with the administration of albendazole. In addition, this drug prevents cysts from growing and even making them shrink (16). This could help the surgeon to operate on the patient with less blood and faster. We also found out that albendazole usage is associated with a decreased time of surgery and even reduced bleeding during the operations.

During 20 years of follow-up, 8.2 % of patients developed recurrent cysts. In existing studies, the recurrence rate after surgery has been reported between 1.1 and 11% (2, 19, 25). This shows that the recurrence rate in our center was not higher than average compared to previous studies.

Finally, we should declare that we performed a descriptive analysis of single-center medical cases. We know that it is necessary to design multiple randomized trials to draw firm conclusions. However, hydatid cyst is not so common to recruit a high volume sample for this mean. As a result, developing a trial with the appropriate sample size may require years of time and expense.

Conclusion

Using albendazole in the perioperative era may be helpful to lower the recurrence rate, time of surgery, and even size of the cysts. The surgeon should keep in mind that the administration of this medicine could not eradicate cysts. There is also a low risk of recurrence even in patients who used the drug preoperatively. Since we have some limitations in the study, further trials in the context are recommended.

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Conflict of Interest

The authors declare that there is no conflict of interests.

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