

Percutaneous treatment of liver hydatid cysts : outcome of direct injection of albendazole under ultrasonographic guidance

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Abstract:

Objectives: To evaluate the efficiency of percutaneous aspiration and intracystic injection of albendazole in the treatment of liver hydatid cysts under ultrasonographic guidance.

Patients and methods: A prospective study of 64 patients underwent percutaneous treatment for 72 hydatid liver cysts under ultrasound guidance in Al-Thawrah & Al-Rayyan hospitals, Sana'a, & Mukalla respectively, Yemen. The PAI (percutaneous aspiration and injection) method was used. The cyst was punctured and most of the cyst content was aspirated, then albendazole solution was injected. Adjuvant oral albendazole was used one week before and one month after procedure. All patients underwent serial ultrasound follow up for three years and the therapeutic response was based on the sonographic changes of the cyst and the serology titers.

Results: PAI was successfully performed for all 72 liver hydatid cysts with about 24 hours median hospital stay. All treated cysts showed collapse and detached endocyst immediately after treatment, and re-expanded to almost its original size during first week, then a progressive decrease in size was noted after the first month. At the last follow up, the main reduction of cyst volume was about 70% and the ultrasound appearances were 63% solid form and 37% of mixed solid and fluid form. Only two cysts showed recurrence (of multivesicular type). Minor complications of the treatment were noted included urticaria, fever, hypotension and slight right pleural effusion.

Conclusion: PAI of albendazole is safe and highly successful in the treatment of liver hydatid cysts especially univesicular type.

Key words: Hydatid cyst, albendazole, aspiration, sonography.

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العلاج عن طريق الجلد للأكياس العدارية الكبدية: نتيجة الحقن المباشر للألبيندازول تحت توجيه الموجات فوق الصوتية

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الملخص :

الهدف: تقييم فعالية اخراج سائل الكيسة العدارية في الكبد وحقنها بعقار ألبيندازول عن طريق الجلد تحت توجيه الموجات فوق الصوتية.

الطريقة: أجريت دراسة لـ 64 مريض خضعوا للعلاج بالحقن عبر الجلد لـ 72 كيس عداري في الكبد تحت توجيه الموجات فوق الصوتية في مستشفى الثورة، صنعاء، و الريان، المكلا، اليمن. تم بسحب ماء الكيس عن طريق الجلد بثقب الكيس واخراج معظم محتواه ثم يتم حقن محلول ألبيندازول، مع استخدام ألبيندازول عن طريق الفم لأسبوع واحد قبل اجراء التداخل وكذلك لمدة شهر واحد من الإجراء. جميع المرضى خضعوا للموجات فوق الصوتية بصورة دورية لمدة 3 سنوات واستندت الاستجابة العلاجية على تغييرات صورة الموجات فوق الصوتية للأكياس و معايير الأمصال.

النتائج: تم تنفيذ الإجراء بنجاح للأكياس الكبدية الـ 72 مع حوالي 24 ساعة متوسطة مدة البقاء في المستشفى. وأظهرت جميع الأكياس المعالجة انفصال في الجدار الداخلي وانهيار في حجم الكيس فوراً بعد العلاج واستعادة حجمه الأصلي خلال الأسبوع الأول، ثم انخفاض تدريجي في حجمه بعد الشهر الأول. في آخر متابعة كان النقص في حجم الكيس حوالي 70%، وكانت 63% منها على صورة صلبة و 37% منها مادة صلبة وسوائل مختلطة. اثنين فقط من الأكياس اظهرت عودة المرض فيها (من نوع متعدد الأكياس). وقد لوحظت مضاعفات طفيفة فقط من العلاج شملت: الشرى، الحمى، انخفاض ضغط الدم وانصباب جنبي طفيف في الجهة اليمنى.

الخلاصة: الإجراء التداخلي لأكياس الكبد العدارية عن طريق الجلد بحقنها بالألبيندازول هو علاج آمن حقق نجاحاً كبيراً في علاج كيسات الكبد المائية (وخاصة النوع الأول والثاني).

الكلمات المفتاحية: كيس مائي (عداري)، ألبيندازول، شفت، موجات فوق صوتية

Introduction:

Hydatid disease is endemic in many parts of the world, most frequently localized in the liver [1]. Treatment of hydatid liver cysts has to be considered mandatory in symptomatic cysts and recommended in viable cysts because of risk of severe complications [2,3]. Surgical treatment used to be accepted as the first choice of treatment, which is unfortunately an invasive method with high rates of morbidity and mortality [4,5]. In addition, long hospital stay, high costs and lack of surgical facilities in poor countries are also considered disadvantages of surgery.

In recent years medical and percutaneous treatment of liver hydatid cyst have been used frequently as an alternative to surgery [6,7]. This conservative treatment was previously contraindicated because of possibility of anaphylactic shock and cholangitis [8]. However all previous published reports of percutaneous treatment of hydatid cyst showed that this procedure is safe and efficient [3,6,7,9,10]. This method was known as puncture-aspiration-injection-reaspiration (PAIR) and was recommended by the WHO as an alternative method to surgery [11].

Several types of sclerosing solutions, such as hypertonic saline, alcohol, hydrogen peroxide and silver nitrates are commonly used for percutaneous treatment of hepatic cysts, but these scolicidal solutions can produce toxic effects to biliary tree [12]. The efficacy of systemic chemotherapy with an abenzimidazole derivatives is limited because only small amounts of the drug can be transported to the hydatid cyst fluid. However, a recent report advocated that direct injection of benzimidazole derivatives (albendazole and mebendazole) solution into the cyst cavity is less toxic scolicidal agent and will provide a high intracystic concentration of the drug [13].

In our study we will evaluate the efficacy of percutaneous direct injection of albendazole solution into the hydatid liver cyst using PAI technique under Ultrasound guidance with long term follow up.

Patients and methods:

This prospective study was conducted in Al-Thawrah General Hospital - Sana'a, and Al-Rayyan specialized Hospital –Mukalla, Yemen between April 2009 and March 2014. 64 patients with 72 liver hydatid cysts (34 males and 30 females) with a mean age of 35 years (range 14-65 years) were treated with percutaneous intracystic injection of albendazole solution under ultrasound guidance. PAI technique

was used.

Inclusion criteria: patients with proved type 1, 2 and 3 hepatic hydatid cysts having single/multiple hepatic hydatid cysts who accepted this procedure as an alternative to surgery, patients who refused surgery or to whom surgery was prohibited, and patients who had relapse after surgery and adequate liver parenchyma (>5 mm) surrounding the cyst.

Exclusion criteria: cysts which were inaccessible to puncture, peripheral cysts having <5 mm of surrounding hepatic tissue according to Rajesh et al [14], cysts with communication to the biliary tree, type 4 and 5 hydatid cysts as they are tumor like and calcified respectively, history of anaphylaxis or atopy, and uncooperative patients.

Hydatid cysts are classified according to Gharbi et al [15]. Oral albendazole (10 mg/kg/day) was given for all patients one week before, and one month after the procedure. In addition, all patients were given anti allergic prophylactic treatment before intervention. Necessary laboratory investigations included serum blood indirect hemagglutination test, liver function tests and coagulation function/bleeding profile were performed before intervention.

A real time US with a 3.5 MHz probe (GE Voluson 730) was used in all patients before treatment to localize the cyst to be punctured. The relation of the cyst to the normal liver tissues was delineated and the site of puncture was marked in such that the cyst could be approached through the normal liver tissue to avoid risk of seeding. Albendazole solution was prepared as 1 oug/ml of normal saline. Under full aseptic conditions in the localized intervention area, local anesthesia were injected intradermally. A 15 or 20 cm long fine needle (20 gauge) was inserted into the cyst cavity and most of the cyst was aspirated under US guidance, and then the solution of albendazole was injected in the cyst cavity in one quarter of the amount of cyst volume.

All patients admitted in the hospital and observed for 24 hours. Then, all patients were followed up by US after the procedure, during hospitalization and at one week, one month, 3 months, 6 months, one year, after 2 years and after 3 years of treatment (cystic changes were recorded in each examination). The aspirated fluid was sent immediately after procedure to the laboratory for the detection of vital scolices. Indirect haemagglutination assay titer was monitored after one month of the procedure and then every 6 months.

The following criteria were used to assess the demise and activity of the cyst: reduction of the cyst size, absence of vital scolices in the aspiration contents and irregularities of cyst wall. Recurrence was defined as increase in cyst dimension or fluid contents, development of daughter cyst, persistence of high indirect haemagglutination assay titer and persistence of living scolices in the aspirated fluid during follow up intervals.

Results:

Most of the treated cysts were simple univesicular (type 1). 10 cysts were type 2 (univesicular with septated laminar membrane) whereas 6 cysts were type 3 (multivesicular). The characters and parameters of the liver hydatid cysts that included in our study were described in table 1.

Table 1: Characters and parameters of liver hydatid cysts of the studied patients

Parameter	Value
Types of cysts n/(%)	
▪ Type I	56 (78%)
▪ Type II	10 (14%)
▪ Type III	6 (8%)
Location of cyst n/(%)	
▪ Right lobe	48 (67%)
▪ Left lobe	18 (25%)
▪ Both lobes	6 (8%)
Number of cysts/patients (%)	
▪ Single cyst	86 %
▪ Multiple cysts	14 %
Cyst diameter (cm)	
▪ Mean	5.8 cm
▪ Range	3 - 14.5 cm
Previous surgery (No. of patients)	4

Patients presented clinically with abdominal pain in 60%, hepatomegaly in 28% and 25% were asymptomatic. The PAI was successfully performed for all 72 liver hydatid cysts with about 24 hours hospital stay after treatment.

There was partial collapse of all cysts immediately after completion of the procedure and then they were re-expanded to almost their initial size during the first month follow up (due to re-accumulation of fluid within the cyst cavity) with detached endocyst from pericyst (figures 1a-c ,2a-b). Then a progressive reduction in the cyst size was observed after the first month and significant reduction of the amount of cyst fluid was noted after 6 months of treatment in most of cases (figures 1d-f, 2c-d, 3b-c). The cysts

almost remained unchanged after the first year follow up (figure 3c-d).

At the end of the last US follow up, two patterns were observed, the first was the solid pattern (63%) which characterized by small irregular-walled cyst filled with thick heterogeneous contents representing misshaped endocyst (figures 1f, 3d, 4b). The second was a liquid and solid pattern (37%) that characterized by small sized cyst containing folded membranes floated in a residual fluid with no vital scolices in the aspirated fluid (figure 2d). 70 out of 72 cysts were cured and only 2 cysts showed recurrence which were type 3. No major complications were developed during or after the procedure, however minor complications were developed in 10 patients and all treated symptomatically. The features of PAI treatment outcome were summarized in table 2.

Table 2: Result outcome of PAI treatment of liver hydatid cysts in ALThawrah Hospital.

Outcome	value
▪ Diameter of cyst at last visit (cm)	
Range	1.4 - 4cm
▪ Decrease in cyst diameter at last follow up (%)	
Mean	78%
Range	55-95%
▪ Serum IgG antibodies titer during follow up (%)	
Negative (less than 1:160)	85%
Progressive decrease	15%
▪ Recurrent cysts No. (%)	2 (3%)
▪ Quantity of aspirated fluid (ml)	
Mean	85ml
Range	15-1200ml
▪ Hospital stay range (hours)	18-30
▪ Follow up (years)	3
▪ Complications (No of patients)	
Urticaria	3
Nausea or vomiting	3
Hypotension	1
Mild fever	2
Slight reactive pleural effusion	1

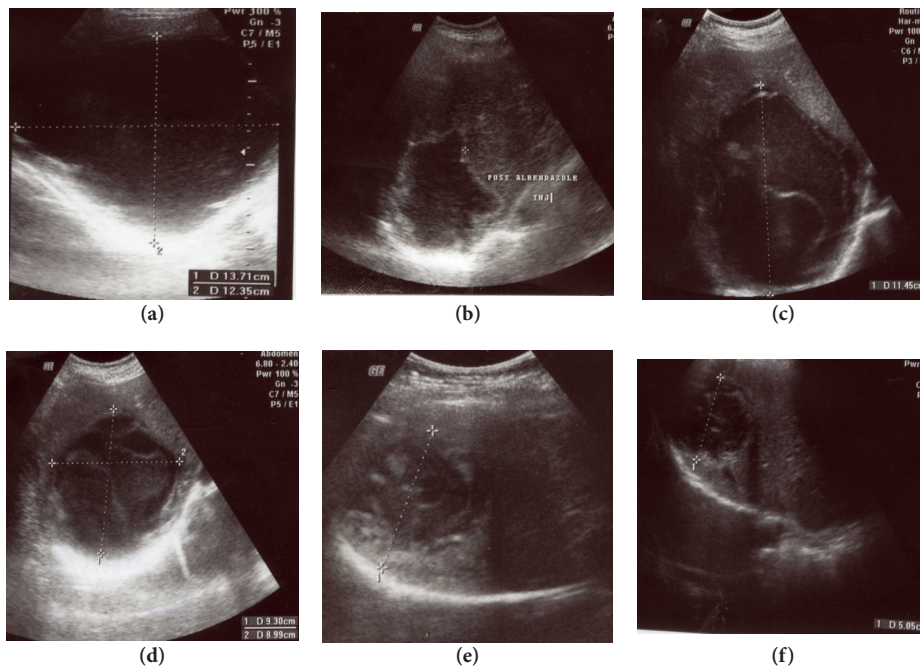


Fig. 1: Serial follow up sonograms for patient with single right hepatic hydatid cyst treated with PAI: (a) Before intervention. (b) Partially collapsed cyst just one hour after PAI. (c) Reexpansion of the cyst with detached endocyst after one week of the treatment. (d& e) Sonogram obtained at 3rd and 6th months follow up visits showed progressive reduction in the cyst volume with progressive increasing solid component, and (f) Small pseudo-mass pattern at last follow up.

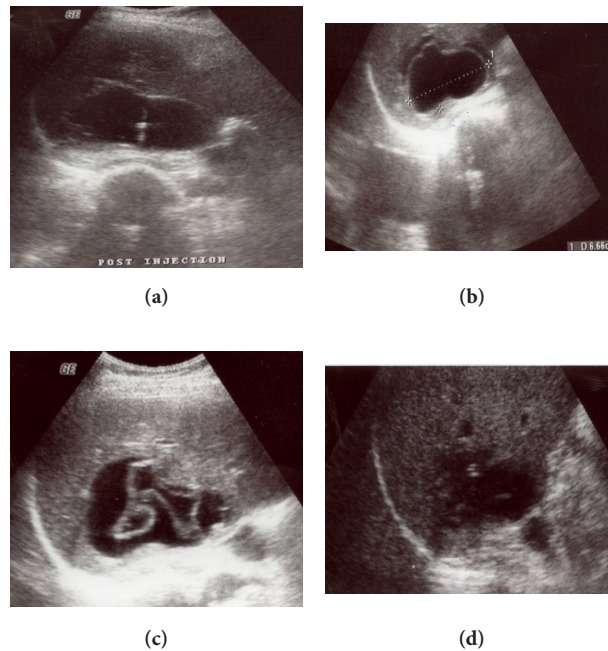


Fig. 2: Another patient with simple hepatic hydatid cyst who treated with PAI, the sonographic follow up show: (a) Tip of needle seen within the cyst during injection of albendazole, (b) Immediately after injection with detached internal membrane. (c) Folded endocyst after 8 months. (d) Small cyst with irregular thick wall and inactive partially hyperechoic content at the final follow up sonographic pattern

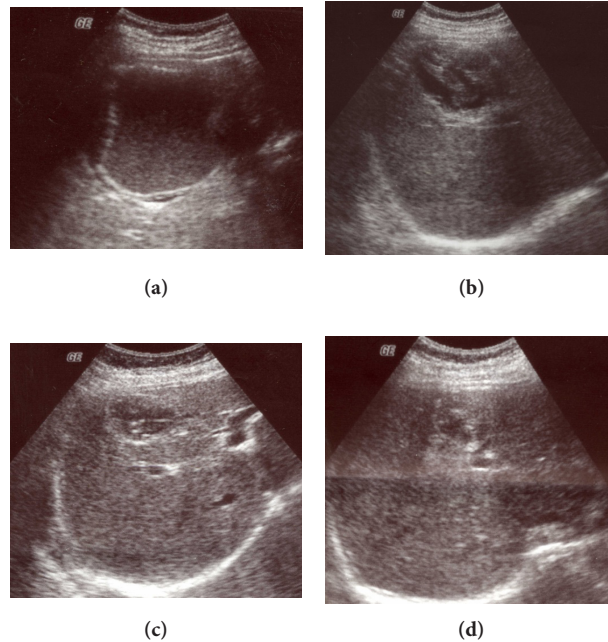


Fig. 3: Type II hepatic hydrated cyst treated with PAI and sonographic follow up shows progressive decrease in the size and fluid content and remained unchanged after the first year. (a)Before aspiration. (b) three months after PAI, (c) after 1 year, (d) after 2 years.

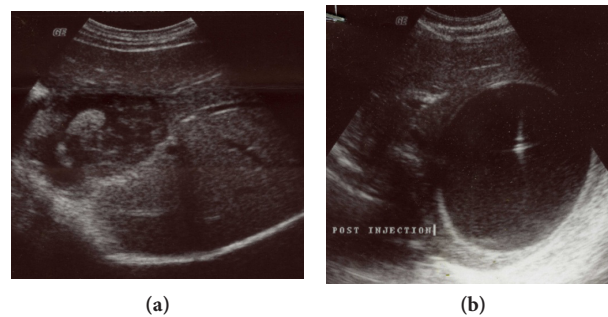


Fig. 3: (a) Typical final sonographic picture (pseudotumoral) for a large hepatic hydrated cyst treated with PIA. (b)The cyst of the same patient during PIA procedure.

Discussion:

Hydatid disease of the liver is a common medical problem in endemic areas because of its severity and frequency of complications [16]. Surgery is still regarded as the standard form of treatment. However the morbidity rate of surgery may be as high as 19%-60% and mortality ranging from 0 to 8% [4]. Moreover recurrences after surgery have been reported to be 2-22% [4,5]. The laparoscopic approach has been introduced to treat selected cases of liver hydatid cysts but conversion rate has been reported as high as 23% [17]. Systemic chemotherapy in the form of me-

bendazole and recently albendazole have been used as an alternative to surgery but the success rate was less than 30% [18].

Over the last decade, there had been growing evidence that percutaneous treatment of uncomplicated hydatid liver disease can be accepted as an alternative to surgery because it offers an effective, safe and inexpensive therapy, especially in the region where the disease is endemic and medical resources are limited [19]. Studies by Kurhoo et al. [6,20] showed that percutaneous treatment of hydatid liver disease proved to be as effective as open surgical drainage, but with reduced complication rate and lower cost than

surgery. Percutaneous treatment of hydatid cyst of the liver was first reported by Mueller et al. in 1985[21] Then, several studies of percutaneous treatment of liver hydatid disease and inject scolical agent that showed successful results have been conducted [3,7,22,23,24,25,26].

The most widely used technique was PAIR (percutaneous aspiration-injection-reaspiration) [27]. Many scolical agents have been used by investigators and the most frequently used agents were 95% Alcohol and 20% hypertonic saline [28]. Unfortunately, these scolical agents can cause serious complications such as cholangitis. However, most reports stated that intracystic injection of albendazole can be effective with less complications in percutaneous treatment of hydatid liver disease [29]. Benzimidazole derivatives alone cannot fully eliminate cysts [30].

In our study, we treated 72 hydatid liver cysts by injecting albendazole solution into the cyst using PAI technique rather than PAIR. PAI technique requires less time and needle may be removed as soon as the scolical injection completed which reduces risk of infection. In addition, the effect of scolical agent is limited to 10-20 minutes in PAIR method whereas in PAI procedure the effect continues for long time. The effectiveness of albendazole as scolical agent is well known [31]. Ten microgram/ml of albendazole solution is enough to kill scolices in vitro, furthermore it is not toxic to liver and biliary system at the applied concentration in contrast to chemical scolical agents [12,31].

To our knowledge, our study is the second worldwide that described the efficacy of the intracystic injection of albendazole in percutaneous treatment of liver hydatid cysts in human and in adequate number of patients. The previous scientific study was conducted by Paksoy Yahya et al. [13] who compared the results of intracystic injection of an albendazole with that of hypertonic saline in 30 patients for each group, and concluded that intracystic injection of albendazole is as effective as hypertonic saline with less side effects.

Our findings of percutaneous intracystic injection of albendazole in relatively larger number of patients confirm the good results in terms of high success rate, feasibility and effectiveness of this procedure in the treatment of hydatid liver disease. As regards the cyst size and the last follow up sonographic patterns, it is emphasized that remarkable reduction of the cystic size (median 70%) with irregular thick cystic wall was seen in all patients and the pseudo tumeral pattern

with slight remnant cystic fluid were the predominant end patterns. The efficacy of the procedure is primarily with sonographic follow ups and serological tests because in the literature, the sonographic finding was correlated well with pathologic findings [13,19].

It should be stressed out that only few minor side effects (less than 5%) were documented in our study such as urticaria, pain and minimal reactive pleural effusion with no major complications detected. However, post-procedural cyst infection was reported by Paksoy Yahya et al [13] as a major complication in one case. Some previous studies that used PAIR and chemical scolical agents reported anaphylaxis and mortality rate of 0.7-1.3%, infection in 1-3% and biliary fistula in 0.5-2% [3,9,10,18,20].

In our study, the recurrence rate as in other series was very low and all cysts of Gharbi type I and 2 were cured. The most notable exception was the multiloculated cysts which showed relapse in two cases in our study. Kurhoo et al. and Giorgio et al. [6,10] reported 20-30% relapse of multiloculated cysts treated percutaneously. Extra-hepatic diffusion and anaphylaxis were never observed in our study. Another advantageous point in percutaneous treatment of liver hydatid cyst was its cost effectiveness and short hospital stay (24 hours in our study) and thus no need of expense of infra-structure in poor countries including our country (in previous series hospital stay rate was 24-36 hours).

Our high success rate along with less complications may be explained by certain methods. First we decided to use albendazole as scolical agent because of its good effectiveness and less side effects. Second, we left injected albendazole in situ without reaspiration in belief that longer contact between the pericyst and scolical agent have greater likelihood of killing the scolices. Moreover refilling of the cyst along with inflammatory response of scolical agent prevent leakage into biliary tree through small fissures in pericyst.

Conclusion:

Percutaneous aspiration and intracystic injection of albendazole is safe and effective in the treatment of liver hydatid cysts. It is especially highly successful in the treatment of univesicular type and relatively limited in multivesicular cysts. PAI requires minimal infrastructure and can be performed in remote poor endemic regions.

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