ULTRASOUND-GUIDED PERCUTANEOUS PUNCTURE, ASPIRATION, INJECTION AND REASPIRATION (PAIR) FOR TREATMENT OF HEPATIC HYDATID CYSTS: A PRELIMINARY REPORT OF UNIVERSITY HOSPITAL

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ABSTRACT

Aim: The purpose of this study was to analyse the effect and preliminary clinical outcomes of percutaneous puncture, aspiration, injection of scolicidal agent and reaspiration (PAIR) in patients with liver hydatid disease.

Materials and methods: Data of a total of 41 patients with a diagnosis of hydatid cyst of the liver who underwent treatment with PAIR procedure were analysed between January 2011 and August 2013. Preprocedural clinical, radiological and laboratory characteristics, and postprocedural morbidity, mortality and length of hospital stay were recorded.

Results: The mean length of stay in hospital was 1.1 days (ranges 1-3). We performed percutaneous drainage of 68 hydatid cysts in 41 patients with a success rate of 95.1% and a morbidity rate of 17% without any mortality. In our series, minor complication (urticaria) occurred in 1 patient and major complications in 3 patients (anaphylactic shock). Three patients had cystobiliary fistula. The third patient presented with cholangitis findings 3 weeks after PAIR procedure and was managed by endoscopic retrograde cholangiopancreatography sphincterotomy (ERCP) and percutaneous catheter drainage. The follow-up period ranged from 6 to 19 months, with a mean of 10.3 months. No recurrence was seen.

Conclusion: Percutaneous puncture, aspiration, injection of scolicidal agent and reaspiration using hypertonic saline with adjuvant medical therapy is minimally invasive, safe and effective therapy in the treatment of type I, II and even III liver hydatid cysts. When considering the morbidity, mortality, hospitalization period and costs of surgical treatment, it can be used as an alternative to surgery.

Key words: Albendazole, hepatic hydatid cyst, ghary classification, percutaneous puncture aspiration irrigation and reaspiration.

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Introduction

Hydatid disease caused by Echinococcus granulosus larvae is a common health problem especially in endemic areas such as Mediterranean countries, the Middle East, South America and Latin American countries1. Despite all the measures taken so far, unfortunately, it still continues to be a major health problem in Turkey. The prevalence of the hydatid disease worldwide is 1-500/100,000 individuals and the incidence is 5-20/100,000. In Turkey, the prevalence is 0.87-6.6/100,000 and the incidence is 3.4/100,0002. When we look at the literature of Turkey, approximately more than 21,303 cases with hydatid disease were reported between 1987 and 1994 in Turkey3. The disease occurs in almost all regions of our country. There are a lot of factors, such as general unhygienic conditions, country’s zoogeographical structure, social and economic conditions, lack of public education about E. Granulosus prevention affect the high prevalence of the infection in Turkey3.

Echinococcus granulosus has both definitive and intermediate hosts1,2. The most common definitive and intermediate hosts of echinococcus are dogs, sheep and cows, respectively. Humans become...
infected as an intermediate host by ingestion of contaminated food or drinks or by direct contact with dogs. Echinococcus eggs that have been deposited in soil can stay viable for up to a year. The cysts are usually found in liver, (in about 65% of cases) but can occur in the lungs (25%), peritoneal cavity (8%), kidney (3%), spleen, nervous tissue (1%), or bone\(^4\).

The traditional mainstay of treatment for liver hydatidosis is surgery\(^4\). But it has several disadvantages such as high rates of morbidity and mortality, long hospital stay, surgical scarring, high cost, and recurrence\(^5\). Recently, medical and percutaneous drainage methods have been progressively replaced, causes mentioned above, as alternatives to surgery for the treatment of the liver hydatid disease. Percutaneous puncture, aspiration, injection of scolicidal agent and reaspiration (PAIR) is a minimally invasive procedure than surgery\(^6\). In this study, we aimed to present our preliminary clinical outcomes and the efficacy of PAIR technique with pre/and postprocedural albendazole treatment.

Materials and methods

A total of 41 patients (21 female and 20 male) with 68 hepatic hydatid cysts (HHD) were treated with PAIR in a period between January 2012 and August 2013 at the department of the interventional radiology and general surgery clinics of Katip Celebi University, Ataturk Training and Research Hospital. All of the cysts were classified according to the Gharbi et al classification\(^7\). Thirty patients had only one cyst (type 1: 14, type 2: 15, type 3: 1), eleven patients had multiple cysts (range: 2 - 8), total of 38 (12 of them type 1, 20 of them type 2 and 6 of them type 3 cyst). The median patient age was 35.8 years (range 17-80 years). 29 patients were recently diagnosed with HHD and had no previous medical treatment or surgical intervention. 12 patients had cyst recurrence following surgical treatment.

PAIR and other treatment modalities were explained and discussed with the patients. After giving written informed consent, every patient administered prophylactic Albendazole (ABZ), 10 mg/kg twice a day by mouth, starting 2 week before the procedure and continuing after PAIR procedure for a total of 3 months to minimize the risk of possible spillage and dissemination into the peritoneal cavity.

All patients were regularly followed up monthly for the first 3 months and at 3, 6 and 12 months to observe both clinical courses after PAIR treatment and side effects of ABZ treatment. The follow-up protocol included clinical assessment, laboratory tests and ultrasonography (US). Abdominal computed tomography (CT) and/or abdominal magnetic resonance imaging (MRI) were only used in some cases (Figure 1A-1B). Follow-up US criteria were the echo pattern, size and wall structure of the cyst. Serologic tests [indirect hemagglutination (IHA) or/and enzyme-linked immunosorbent assay immunoglobulin G (ELISA IgG)] were determined during the first 6 months in all patients and once for later years or at the patient’s convenience. In our laboratory, serology for Echinococcus by ELISA was cut-off >1.1 and IHA, a titer of ≥1/160 was evaluated as positive.

Fig. 1 A: 35 year-old man with hydatid cyst of liver. T2W MRI obtained before PAIR treatment shows one hydatid liver cyst.

Fig. 1 B: CT image obtained done month after PAIR procedure of the same patient shows marked volume reduction.

The cysts were classified by US according to the Gharbi et al classification\(^7\): type I, a simple hydatid cyst with pure fluid collection; type II, fluid collection with septa (honeycomb sign); type III, heterogeneous echographic patterns (daughter cysts); type IV, a cyst with a heterogeneous echo pattern and filled with a matrix or amorphous mass; and type V, a cyst with a thick and calcified wall. Inclusion or exclusion criteria were determined by surgeons and radiologist mainly in accordance with patient’s status, comorbidity, and the sonographic and tomographic findings. PAIR treatment was just used in the patients with type I, type II liver hydatid cysts, and type III hydatid cysts with drainable content.
The most common presenting symptoms were right upper quadrant pain with abdominal discomfort (n = 32) and swelling (n = 9). While three patients had concomitant abdominal swelling and right upper quadrant pain, other three were asymptomatic and were incidentally diagnosed. The diagnosis was mainly obtained by US and BT, if needed MRI.

Thirty patients had one cyst and 11 patients had multiple liver cysts\(^{2-8}\). Seven patients also had extra hepatic disease in the lung (n = 4), kidney (n = 1) and spleen (n = 2). The cysts were most frequently found within the right lobe of the liver. Thirty-two cysts (78\%) were located in the right lobe, 6 (14.7\%) in the left lobe, and 3 (7.3\%) in the right and left lobes. The size of the cysts was 12.6 ± 5.79 cm (range 4 - 18 cm).

**PAIR Technique**

Patients with uncomplicated active and transitional echinococcal cysts located in the liver were included in the study and treated with PAIR. The patient fasted overnight. The procedure was performed under heavy sedation (midazolam 0.1 mg/kg, intravenously (IV), propofol 2 mg/kg, IV) with close monitoring by an anaesthesiology team to treat any potential complication including anaphylaxis. Under aseptic conditions, a Teflon sheath needle (20 gauge, 20 cm long) was introduced percutaneously into the cyst under US guidance (Mindray DC-3). The puncture was made through normal liver tissue surrounding the cyst and whenever possible the right intercostal route was used to minimize the risk of hydatid fluid spillage into the peritoneum (Figure 2).

The technique of the procedure was chosen mainly according to the size of the cyst. PAIR technique was used for the cysts under 6 cm diameter. In this technique, once the cyst is punctured, approximately 60\% of the cysts fluid was aspirated for decompression. Then, hypertonic saline solution one-half of aspirated fluid volume was instilled and left in the cavity for 15 minutes. After separation of germinative membrane was seen, the fluid was then reaspirated as much as possible (Figure 3). For the cysts larger than 6 cm diameter, modified PAIR technique described by Akhan et al\(^{8}\) was always used. In contrast to PAIR technique, after hypertonic saline solution injection, 6-8F drainage catheter was inserted into the cyst cavity. Following reaspiration, catheter was left in cavity until daily drainage dropped under 10 cc (24-72 hours).

Once the cyst was almost empty, injection of contrast medium under fluoroscopic control was performed to exclude cyst communication with the biliary system. If cystographic study through the catheter shows communication, alcohol should not be used because this may result secondary sclerosing cholangitis. For the complete destruction of the germinative membrane, 96% alcohol was applied through the catheter and left in the cavity for 10-12 minutes. Hence, catheterization is essential to ensure quicker and more effective involution of the cavity; alcohol may further promote this involution with its sclerosing effect. Whole of the cyst content was aspirated and drainage catheter removed in the end of the procedure. After that, the patients were closely observed for possible complications for 24 hours. The complications were defined according to the Society of Interventional Radiology (SIR) guidelines\(^{9}\).

![Fig. 2](image2.png)

Fig. 2: The puncture was made through normal liver tissue surrounding the cyst to minimize the risk of hydatid fluid spillage.

![Fig. 3](image3.png)

Fig. 3: It is apparently showed that separated germinative membrane from the cyst wall by US.

**Results**

We performed percutaneous drainage of 68 hydatid cysts in 41 patients with a success rate of 95.1\% and a morbidity rate of 17\% without any mortality. In our series, minor allergic complication (urticaria) occurred in 1 patient and major allergic complication (anaphylactic shock) in 3 patients (Table 1). Totally, 4 patients (9.7\%) needed surgical
intervention, two of them had cysts with thick walls or not drainable content. Because of this, puncture and aspiration procedures failed. Also, one of these patients had anaphylactic shock during the PAIR procedure. The other two patients underwent successful PAIR procedures for the hydatid cyst of the liver but they also had Type IV spleen hydatid cysts.

Three patients had cystobiliary fistula. Two of them were found during cystogram and underwent catheter drainage for 10 days and resolved without any additional procedure. The third patient presented with cholangitis findings 3 weeks after PAIR procedure and was managed by ERCP and percutaneous catheter drainage. All three patients had good clinical outcomes and they went on their routine follow up without any problem. During procedure, anaphylactic shock characterized by hypotension, lower oxygen saturation and shallow breathing occurred in three patients and treated uneventfully, with attention paid to their respiratory support and medical treatment. PAIR procedure was successfully performed for two and the other also had thick cyst wall so this patient referred for surgery.

Follow-up US criteria were the echo pattern, size and wall structure of the cyst. In the follow-up period, fluid contents totally disappeared; thickening and irregularities were also observed in the cyst walls and a solid, hyperechogenic, heterogeneous pseudotumor appearance, representing a degenerated membrane, was seen in all patients. Hypertonic saline solution inactivated the scolices from the beginning of the treatment.

In two patients, there were more fluid contents than expected therefore we repeated the percutaneous drainage. The mean length of stay in hospital was 1.1 days (ranges 1-3). The follow-up period ranged from 6 to 19 months, with a mean of 10.3 months. No recurrence was seen, but one of our patients, from rural area, had an abdominal pain after 2 months from PAIR procedure and underwent surgery due to the diagnosis of hydatid cyst in another hospital.

### Table 1: Perioperative and postoperative complications.

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylactic shock</td>
<td>3</td>
<td>Anaesthesiologist intervention.</td>
</tr>
<tr>
<td>Intrabiliary fistula</td>
<td>3</td>
<td>ERCP sphincterotomy+Antibiotics and follow up percutaneous drainage in 1 patient with cholangitis. Percutaneous drainage in other 2 patients.</td>
</tr>
<tr>
<td>Failure PAIR</td>
<td>2</td>
<td>Surgery</td>
</tr>
<tr>
<td>Urticeria</td>
<td>1</td>
<td>Medical</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Surgery has been the mainstay of treatment for liver hydatid disease over the years. However, the surgical treatment of the liver hydatidosis suffer from both mortality and important complications such as bleeding, dissemination of viable scolices, infection, anaphylactic shock, recurrence and bile fistula. Additionally, the surgical treatment of cyst which located near major biliary or vascular structures may cause serious complications. Although many surgical techniques have been described there is no ideal surgical method for the treatment of liver hydatid cysts yet and surgery is not usually 100% effective. In the literature, mortality rates related to surgery have been reported to be 0-6.3%, the operative complication rate varies between 12.5% and 80%.

Smego et al. (12) reported a meta-analysis of surgical treatment for hydatid disease, minor and major complication rates were 33% and 25.1%, respectively, and mortality rate was 0.7%. On the other hand recurrence, which is most important complication after surgery, has been reported to be 2.2-25%.

Recently, medical and percutaneous drainage methods have been progressively replaced, causes mentioned above, as alternatives to surgery for the treatment of the liver hydatid disease. PAIR is a minimally invasive procedure than surgery. Firstly, PAIR was introduced by Ben Amor et al. (15) in 1986. Moghadam et al. (16) suggested that the superiority of PAIR compared with surgical treatment, for some selected patients with hydatid disease. It’s advantages are: cost effective, shorter hospitalization period, more patient’s comfort, easily repeatable if needed and it can often be performed on an outpatient basis. The advantages of this technique in selected cases of HHD have been reported in the literature over the last 20 years. Smego et al reported that PAIR has greater clinical efficacy, low rates of major and minor complications, mortality, recurrence rate and short hospitalization days.

In Turkey PAIR procedure has been performed for treatment of the hydatid disease since the 1990s.
Firstly, Akhan et al.\(^8\) reported long-term results indicating that PAIR in treatment of liver hydatid cysts is an effective and safe method in selected cases. Afterwards, some authors presented their series at the different centre in Turkey\(^ {10,17-21}\). These studies obviously showed that PAIR was used successfully to treatment of type I-III liver hydatid cysts. Aygun et al.\(^20\) reported that PAIR was performed over 83 hydatid cysts in 45 patients with a success rate of 100% and a morbidity rate of 6.6%. In their study, mean follow-up was 30 months without recurrence and they administered ABZ orally (10 mg/kg daily) as a prophylactic measure 48 hours before and for 2 months after the percutaneous irrigation to all patients. Therefore, they advocated that PAIR may be a first line therapy in type I and type II liver hydatid cysts.

No doubtful, PAIR has some complications such as anaphylactic shock or other allergic reactions, haemorrhage, infections, recurrent fluid collection, biliary fistulas, persistence of satellite daughter cysts and secondary echinococcosis caused by spillage. Other complications include pleural effusion, abdominal pain, etc.) generally are minor and infrequently seen. In presented series, although anaphylactic shock occurred in three patients, death due to anaphylaxis was not observed. Urticaria was only seen in one patient. Although it has been reported postprocedural abdominal pain, fever, related PAIR procedure which are common complications, but these complications weren’t seen in any our patients.

Intrabiliary rupture, a communication of the cyst cavity with the biliary system, is one of the most common and serious complications. However, patients with intrabiliary ruptures may course clinically silent, without any specific radiological or laboratory findings. Zeybek et al.\(^4\) reported that cystobiliary fistula rate was 18% (6 of 33 patients). A multidisciplinary team consisting of radiologist, gastroenterologist and surgeon managed these patients. In refractory cases, reducing the pressure in biliary system by endoscopic papillotomy may solve the problem. In this study, biliary fistula was seen in three patients. Two of them were found during cystogram and underwent catheter drainage for 10 days and resolved without any additional procedure. The third patient presented with cholangitis findings 3 weeks after PAIR procedure and was managed by ERCP and percutaneous catheter drainage and resolved within 14 days.

Some authors reported cholangitis, high bilirubin and Alkaline phosphatase (ALP) levels, cysts larger than 10 cm and suggestive US findings as clinical predictors of intrabiliary rupture. ERCP was suggested to delineate the presence of cyst-biliary communication in these cases\(^ {12,23}\). Kilic et al.\(^22\) reported that the presence of irregular linear echogenic structures without acoustic shadowing in the bile duct and/or the dilated biliary tract was pointed to as suggestive USG findings of intrabiliary rupture. All of the patients with these USG findings were further evaluated with either abdominal CT or magnetic resonance cholangiopancreatography (MRCP). In our patients, we did not find any suggestive findings related to cystobiliary fistula before PAIR procedure. It was not a rule but according to our experience, cysts larger than 10 cm had increasing possibility of cystobiliary fistula.

In this study, ultrasonography is the first preferred imaging modality for the diagnosis of hydatid disease as being a non-invasive method. It is also helpful in guiding the physician during PAIR procedure and following up the course of disease. Although MRI is important tool for hydatid disease, we just used in a few selected patients for the extent of lesion, clear identification of involved structures and surgical or PAIR planning.

Benzimidazole compounds (i.e., albendazole and mebendazole) alone or combined with other treatment methods have been used in the treatment of hydatid cyst for many years. This agent causes the reduction of adenosine triphosphates, pyruvate kinase, and phosphoenol pyruvate carboxylase in the cyst wall and blocks glucose intake, therefore, causes the death of scolices\(^ {26}\). However, the efficacy of the systemic effect of these agents in treatment has been limited because of a small proportion of the drug is transported to the cyst fluid through the gastrointestinal system\(^ {24,25}\). It has been reported that the different factors can affect the therapeutic results of medical treatment such as age of cyst, age of patient, intrinsic sensitivity and morphology of cyst\(^ {20}\). Currently, ABZ is the most effective and useful drug for the medical treatment of hydatid disease and it also is an effective adjuvant therapy in the management of hepatic hydatid cyst\(^ {24,26}\).

In the literature, most authors showed that cyst size reduction was best achieved by the combined therapy when compared to ABZ or percutaneous drainage alone\(^ {10}\). Although there has been ongoing debates about their highly curative efficacy and duration of ABZ treatment of hydatid cyst in the literature the most authors has been proposed that these agents should be used for prophylactic purposes to prevent
the spreading and recurrence after both surgical and PAIR treatment\(^{(1)}\). The usually recommended oral dosage of ABZ for treatment of liver hydatidosis is 10-15 mg/kg per day for several days or weeks before PAIR and several months’ courses separated by 14 intervals after PAIR\(^{(1)}\). Otherwise some authors reported that might be used highest dose using\(^{(27)}\). WHO Informal Working Group on Echinococcosis proposed that chemotherapeutic agent(s) should be combined with PAIR procedure to minimize risks of recurrence. They advocated that four days of treatment with benzimidazoles before PAIR is mandatory and should last for 1 month (ABZ) or 3 months (mebendazole) after the procedure\(^{(28)}\).

In our study, we gave ABZ 2 weeks before the procedure and continuing after PAIR procedure for a total of 3 months.

But this protocol’s boundary was not drawn exactly. Liver function tests and haematological tests were studied for ABZ toxicity and also indirect hemagglutination test (IHA), abdominal CT and US were applied in certain intervals.

In other hand, there is no consensus regarding an ideal scolicidal agent in the PAIR procedure. It has been used as scolicidal solutions include mebendazole, 10% to 20% hypertonic saline, 95% alcohol, 0.05% silver nitrate, iodine and hydrogen peroxide in the PAIR procedure\(^{(1)}\). Aygün et al\(^{(29)}\) reported their success rate 100% with using 0.05% silver nitrate. But this should not be associated only the scolicidal agent used. Because, like surgery cases, many factors can influence the rate of recurrence after PAIR procedure. In the literature, we saw that scolicidal agents were mainly used 20% hypertonic saline and 95% ethanol solution. We used these agents in our study, too. However, our short-term follow-up, we did not encounter any recurrence.

Recurrence is one of the most serious problems after surgical therapy in the patients with HHD. Many factors may have a role in recurrence. The most important factors are the immunity of the patient, surgical procedure applied, the localization of the cyst, the period of hospitalization, the lavage fluid used during the surgical period, preoperative and postoperative ABZ usage. In our study 12 patients were already underwent surgical intervention for hepatic hydatid disease before being admitted to our Department. As our experiences, the patients with recurrent HHD have high mortality and morbidity rates for second surgical treatment. Because of this, especially in these cases, PAIR can be a good alternative procedure instead of a second surgery.

PAIR procedure should not be seen as a miracle treatment for every patients whose have hepatic hydatid cyst. But, when compared with surgery, PAIR procedure is getting remarkable because of its short hospital stays, low cost, low morbidity and mortality rate and also has minimally invasive characteristic. These patients were managed by a multidisciplinary team consists of radiologist, gastroenterologist and surgeon to have a high success rate.

Our preliminary report showed that PAIR with adjuvant medical therapy is minimally invasive, safe and effective therapy in the treatment of types I, II and even III of HHD with adjuvant medical therapy. When considering the morbidity and mortality and costs of surgical treatment, it can be used as an alternative to surgery.

References

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