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3% Hydrogen peroxide as a scolicalid agent in an ultrasound-guided percutaneous treatment of liver hydatid cysts

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Abstract

Aim: By employing 3% hydrogen peroxide (HP) as a scolicalid agent in PAIR therapy for the treatment of hepatic hydatid disease, the clinical outcomes and efficacy of the intervention will be assessed.

Materials and Method: Fifty Hydatid cysts were treated in forty patients via the PAIR procedure with 3% HP as a scolicalid agent. Clinical, radiological, and laboratory characteristics were documented prior to the procedure, as were post procedural morbidity, mortality, and duration of hospital stay.

Results: Fifty hydatid cysts were treated with PAIR in forty patients, yielding a success rate of ninety-five percent and no fatalities. The average duration of hospitalization was three days. Seven patients in our series experienced minor complications, while four patients encountered significant complications. The mean duration of the follow-up period was 15.3 months, ranging from 12 to 18 months. 2 patients experienced recurrence.

Conclusion: PAIR therapy is a minimally invasive approach utilized to treat hepatic hydatid lesions of the Gharbi type I-III. It is a relatively risk-free procedure that substantially shortens the length of hospitalization. It was our conviction that HP exerts some influence on the results and consequences of PAIR on its own.

Keywords: Minimally invasive, patients, influence

Introduction

Hydatid disease, which is predominantly prevalent in regions where *Echinococcus granulosus* larvae are prevalent, is a prevalent health concern [1,2]. *Echinococcus granulosus* inhabits intermediate and definitive hosts. Dogs, sheep, and cows are the absolute and intermediate hosts that occur most frequently. Humans may get the infection as an intermediate host through direct contact with the animals or by consuming contaminated food or beverages [3].

Hydatid cysts comprise tissue from both the host and the parasite. The pericyst, a dense and fibrous tissue, is produced when the liver reacts to the presence of the parasite. The endocyst, on the other hand, is composed of two layers: an outer laminated layer and an inner germinal layer [4].

Although the development of this condition can transpire in any bodily organ, it is most frequently observed in the liver (50–80%). More frequently, the right lobe of the liver is impacted compared to the left. Lungs constitute the second most frequent site, accounting for 5–30 percent. Less frequently, cysts have been identified in the bones, spleen, kidney, heart, and central nervous system, among other organs [5]. Despite the fact that hydatid cysts are typically benign and are detected incidentally on ultrasonography, treatment is required for symptomatic and active cysts due to the high risk of fatal complications [6].

Surgery has long been the prevailing approach for managing hepatic hydatid cysts. Regrettably, this method is invasive in nature, carrying significant risks including mortality and morbidity, extended hospital stays, surgical scarring, substantial financial investment, and recurrence. In the last thirty years, non-surgical treatments for the disease (medical and percutaneous approaches) have been gradually supplanted by surgical alternatives. At the moment, albendazole and mebendazole are prescribed for medical purposes [7].

The inception of percutaneous therapy for hepatic hydatid cysts was documented by Mueller *et al.* in 1985 [8].

Subsequently, this approach has gained widespread adoption as a result of its minimal occurrence of adverse effects and mortality rates. PAIR (Percutaneous puncture, aspiration, scolicedal agent infusion, and reaspiration) is a less invasive alternative to surgery. Two frequently utilized strategies are injecting a scolicedal agent into the unopened cyst and enclosing the operative field with sponges saturated in a scolicedal agent [9]. Compounds such as ethyl alcohol, hydrogen peroxide, hypertonic saline, cetrimide, and chlorhexidine are utilized as scolicedal agents in the PAIR procedure [10]. Each is dependent on concentration, and the degree to which it dilutes in the cyst contents is highly unpredictable.

The purpose of this study was to demonstrate the efficacy of the PAIR technique, which combines pre/post-procedural albendazole treatment with 3% hydrogen peroxide solution used as a scolicedal agent, in addition to preliminary clinical results.

Materials and Methods

The investigation for this prospective interventional study was conducted within the radiology department. Forty patients (20 females and 20 males) with fifty hepatic hydatid cysts underwent PAIR technique treatment and were monitored for a maximum of eighteen months. The range of patients was 15–65 years, with a median age of 40 years. A total of thirty-seven patients were recently identified as having hydatid liver lesions, with no history of surgical intervention or prior medical treatment. Prior to the intervention, three patients had undergone surgery to address a hydatid cyst; upon relapse, they had submitted applications for percutaneous treatment. Eight patients had multiple hydatid cysts, whereas thirty-two patients had a single cyst. The classification of every cyst was based on the Gharbi classification.

Inclusion criteria

- patients having single/multiple hepatic hydatid cysts of Gharbi type I, type II, type III
- cysts with drainable matrices
- with adequate liver parenchyma (>5 mm) surrounding the cyst
- cyst size >4 cm

Exclusion criteria

- patients with Gharbi type III cysts with non-drainable contents
- with severe septation with innumerable daughter cysts
- type IV and V cysts
- peripheral cysts having <5 mm of surrounding hepatic tissue
- cysts with communication to the biliary tree
- history of anaphylaxis or atopy
- uncooperative patients
- patients who were pregnant or who had infected cysts at the time of initial aspiration

Prior to the procedure, written informed assent was obtained from all patients. After a comprehensive history and clinical examination, sonography and an enzyme-linked immunosorbent assay (ELISA) serological test confirmed the diagnosis. A computed tomography (CT) scan was exclusively conducted in cases where calcification in the

lesions and their relationship to the vessels and biliary tree required clarification. In addition to conducting liver function tests, blood counts and coagulation functions were assessed. A prophylactic oral albendazole solution containing 10–15 mg/kg twice daily was administered to all patients undergoing percutaneous drainage. This treatment commenced one week prior to the PAIR procedure and continued for a total of eight weeks afterward. The objective was to reduce the likelihood of scolices spilled during the interventional procedure seeding intraperitoneally. Anti-allergic prophylaxis (diphenhydramine, 10–50 mg/kg and hydrocortisone sodium succinate, 100 mg IV) was administered intravenously for 15 minutes prior to the intervention in every case. Preparation of an emergency tray containing essential medications and apparatus was conducted within the procedure unit. The patients observed a nightly fast.

PAIR Technique

After establishing aseptic conditions in the intervention area, the procedure was conducted under local anesthesia using 2% lidocaine at the puncture site. However, in the case of irascible, uncooperative, or patients with large cysts, the procedure was carried out under heavy sedation (midazolam 0.1 mg/kg intravenously (IV), propofol 2 mg/kg IV) with close monitoring by an anesthesiology team in order to manage any potential complications that may arise. A 3% solution of hydrogen peroxide (HP), which was prepared in the laboratory, was administered as the scolicedal agent to all patients. The incision was performed via the normal liver parenchyma that encircled the cyst. To reduce the likelihood of hydatid fluid leakage into the peritoneum, the right intercostal route was utilized whenever feasible. A 15 or 20 cm Teflon sheath needle was inserted into the cystic cavity via a transhepatic route guided by sonography (HD11 XE, Philips), ensuring aseptic conditions and avoiding direct penetration of the cyst. After aspirating the majority of the cyst contents, a three percent sterile HP solution was injected into the cyst cavity for 15–20 minutes in an amount equal to half of the aspirated liquid. The solution was left in place until the cyst was nearly emptied. Once the germinative membrane had separated, the cyst cavity was rinsed with normal saline and the fluid was re-aspirated to the greatest extent feasible.

Critical signs were continuously monitored during the procedure. Upon aspiration, the cyst liquid was subjected to cytologic, histopathologic, and parasitologic examinations to confirm the diagnosis and evaluate the efficacy of the drainage procedure. These analyses were conducted to identify any fragments of laminated membranes, hooklets, and scolices. The bilirubin concentration in the aspirated fluid was assessed using a semi-quantitative method (Combur-Test; Roche Diagnostics, Indianapolis, IN) just moments prior to HP injection at each PAIR in order to rule out the existence of a biliary fistula. Following that, the patients were monitored attentively for 24 hours to identify any potential complications.

Follow-up

In the protocol for follow-up, clinical evaluation, laboratory analyses, and ultrasonography were all included. Abdominal CT was utilized infrequently. The following day, the patients were evaluated using the US following the intervention. Subsequent US evaluations were conducted at

one month, three months, six months, one year, and the conclusion of the follow-up period, for a total of 12–18 months of follow-up. All patients' indirect hemagglutination (IHA) titers were determined at the same time intervals. The functions of the liver were evaluated.

Results

According to Gharbi classification, the majority of the cysts were Gharbi type I (n=36; 72 per cent). 8 cysts were type II (16 per cent). 6 patients were type III cysts (12 percent).

Table 1: Distribution of cysts according to Gharbi classification prior to intervention

Gharbi classification	Lesion features	No of treated cysts with PAIR
Type I	Pure cystic lesion	36(72%)
Type II	Cystic formation containing segregated membranes	8(16%)
Type III	Cyst containing multiple septa/daughter vesicles	6(12%)
Type IV	Semisolid heterogeneous lesion	-
Type V	Calcified wall hyperechogenic lesion	-
Infected	Abscess-like lesion	-
Total		50

Table 2: Outcomes after treatment with PAIR

Outcome	
Follow-up (months)	12-18
Hospital stay (days)	3 (ranges 1- 8)
Minor complications	7 patients (17.5%)
Major complications	4 patients (10%)
Anaphylaxis shock	1 patient (2.5%)
Cyst haemorrhage	1 cyst (2.5%)
Biliary fistula	1 cyst (2.5%)
Abscess	1 cyst (2.5%)
Recurrence	2 patients (5%)

A total of seven patients (17.5 percent) who received treatment experienced minor complications. These complications included urticaria (one case), fever (one case), hypotension (two cases), nausea and vomiting (two cases), and abdominal pain lasting over two hours (one case). Antipyretics, intravenous fluids, and antihistamines were generally sufficient to manage these reactions.

Out of the patients who received treatment, four (10 percent) experienced major complications. Anaphylaxis shock (one case), cyst hemorrhage (one case), biliary fistula (one case), and abscess were the complications.

Recurrence occurred in two patients during the follow-up phase. They had multiloculated cysts, which during the follow-up period produced new, viable daughter cysts within the heterogeneous structures that had been treated. Following this, each of these patients was treated with an additional session of the PAIR procedure. The daughter cysts resolved by the conclusion of the second month of treatment, and the most recent US examination revealed the presence of a consistent pattern.

Follow-up

Type I cysts treated with the PAIR method exhibited additional endocysts detaching from pericysts floating in the cyst cavity at the initial follow-up during the first month. On the other hand, type II cysts demonstrated further detachment and inner membrane folding. A gradual decline in dimensions is observed subsequent to the initial month due to endocyst degeneration. Following a two-month follow-up, the cysts exhibited a mean size of 4.2cm, signifying a reduction of approximately 50 percent in size

Prior to treatment, the cysts exhibited a mean size of 8.4 cm, with a range of 5–12 cm. The pre-procedure cyst volume was 220cc on average (with a range of 32–665cc), whereas the post-procedural volume was 115cc with a range of a few cc to 280cc. The volume of HP injected per procedure varied from 10 to 200 mL, with an average of 44 mL. The mean duration of each interventional procedure was forty-eight minutes, with a variation of thirty to sixty minutes. Three days was the mean length of hospitalization (intervals: 1–8 days).

from their initial dimensions. Following a duration of six months, a notable and gradual decline in the quantity of cyst fluid was observed, as evidenced by an average cyst diameter of 3cm. This diameter corresponds to an approximate 65% reduction in size, and in certain instances, the fluid component entirely disappeared. The degenerated and detached membranes were represented by a solid hyperechoic lesion that gave the appearance of a heterogeneous pseudotumour. During the follow-up phase, irregularities and thickening of the cyst walls were also detected; these characteristics were regarded as cure criteria in our study. The time required to obtain the final ultrasonographic pattern was highly variable. In general, ultrasonographic pattern changes became apparent more rapidly in smaller type 1 cysts (1-3 months), while larger, more complex cysts required a prolonged duration (up to 18 months).

Discussions

Surgical intervention was the treatment of choice for hydatid lesions of the liver for decades.¹¹ Nevertheless, surgery carries with it substantial rates of morbidity and mortality. Surgical mortality rates ranging from 0% to 4% have been documented in the literature, contingent upon the specific surgical procedures performed.¹² Recurrence, the most significant complication following surgery, has been estimated to occur between 2% and 25% of the time. Furthermore, severe complications may arise from the surgical treatment of cysts situated in close proximity to significant biliary or vascular structures^[13, 14]. In a meta-analysis of surgical treatment for hydatid disease, Smego *et al.*^[15] found that the rates of severe and minor complications were 25.1% and 33%, respectively, with a mortality rate of 0.7%.

In recent years, minimally invasive therapeutic approaches (e.g., percutaneous therapy and laparoscopic surgery) and medical treatment have gradually surpassed surgical intervention in the management of hepatic hydatid disease. PAIR is an intervention that requires less incision than surgery. In the first place, Ben Amor *et al.* introduced it in 1987.^[16] In Gharbi type I-III cysts, US-guided PAIR is now frequently performed in conjunction with drug therapy comprised of albendazole or mebendazole administered

prior to and following drainage. This approach is highly effective and yields a more favorable prognosis than surgery. Literature from the last two decades has documented the benefits of this technique, which include increased clinical efficacy, decreased mortality, recurrence, and complications, low cost, shorter hospital stay, increased patient comfort, ease of repetition if necessary, and frequent outpatient availability^[17].

Despite the World Health Organization's (1996)^[18] recommendation for hypertonic saline as a scolical agent, we opted to utilize 3% hydrogen peroxide (HP) in our investigation due to its accessibility and lack of adverse effects. At the concentration administered, HP does not exhibit toxicity towards hepatic and biliary structures, thereby reducing the likelihood of chemical sclerosing cholangitis, a widely recognized adverse effect associated with chemical scolical agents^[19].

In seven patients (17.5%), minor complications including urticaria, abdominal pain, fever, hypotension, and nausea and vomiting occurred during the procedure. According to research conducted by Etlik O *et al.*^[20] and Men S *et al.*^[21], the incidence of complications varied from 18 to 84%.

One participant experienced severe anaphylactic reactions during our research. The patient made a speedy recovery after receiving the proper medication, which is consistent with the conclusions drawn by other researchers^[20]. In one patient, the presence of bile-stained fluid collected during the second aspiration indicated the existence of a biliary fistula. Our study documented a significantly lower incidence of biliary fistula formation (2.5 percent) in comparison to the approximately six percent reported in the studies by Ustunsoz *et al.*^[2] and Men *et al.*^[21] According to Zeybek *et al.*^[23] the incidence of cystobiliary fistula was 18% (six out of 33 patients).

Following surgical and percutaneous treatment, recurrence is one of the most severe complications reported by patients with hydatid liver disease. In contrast, the recurrence rate was significantly lower with PAIR compared to surgery. The incidence of recurrence subsequent to percutaneous treatment was 5% in our study (two patients out of forty). During a follow-up period of 12–24 months, the ratio was reported to be 4% (five out of 120 cysts) in the series by Gargouri *et al.*^[24] It is possible that the absence of disease recurrence in other liver segments or other anatomical sites (peritoneum and thorax)—possibly due to hydatid fluid leakage—contributes to this finding. Systemic prophylaxis with albendazole, which has been demonstrated to reduce relapse of hydatid disease following surgery and percutaneous treatment, may have played a role in this phenomenon.

The study is limited by several factors, including the relatively brief duration of follow-up observations, the small number of cases examined, and the absence of comparisons with surgical methods. Nevertheless, the sole objective of this research was to compare percutaneous interventions. PAIR therapy demonstrated superior clinical efficacy (i.e., a greater incidence of cure) in comparison to surgically treated patients. Additionally, it was associated with reduced rates of major and minor complications, mortality, and disease recurrence, as well as a shortened duration of hospitalization.

Conclusion

PAIR utilizing HP as the scolical agent is a minimally

invasive, relatively safe, and cost-effective alternative to surgery for patients with Gharbi type I-III hepatic hydatid cysts, according to our findings. Despite their rarity, however, life-threatening complications necessitate that this therapeutic modality be restricted to facilities equipped with resuscitation techniques and surgical capabilities.

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