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Original Article

Percutaneous US-guided combined ethanol and tetracycline injection for treating symptomatic simple and hydatid hepatic cysts

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ABSTRACT

Introduction: Percutaneous treatment of simple or hydatid liver cysts is widely used in clinical practice and ethanol is the commonest sclerosant used. Abdominal discomfort and pain commonly occurs after ethanol injection which increase with increased ethanol volume.

Purpose: To evaluate the safety and efficacy of the combination of tetracycline and ethanol for percutaneous sclerotherapy of either symptomatic simple hepatic cysts or unilocular hepatic hydatid cysts.

Patients and methods: A total of 34 adult patients with symptomatic simple cyst and 36 unilocular hydatid cysts underwent clinical, laboratory and radiological evaluations followed by diagnostic cyst aspiration. Each was divided into 2 arms. The first arm was treated by ethanol sclerotherapy and the second was treated by combined ethanol and tetracycline sclerotherapy.

Results: Combined ethanol and tetracycline sclerotherapy was associated with fewer sessions than ethanol sclerotherapy ($P = \leq 0.001$) and higher rate of sustained cyst size reduction on follow up ($P = \leq 0.001$). Also second arm was associated with less pain than alcohol alone due to the beneficial effect of tetracycline. Conclusion: combined ethanol and tetracycline seems to be more effective, non expensive, more sustained action and more comfortable to our patients than single ethanol use.

1. Introduction

Simple liver cysts are variable sized cystic lesions from few millimeters to huge cysts. Most of the simple cysts are small and asymptomatic but when enlarged or complicated it may cause symptoms. Simple hepatic cysts don't communicate with the biliary tree [1–4].

Simple liver cyst must be differentiated from the other similar cystic liver lesions since the management is clearly different. Simple cyst when symptomatic may cause right hypochondrial pain if enlarged and less commonly a palpable swelling may occur. Simple liver cyst may cause complications like cholestatic jaundice due to mechanical compression, infection, acute abdomen due to torsion of a superficial cyst [5–8].

Treatment is indicated only for symptomatic or complicated simple liver cysts. Many treatment options are available including cyst aspiration, cyst aspiration with percutaneous sclerosis, cystojejunostomy, unroofing and cyst resection. Percutaneous aspiration of the simple cysts without sclerosis is associated with high failure rate and rapid recurrence [9–12].

Hydatid liver cyst results when humans are infected by the metacestode stage of the echinococcus species. Hepatic affection is the most common and this occurs in about two third of cases in E- granulosus infection [13,14].

The World Health Organization (WHO) classified cystic echinococcosis according to the sonographic appearance by type and size. According to the WHO CE1 and CE2 are active cysts. The CE1 cysts are unilocular and CE2 cysts are multilocular. The CE3 cysts are degenerating cysts. The CE3a cysts show the water-lily sign and the CE3b cysts are predominantly solid with daughter cysts. CE4 and CE5 are inactive cysts [12,15].

According to the WHO-IWGE expert consensus; Stages CE1 and CE3a cysts which are smaller than 5 cm may be treated with

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albendazole or albendazole plus PAIR (puncture, aspiration, injection, and reaspiration); while cysts that are larger than 5 cm may be treated with albendazole plus PAIR. Intracystic injection of a scolicidal agent (e.g., hypertonic saline or 95% ethanol), after cyst puncture and aspiration followed by reaspiration of the cyst content. PAIR was first considered In 1980 s. Ultrasound or computed tomography (CT) are used to guide PAIR and reaspiration is performed after at least 10–15 min [16–18].

2. Patients and methods

2.1. Patients characterization

The study is prospective and all tested patients are examined in the endemic medicine, hepatology and radiology departments by abdominal ultrasonography over 3 years (2013–2015). Inclusion criteria: adult patients with symptomatic hepatic cyst and sonographic cystic picture (anechoic, post cystic acoustic enhancement and more than 3 cm), on the other hand, exclusion criteria are cases with any suspicion of malignancy.

This prospective study included 34 patients with simple hepatic cysts and 36 patients with hydatid cysts. Mean age of patients was 44.6 years. The study included 44 males and 26 females. 21 patients complained from right hypochondrial pain, 18 ones complained from right hypochondrial swelling and other 31 complained from both right hypochondrial pain and swelling.18 out of 34 patients with simple hepatic cysts underwent alcohol injection alone while remaining 16 patients underwent combined alcohol and tetracycline injection. 15 out of 36 patients with hydatid cysts underwent alcohol injection alone while remaining 21 patients underwent combined alcohol and tetracycline injection.

Selected patients underwent CT or MRI to confirm benign nature of the cysts followed by cyst aspiration and cytological study before starting treatment. The cysts were classified into simple non infectious cysts and hydatid hepatic cysts according to laboratory results. Then therapeutic workup classify the patients haphazardly into 2 arms, first arm was treated by combined absolute ethanol and tetracycline therapy and second arm treated by ethanol alone. Conscious sedation is the role using intravenous midazolam with constant hemodynamic monitoring.

Informed consent was taken from each patient. The research protocol was approved by the Ethical Committee.

2.2. Radiological examination

Ultrasound is the best simple, rapid and sensitive reliable radiological test for evaluation of abdominal pain; Followed by more evaluation by computed tomography or magnetic resonance imaging [19,20]. Abdominal ultrasonography can diagnose hepatic hydatid cyst with an accuracy of more than 90% [21].

2.3. Laboratory workup

Routine laboratory tests for liver functions (transaminases, alkaline phosphatase, albumin level, gamma glutamyl transferase), renal function, complete blood picture, bleeding profile including prothrombin time, tumors markers (alpha fetoprotein, carcinoembryonic antigen), serum amylase, ELISA for hydatid disease and stool analysis for parasitic infestation. Biochemical analysis of cyst fluid for: (protein content, creatinine, bilirubin, urea nitrogen, electrolyte). All of these help to differentiate cyst type.

2.4. Cyst aspiration

Fluid aspiration and cytological evaluation to detect any malignant cells, scolices or inflammatory cells; also culture and sensitivity was done for bacteriological study.

2.5. Percutaneous treatment

The study compares percutaneous alcohol injection and reaspiration (PAIR) versus the combined tetracycline and ethanol aiming to decrease the number of sessions and amount of alcohol to avoid side effects with high efficacy.

2.5.1. Alcohol alone (PAIR)

Through Chiba needle the whole cyst is aspirated and then 95% ethanol is injected after exclusion of biliary communication. The volume of the injected ethanol is about 20–25% of the aspirated fluid with a maximum of 100 ml in adults to prevent toxicity. Strict observation for signs of ethanol toxicity is essential. Frequent change in the patient position every 5 min to ensure that alcohol contacts the epithelial lining of the whole cyst is done followed by complete reaspiration after 20 min. Percutaneous catheter is avoided to avoid development of pyogenic infection [22,23].

2.5.2. Combined alcohol and tetracycline

In this group we use lower amount of alcohol median (shown in Table 1) in combination with 1 g of tetracycline , installing tetracycline using four 250 mg capsules mixed with sterile saline in 10 ml syringe and injected in the cyst without reaspiration. Tetracycline chloride is a strong chemical irritant which was investigated by many authors as a sclerosant agent for percutaneous sclerosis of symptomatic hepatic cyst [24,25].

3. Results

The mean values of initial size of the cyst, volume of aspirated cyst fluid, number of sessions, volume of injected alcohol, final size of the cyst, cyst reduction rate, follow up duration and complications are shown in Table 1.

3.1. Patients with simple hepatic cysts group

Significant difference was observed in number of sessions (38 sessions using alcohol injection alone in comparison with 18 sessions using combined alcohol and tetracycline injection) ($p < 0.001$). Significant difference was also observed in cyst reduction rate (56.66 ± 6.91% using only alcohol injection in comparison with combined therapy reduction rate was 78.56 ± 8.51%) ($p \leq 0.001$). As regard final cyst size p-value was significant ($p < 0.05$) (3.41 ± 1.23 cm for that injected with alcohol alone in comparison with combined injection therapy which was 2.29 ± .91 cm). Other comparing parameters between simple cysts injected with alcohol alone and that were injected with combined therapy included initial size of the cyst, volume of aspirated cyst fluid, volume of injected alcohol or follow up duration and complications showed no significant difference (all $p > 0.05$) (Table 1).

3.2. Patients with hepatic hydatid cysts group

Significant difference was observed in number of sessions (36 sessions using alcohol injection alone in comparison with 27 sessions using combined alcohol and tetracycline injection) ($p < 0.001$). 21 out of 36 patients had cyst > 5 cm are injected with combined ethanol and tetracycline but 15 patients who are injected with ethanol alone were divided into 2 groups according to cyst size (< 5 cm; n = 6 and > 5 cm; n = 9). Significant difference was also observed in cyst reduction rate (60.00 ± 0.65% using only alcohol injection in comparison with combined therapy reduction rate was 75.14 ± 1.41%) ($p \leq 0.001$). As regard volume of injected alcohol p-value was significant ($p < 0.001$) (75.00 ± 9.25 ml for that injected with alcohol alone in comparison with combined injection therapy which was 51.42 ± 16.59 ml). There was no significant difference in final size of the cyst, alcohol intoxication and anaphylaxis between Ethanol injection group and Ethanol with