Percutaneous treatment of symptomatic non-parasitic hepatic cysts. Initial experience with single-session sclerotherapy with polidocanol.

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Abstract

Aims: Hepatic cysts have a prevalence of 2.5-7% and most of them are asymptomatic. However, large cysts may cause complaints; in such cases an appropriate treatment is necessary (open surgery, laparoscopic deroofing, percutaneous removal of cystic fluid and injection of a sclerosing agent. The aim of this study was to assess the efficacy and safety of a single session technique with polidocanol in the therapy of symptomatic non parasitic hepatic cysts. Material and methods: The study included 13 patients with symptomatic liver cysts (range 4-10 cm). All patients underwent percutaneous aspiration of the liver cyst under ultrasound guidance followed by instillation of polidocanol (3%, 4-10 ml). The patients were followed up at 1, 3 and 12 months. The disappearance of the cyst or reduction in volume more than 90% was considered successful. If the fluid was accumulated at 1 month the procedure was repeated. If after the second injection the fluid accumulation was more than 50% of the initial volume the case was considered a failure and a laparoscopic deroofing was performed. Results: The procedure was successful in 10 patients, 9 after the first instillation and one after the second (76.9%). The mean initial volume of cysts was 228 ml and the mean reduction in volume at 1, 3 and 12 months was 80.2%, 91.9% and 96.7%. The cyst resolution was gradual with clinically significant cyst reduction achievement within 1 year after therapy. In 3 patients the fluid reaccumulated at the same volume despite 2 instillations. Those 3 cases the procedure was considered failure and the patients were sent to surgery. In 2 patients (one successfully treated and one with treatment failure) bleeding during the first puncture and aspiration appeared and the therapy was postponed for 1 month. There were no significant adverse effects, and all the patients had relief of symptoms after therapy. Conclusions: This initial experience with percutaneous aspiration and polidocanol sclerosis of hepatic cysts demonstrated that the technique is efficient and safe.

Keywords: hepatic cyst, ultrasonographic guided aspiration, sclerotherapy, polidocanol

Introduction

Hepatic cysts have a prevalence of 2.5-7% and most of them are asymptomatic [1]. However, large cysts may cause complaints such as pain, nausea, meteorism, vomiting, early satiety and even obstructive jaundice [1-3]. In such cases an appropriate treatment is necessary. Open surgery (internal drainage with cysto-jejunostomy, varying degrees of liver resection, liver transplantation) or laparoscopic deroofing are used to treat symptomatic patients with high success rates [4,5]. However, surgery is associated with substantial morbidity and mortality and requires technical expertise and is used only in selected cases [5].

Percutaneous treatment usually with ultrasound guidance is a minimally invasive therapeutic option for these patients. The technique consists of the aspiration of cystic fluid with or without injection of a sclerosing agent [4]. Due to the presence of epithelial cell lining the simple needle aspiration is associated with high recurrence rate (78-100%) [5].
The most used and studied sclerosing agent is ethanol [6-12]. Ethanol destroys the cell lining of the cystic cavity thus disabling the cystic fluid secretion. It is a relatively safe and effective therapy of solitary large hepatic cysts [13]. Various techniques have been used over time [6-12] but ethanol may leak from the cystic cavity into peritoneum or bile ducts and may be systemically absorbed [5]. Therefore other agents were studied such as tetracycline chloride [13,14], minocycline chloride [15,16], hypertonic saline solution [17] and ethanolamine oleate [5,18].

Polidocanol is a sclerosing agent that has been extensively used for the treatment of venous malformations, varicose veins and lymphoceles [19]. Renal cysts, hydroceles, and epididymal cysts were also successfully treated with polidocanol sclerotherapy [20].

The aim of this study was to assess the effectiveness and safety of ultrasound guided percutaneous aspiration and polidocanol sclerosis of symptomatic hepatic cysts.

**Material and methods**

From June 2008 through June 2013, 13 patients (11 women, 2 men, mean age 57.7, range 35-71) consecutively referred to our department with symptomatic liver cysts (solitary or multiple) were included in this prospective study. Patients with polycystic liver disease were excluded. The demographic characteristics of the study group are presented in table I. All patients gave a written consent for the study, and the study protocol was approved by the Ethics Committee at our institution.

Simple liver cysts were diagnosed by ultrasound (US) as anechoic structures with smooth borders and strong posterior echo enhancement. The volume of the cyst was estimated as the volume of an ellipse, multiplying the product of the three orthogonal diameters by 0.523 (volume = height x width x length x 0.523).

The procedure was performed on an inpatient basis. The puncture site, needle angle, and depth were chosen in real time at US examination. After antiseptic preparation of the skin and local anesthesia with lidocaine, the cyst was punctured with an 18-gauge aspiration needle using the percutaneous tranhepatic approach. The content of the cyst was aspirated and the cystic fluid was sent for cytological and bacteriologic examination. To avoid leakage of the sclerosing agent, a puncture line traversing normal liver parenchyma was chosen. The fluid aspirated was then checked to exclude the presence of bile and a possible cysto-biliary fistula (in 5 patients). In the other 8 patients the cyst was opacified by injection of a diluted US contrast agent (2-4 drops of SonoVue, Bracco, Milan, Italy in 40-200 ml 0.9% saline) to verify the absence of communication between the cyst cavity and the biliary tree and the into the peritoneal cavity. The amount of contrast agent injected was the same or lower as the volume aspirated from the cyst cavity [21]. During contrast enhanced US (CEUS) cystography in this study, no communication was visible before the injection of the sclerosing agent.

<table>
<thead>
<tr>
<th>Patient no</th>
<th>Gender</th>
<th>Age</th>
<th>Symptoms</th>
<th>Location (liver segment)</th>
<th>Size (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>female</td>
<td>43</td>
<td>pain in RUQ</td>
<td>VI</td>
<td>10/8/8.5</td>
</tr>
<tr>
<td>2</td>
<td>male</td>
<td>60</td>
<td>pain in RUQ</td>
<td>VI</td>
<td>9/8.7/6</td>
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<tr>
<td>3</td>
<td>female</td>
<td>68</td>
<td>nausea</td>
<td>III</td>
<td>8.1/7.8/6</td>
</tr>
<tr>
<td>4</td>
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<td>71</td>
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<td>10.2/5.2/5.8</td>
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<tr>
<td>5</td>
<td>female</td>
<td>66</td>
<td>thoracic pain</td>
<td>IV</td>
<td>7.7/5.1/6</td>
</tr>
<tr>
<td>6</td>
<td>female</td>
<td>52</td>
<td>epigastric pain</td>
<td>III</td>
<td>9/8/8.6</td>
</tr>
<tr>
<td>7</td>
<td>male</td>
<td>69</td>
<td>pain in RUQ</td>
<td>VI</td>
<td>7/6/6.5</td>
</tr>
<tr>
<td>8</td>
<td>female</td>
<td>35</td>
<td>compression</td>
<td>III</td>
<td>5.3/4.4/6</td>
</tr>
<tr>
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<td>III</td>
<td>6.8/7/5.8</td>
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<td>53</td>
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<td>II</td>
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<tr>
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<td>VI-VII</td>
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</tr>
<tr>
<td>12</td>
<td>female</td>
<td>68</td>
<td>pain in RUQ</td>
<td>VII</td>
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<tr>
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<td>female</td>
<td>57</td>
<td>pain in RUQ</td>
<td>VI-VII</td>
<td>9.6/9.2/11</td>
</tr>
</tbody>
</table>

RUQ- right upper quadrant

Table I. Demographic characteristics of the patients with hepatic cysts.
Two-four vials of polidocanol 3% (Aethoxysclerol, Kreussler & Co GmbH, Germany) (4-8 ml) were injected into the cyst cavity and then the needle was removed. The patients were examined the next day for possible complications and then discharged. Follow-up US examinations were done after 1, 3 and 12 months post procedure. The treatment was considered efficient if the cyst had disappeared or was replaced by an echogenic area (fig 1). A reduction more than 90% in volume at 12 month of follow up was considered also efficient.

In patients in which at the 1-month follow up the fluid was found to be recollected, the procedure was repeated. If after the second procedure the fluid accumulation was more than 50% of the initial volume the case was considered a failure and a laparoscopic deroofing was planned.

The ultrasound guided sclerotherapy and US follow up were performed using a GE Logiq 7 scanner with a 3.5 MHz probe, an Aloka system with a 3.5 MHz probe and an Acuson 128XP system with a 3.5 MHz convex probe.

**Results**

The aspirated fluid was clear or slightly turbid, yellow in color with the exception of the 3 cases with intracystic bleeding where the aspect was dark red. The cytopathological examinations were negative for malignant cell and revealed no inflammatory cells. No signs of bacterial or parasitic infections were present in the aspirated fluid.

The procedure was successful in 10 of 13 cases (76.9% success rate), 8 after the first injection and 2 after the second. The mean± SD aspirated volume was 228±133.6 ml, range 97-560 ml. The successfully treated cysts had a lower volume in comparison with those with treatment failure: 204.9 ml vs. 305.3 ml. In successfully treated cases the mean reduction in volume was 80.2% (range 62-96.9%) at 1 month, 91.9% (range 81.7-97.2%) at 3 months and 96.7% (range 92.1-100) at 12 months (table II).

In 3 patients the treatment was unsuccessful and the patients were sent for laparoscopic deroofing. In 2 of

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**Table II. Results and complications of the percutaneous aspiration and the polidocanol sclerosis of the symptomatic hepatic cysts.**

<table>
<thead>
<tr>
<th>Pt no</th>
<th>Estimated volume (ml)</th>
<th>Aspirated volume (ml)</th>
<th>Amount of polidocanol injected (ml)</th>
<th>Cyst volume (ml) 1mo</th>
<th>Cyst volume (ml) 3mo</th>
<th>Cyst volume (ml) 12mo</th>
<th>Percentage reduction (%) 1mo</th>
<th>Percentage reduction (%) 3mo</th>
<th>Percentage reduction (%) 12mo</th>
<th>Final result, complications</th>
</tr>
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<td>362</td>
<td>8**</td>
<td>350*</td>
<td>340</td>
<td>–</td>
<td>3</td>
<td>92.3</td>
<td>95.4</td>
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<td>2</td>
<td>265</td>
<td>247</td>
<td>6</td>
<td>19</td>
<td>11.3</td>
<td>0</td>
<td>92.3</td>
<td>95.4</td>
<td>100 success</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>189</td>
<td>198</td>
<td>6</td>
<td>185*</td>
<td>192</td>
<td>–</td>
<td>7</td>
<td>3</td>
<td>success</td>
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</tr>
<tr>
<td>4</td>
<td>158</td>
<td>150</td>
<td>4</td>
<td>18</td>
<td>11</td>
<td>9</td>
<td>88</td>
<td>92.7</td>
<td>94</td>
<td>success</td>
</tr>
<tr>
<td>5</td>
<td>122</td>
<td>137</td>
<td>4</td>
<td>17.2</td>
<td>11.8</td>
<td>–</td>
<td>87.5</td>
<td>91.4</td>
<td>–</td>
<td>success</td>
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<tr>
<td>6</td>
<td>317</td>
<td>300</td>
<td>8</td>
<td>47.1*</td>
<td>31.9</td>
<td>–</td>
<td>84.3</td>
<td>89.4</td>
<td>–</td>
<td>success</td>
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<tr>
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<td>140</td>
<td>150</td>
<td>4</td>
<td>57*</td>
<td>27.4</td>
<td>11.9</td>
<td>62</td>
<td>81.7</td>
<td>92.1</td>
<td>success</td>
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<tr>
<td>8</td>
<td>87</td>
<td>97</td>
<td>4</td>
<td>7</td>
<td>–</td>
<td>–</td>
<td>92.8</td>
<td>–</td>
<td>–</td>
<td>success</td>
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<tr>
<td>9</td>
<td>151</td>
<td>142</td>
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<td>11.8</td>
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<td>91.7</td>
<td>–</td>
<td>94.5</td>
<td>success</td>
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<tr>
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<td>121</td>
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<td>9.7</td>
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<td>92</td>
<td>95.6</td>
<td>100 success</td>
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<td>11</td>
<td>344</td>
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<td>312</td>
<td>305</td>
<td>–</td>
<td>13</td>
<td>14.4</td>
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<td></td>
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<tr>
<td>13</td>
<td>541</td>
<td>560</td>
<td>10**</td>
<td>17.9</td>
<td>4.2</td>
<td>–</td>
<td>96.9</td>
<td>99.2</td>
<td>–</td>
<td>intracystic bleeding, success</td>
</tr>
</tbody>
</table>

*Second injection

** Injection after 1 month
them the surgical treatment was efficient, the other presented a relapse 6 months later. In one case bleeding occurred during aspiration and in this case sclerotherapy was postponed for one month. In this case a second injection was required but due to the failure in the cyst’s volume reduction, the patient was sent for surgery.

In another patient the fluid accumulated at 1 month follow up, with important septa formation inside. A second attempt was made but due to the presence of septa the aspiration of the fluid was only partial and the second sclerotherapy procedure was performed (fig 2). The patient was monitored for one month without a change in the cyst aspect. Laparoscopic surgery revealed a cyst with several membranes inside, without hydatid features.

One patient successfully treated (case 13 from table I) had an intracystic bleeding during aspiration with clot formation. Sclerotherapy was postponed for one month. At 1 month after sclerotherapy the cyst was significantly smaller with the clot inside. At 3 months the size was even more reduced (fig 3).

No other local or systemic complications were encountered during polidocanol sclerotherapy.

Discussions

In the last years the treatment of hepatic cyst has switched from a surgical approach to less invasive techniques such as laparoscopic deroofing and image-guided percutaneous treatment. The latter has gained wide acceptance by the patients and physicians as a simple, less invasive, repeatable and efficient treatment. The treatment consists of evacuation of the cystic content (either by aspiration or drainage through a catheter) followed by sclerotherapy of the inner epithelium by several substances (ethanol, tetracycline chloride, minocycline chloride, hypertonic saline solution and ethanolamine oleate [5-8,13-18].

The most used substance for sclerotherapy of hepatic cysts was ethanol [6-12]. Both single and multiple sessions were used, in almost all studies the evacuation of the fluid content being performed through 6-8 F catheters [4-9]. Performing sclerotherapy in one session was less effective in achieving a complete damage of the entire epithelium in comparison with prolonged drainage [1]. In ethanol sclerotherapy different volumes (10 to 50% of the cyst volume) and concentrations of ethanol (95-99%) were used. The exposure time to the sclerosing agent varies widely, from 10 minutes to 4 hours [10, 11].

After ethanol sclerotherapy an 80-100% reduction of cyst volume was achieved in most cases [1,6,9-11,22]. However, this technique may be associated with several complications and drawbacks. The main complications that may occur during ethanol sclerotherapy are pain, ethanol induced fever or hyperthermia, intoxication, intracystic bleeding and iatrogenic pleuritis [4,5,13,23]. Intense pain may occur during instillation of ethanol in

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Fig 2. a) US aspect of a benign non parasitic liver cyst; b) after percutaneous sclerotherapy with polidocanol an inflammatory reaction with septa formation (>) occurring within the cyst.

Fig 3. a) Large hepatic cyst in the right lobe; b) US aspect after evacuation and intracystic bleeding; c) US aspect 1 month after polidocanol sclerotherapy; note the presence of the clot inside the cystic cavity; d) US aspect after 4 months.
the cysts or intraperitoneal ethanol diffusion at catheter withdrawing [23]. The first can be prevented by injecting lidocaine into the cyst before ethanol instillation. Ethanol intoxication and even ethanol induced coma are serious events that may occur especially in the case of larger cysts where a high amount of ethanol is injected. These events may be prevented by limiting the exposure to ethanol to maximum 60 minutes, time interval being optimal for sclerosing effect [1,23].

Patients are often hospitalized for at least 24 h and in rare cases general anesthesia may be necessary. For the treatment of large cysts several injections are necessary, in these cases the catheter is left in place for several days with a subsequent risk of dislodgement or leakage around the catheter with pain [12,24].

Before performing the procedure a communication of a cyst with the biliary tree should be ruled out. We did this in 8 cases using CEUS.

Taking into account the good results of ethanol in achieving a complete sclerotherapy but also the relatively complicated technique (with multiple instillation and aspirations) and the possible complications, several other substances with better safety profiles, easiness to use and low cost were tested. Tetracycline chloride, minocycline chloride, hypertonic saline were tested with good sclerosing results and few complications. The technique in these studies consisted of evacuation of a part of the cyst content through a needle (in most studies) and instillation of a sclerosing agent which was left in place. The method seems to be cheaper, faster and easier to use in comparison with the classic ethanol technique [5-8,13-18].

Injection into the cyst destroys the biliary epithelium chemically, leading to a reduction in liquid secretions. The residual fluid is progressively resorbed through microscopic communications which may exist between the cyst and the surrounding liver parenchyma so the volume of the cyst is reduced gradually [13].

We performed sclerotherapy with polidocanol, a sclerosing agent that has been extensively used for the treatment of venous malformations, varicose veins and lymphoceles [19].

Polidocanol consists of 5% ethyl alcohol as a preservative and 95% hydroxypolyethoxydodecane as the active component of the product [25]. It poses a detergent action that produces a rapid overhydration of the cells, with consequent destruction. Its sclerosing effect can be obtained with a small volume of substance so its use is easier than that of ethanol. Being extensively used in varicose vein sclerotherapy its safety well known so it may be used without reaspiration. Polidocanol can be left in the cystic cavity to destroy the lining epithelium with only one step application [25]. As its application is painless, no intracystic anesthesia or sedation is required.

Renal cysts, hydroceles, and epididymal cysts were successfully treated with polidocanol sclerotherapy [20]. To our knowledge this is the first study on the application of liquid polidocanol in the treatment of symptomatic non parasitic hepatic cysts. The results of our study showed that our proposed technique of polidocanol sclerotherapy in symptomatic hepatic non parasitic cysts is a good, simple, fast and safe procedure. The efficiency was only 76.9%, lower than that obtained in studies with ethanol sclerotherapy. The three failures may be explained by the following factors: a) All three unresolved cysts had large volumes which would have required larger amounts of polidocanol; b) In two of them a complication occurred during or after the procedure. In one patient a bleeding started during evacuation of the fluid so the procedure was postponed for a month. The presence of the clot inside the cyst cavity may have been limiting the diffusion of polidocanol in the cyst cavity. In one successfully treated patient a similar event occurred without influencing the final outcome. Normally, the sclerotherapy is contraindicated in hemorrhagic hepatic cysts, in such cases the patients being managed conservatively by percutaneous transhepatic drainage with or without arterial embolisation and most of them surgically (unroofing, hepatic resection, or cyst enucleation) [26]. One very recent study comprising 20 patients with hemorrhagic hepatic cysts demonstrated that percutaneous sclerotherapy with ethanol is as effective in hemorrhagic as in simple hepatic cysts [21]. The authors concluded that sclerotherapy should not be contraindicated for this complication but have also recommended an arbitrary delay of at least 3 months between the diagnosis of hemorrhagic content and treatment [21]. Because in our study the bleeding occurred during aspiration we postponed the procedure for one month. Another patient developed an inflammatory reaction inside the cyst with echogenic septa and reaccumulation of fluid. A second aspiration was tried but without success. After sclerotherapy, cytological and biochemical signs of acute or subacute inflammatory reaction are present in all cysts [27]. Changes in capillary permeability and cystic epithelial function are also present after sclerotherapy. These inflammatory reactions may lead to fluid production (which may decrease over time) but also to membrane formation with limitation of sclerosing agent distribution in the cyst; c) Performing the evacuation of the cystic content as a one step procedure through a needle leads to the collapse of the cyst, so many folds and adherence areas are created which are inaccessible to the sclerosing agent. In such cases the intracystic distribution may be enhanced by using foam
sclerosants (liquid sclerosants mixed with air) instead of liquid sclerosants. The advantage of foam sclerotherapy with polidocanol was demonstrated in the treatment of varicose veins but also in 3 patients with hepatic cysts [28]. Using a needle to evacuate the cystic contents and injecting the sclerosant agent may lead to bleeding when the needle tip stick to the cyst wall. This may be prevented by using small size catheters (6-7F) instead of 18G aspiration needles. The catheters can be introduced in a “one step procedure”.

In successfully treated cases the reduction in cysts volume started at one month (80%) exceeding 90% after 3 months. In 3 patients the cyst was no longer visible after 1 year.

No adverse affects of polidocanol were present in our study which demonstrates the safeties of this agent.

The present study has some limitations. The number of patients was low which has clearly influenced the efficacy assessment. Secondly the patients were followed up only for one year but the results of previous studies have shown that recurrence is a rare event after one year.

In conclusion, the results of this prospective preliminary study have demonstrated that sclerotherapy with polidocanol is an effective, safe and simple method to treat symptomatic non parasitary hepatic cysts. The efficacy and safety may be clearly improved by using foam polidocanol as a sclerosing agent and small bore, “one-step” catheters for evacuation of the cyst content and instillation of the sclerosing agent.

**Conflict of interest:** none

**References**


