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Article *in* British Journal of Radiology · January 2017

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Received: 25 July 2016 | Revised: 12 January 2017 | Accepted: 24 January 2017

https://doi.org/10.1259/bjr.20160640

Cite this article as:
Shera TA, Choh NA, Gojwari TA, Shera FA, Shaheen FA, Wani GM, et al. A comparison of imaging guided double percutaneous aspiration injection and surgery in the treatment of cystic echinococcosis of liver. *Br J Radiol* 2017; **90**: 20160640.

FULL PAPER

A comparison of imaging guided double percutaneous aspiration injection and surgery in the treatment of cystic echinococcosis of liver

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Objective: To compare the results and complications of treatment by double percutaneous aspiration injection (DPAI) in cystic echinococcosis (CE) of the liver with those of surgery. To the best of our knowledge, such a study has not been carried out till date.
Methods: From November 2012 to November 2015, 43 patients were randomly allocated to DPAI group ($n = 22$) and surgery group ($n = 21$). After the intervention, patients were evaluated monthly for 3 months, then at the sixth month and 6 monthly thereafter.
Results: Average hospital stay was 2.38 days in DPAI group and 8.23 days in the surgery group. Response to DPAI was categorized as successful in 95.3% ($n = 20$) patients and incomplete in 4.7% ($n = 1$) patients. Response to surgery was characterized as successful in 85.7% ($n = 18$) patients and incomplete in 4.7% ($n = 1$) patients, and recurrence was seen in 9.5% ($n = 2$) patients. Using a 10% margin for non-inferiority, treatment response in the DPAI group was non-inferior to that of the surgery group. In the DPAI group, 19 patients had no complications, minor complications were seen in 4.7% ($n = 1$) patients and a major complication was seen in 4.7% ($n = 1$) patients. In the surgery group, no complications were seen in 13 patients, major complications were seen in 28.57% ($n = 6$) patients and minor complications were seen in 9.5% ($n = 2$) patients.
Conclusion: Over a follow-up period of 3 years, DPAI is non-inferior to surgery in the treatment of CE of the liver, while there is a statistically significant difference in the hospital stay and occurrence of complications.
Advances in knowledge: DPAI offers advantages such as a short hospital stay, minimal invasiveness and morbidity, while being non-inferior to surgery. Total Immunoglobulin G antibody titres have limited utility in follow-up of patients treated.

INTRODUCTION

Echinococcosis in humans is a parasitic infection caused by larva of cestodes from the genus Echinococcus in whose life cycle humans play the role of an accidental intermediate host. The major clinically important species are *Echinococcus granulosus* and *Echinococcus multilocularis*, which cause cystic echinococcosis (CE) and alveolar echinococcosis, respectively.[1,2] The incidence of CE is variable, ranging from <1 in non-endemic areas to 220 per 100,000 in some endemic areas.[3] CE may involve almost any organ, with up to 80% patients having single organ involvement, which in approximately two-third of cases is the liver; in about 20% cases, it is in the lungs and less frequently in the spleen, kidneys, muscles, heart, abdominal cavity, bones, central nervous system, skin, eyes, urinary bladder, testis, ovaries *etc.*[4] The clinical manifestations are therefore protean, depending on the site and size of the cyst, but resemble those of a slow-growing tumour that causes gradually increasing mass effect.[5] Complications of hepatic CE include peritoneal rupture, leading to peritoneal hydatidosis, intrabiliary rupture, leading to cholangitis or cholestasis, rupture into the thoracic cavity and secondary infection forming liver abscesses. In addition, immunological reactions may be observed such as urticarial rash, anaphylaxis or membranous nephropathy.[6]

CE is diagnosed by first identifying cysts in patients suspected either clinically or incidentally on ultrasonography, CT, X-ray and/or MRI, followed by detection of specific antibodies in serum by immunodiagnostic tests to confirm the aetiology. However, the immunodiagnosis may be false

negative in 10–20% with hepatic cysts and up to 40% with pulmonary cysts.[6–8]

The World Health Organization Informal Working Group on Echinococcosis has classified types of *E. granulosus* cysts of liver sonographically as Type CL—unilocular, cystic lesions (CLs) with uniform anechoic content, cyst wall not visible; Type CE 1—unilocular, simple cyst with uniform anechoic content, cyst wall is visible; Type CE 2—multivesicular, multiseptate cysts; Type CE 3—anechoic content with detachment of laminated membrane from the cyst wall; Type CE 3b—predominantly solid with daughter vesicles; Type CE 4—heterogeneous hypoechoic or hyperechoic degenerative contents; and Type CE 5—cysts characterized by thick calcified wall with degree of calcification varying from partial to complete.[7]

There are four treatment options for hepatic CE: surgery, chemotherapy, percutaneous drainage and just observation. Historically, the treatment of choice was open surgery with meticulous operative site packing to prevent spillage.[9] Surgical options include conservative techniques such as open cystectomy (with or without omentoplasty/capitonnage or other methods of management of residual cavity) and (palliative) tube drainage of infected cysts or more radical procedures such as pericystectomy, partial hepatectomy or lobectomy. While the results of surgery have been validated over time, it is an invasive modality compared with the relatively benign nature the disease exhibits in most cases.[4,7,10–13] Chemotherapy alone is indicated for patients who are inoperable with hepatic echinococcosis and for patients with multiple cysts in two or more organs.[14]

Since the late 1980s, a number of techniques for percutaneous treatment (PT) of liver hydatid cysts have been developed,[15] in which after percutaneous aspiration of the cyst under ultrasonography or CT guidance, a scolicidal agent is injected into the cyst cavity with or without reaspiration of the cyst contents.[16–19] In 1992, Giorgio et al[19,20] first presented a modified technique of PT of CE called double percutaneous aspiration and ethanol injection [double percutaneous aspiration injection (DPAI)], characterized by no reaspiration of the ethanol injected to replace the aspirated fluid and repetition of the procedure at an interval of 3–7 days. DPAI is less invasive and in the case of uncomplicated hepatic CE, DPAI in combination with benzimidazole therapy is a safe and effective alternative to surgery, requires a shorter hospital stay, permits early return to work, has a low complication rate and is cost effective for the state, the hospital and the patient.[16–19]

The objective of this study was to compare surgery and DPAI in the treatment of hepatic CE with regard to efficacy, hospital stay and complications.

METHODS AND MATERIALS

This study was a prospective randomized controlled trial, registered with the Clinical Trial Registry of India (CTRI/2015/10/006231) and was approved by the institutional ethics committee. Patient recruitment took place between November 2012 and May 2014, and the patients were followed up to the date of analysis in November 2015. The outcomes studied were change in cyst volume, sonographic appearance of the cyst, antibody titres, hospital stay and complications.

The study group comprised of newly diagnosed cases of hepatic CE. Diagnosis was established by the presence of a liver cyst with a positive hydatid serology or a liver cyst with sonographic appearance typical for CE 1 or CE 3a hydatid cysts. The exclusion criteria used are given in Table 1.

For calculation of sample size, review of previous studies showed a cure rate of 99.3% for unilocular cysts treated with DPAI.[19–21] A meta-analysis of multiple studies on treatment of CE showed a cure rate of 89.8% for patients undergoing surgery.[22] Considering a 10% difference in cure rates to be clinically important, 44 patients are required to be 90% sure that the upper limit of a one-sided 95% confidence interval (CI) (or equivalently a 90% two-sided CI) will exclude a difference in favour of the standard group of >10%. A sample size of 44 patients was therefore selected. During the study period, we managed to enrol 43 patients in the study. Eligible patients were randomly allocated either into the surgery arm or the DPAI arm with the use of sealed envelopes in 1 : 1 ratio. The patients, radiologists, physicians and surgeons were not blinded to the arm allocation. Baseline patient characteristics of the two groups were comparable (Table 2).

The interventions in the two groups were carried out as follows. All patients in both groups were put on albendazole (10 mg/kg/day) for 1 week before either procedure.

In the DPAI group, patients were in addition put on dexamethasone 2 mg bid (bis in die) for 2 days before the procedure to decrease possible hypersensitivity reactions. The procedure was performed by an interventional radiologist with at least 10 years' experience in performing CT-/Ultrasonography (USG)-guided procedures. The procedure was performed under local anaesthesia with intensive monitoring and in the presence of an anaesthetist. Under aseptic precautions and after

Table 1. Exclusion criteria

Children <12 years
Complicated cysts (ruptured or infected)
Solid (pseudotumour) sonographic pattern
Calcified cyst
Multiple liver cysts
Cysts in extrahepatic location
Multivesicular cysts
Pregnant females or females intending to conceive during the treatment period
History of hypersensitivity to albendazole
Patients with CE of other organs
Superficial cysts with <1 cm of overlying liver parenchyma

CE, cystic echinococcosis.

Table 2. Baseline characteristics

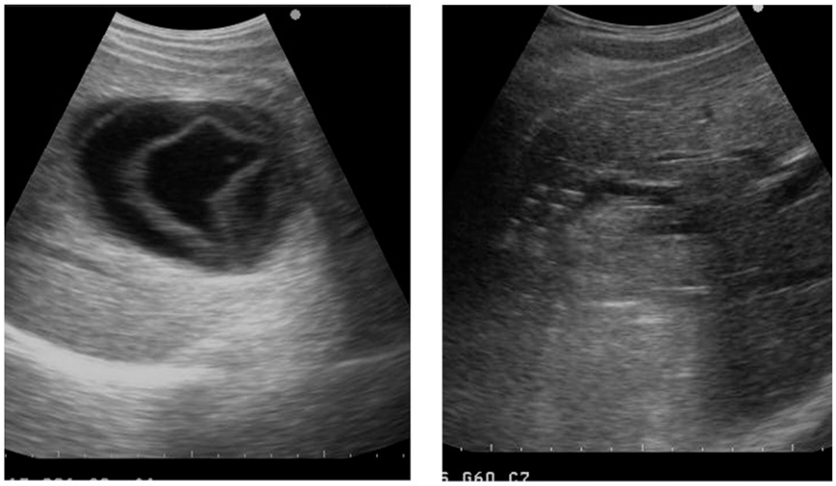
Characteristic	Surgery arm	DPAI arm	*p*-value
Number of patients	21	21	
Age (years)	28.9 ± 14.5	27.9 ± 16.33	0.824
Sex (M : F)	12 : 9	10 : 11	0.537
Locality (rural : urban)	14 : 7	13 : 8	0.747
Presentation			
Incidental	7	6	0.739
Symptomatic	14	15	
Symptoms			
Abdominal pain	14	12	0.778
Nausea/vomiting	2	4	
Fever	1	3	
Jaundice	4	2	
Abdominal mass	2	1	
Anorexia	1	1	
Serology			
Negative	4	4	>0.9
Equivocal	5	4	
Positive	12	13	
Geometrical mean titre	1 : 154.80	1 : 131.25	0.522
USG			
Location			
Right lobe	17	15	0.2772
Left lobe	4	6	
WHO type			
CE 1	16	18	0.6965
CE 3a	5	3	
Mean cyst volume (ml)	200.9 ± 142.4 (range 80–700)	192.6 ± 155.6 (range 60–800)	0.854

CE, cystic echinococcosis; DPAI, double percutaneous aspiration injection; F, female; M, male; USG, Ultrasonography; WHO, World Health Organization.

administration of local anaesthesia at the point of puncture, a spinal needle (22, 20 or 18 gauge) was inserted into the cystic cavity by a transhepatic route under ultrasonography or CT guidance depending on the size and location of the cyst. Cyst contents were almost completely aspirated. After excluding the presence of bilirubin in the aspirated fluid by a rapid dipstick test (UroColour™ 10: SD Bio Standard Diagnostics Pvt. Ltd, India) in order to rule out a biliary communication, 95% sterile ethanol was injected into the cyst and left *in situ* to replace 50–60% of the amount drained up to a maximum of 2 ml per kilogram of body weight. The injected alcohol is not reaspirated. Immediately after aspiration, parasitological examination of the fluid was performed for detection of scolices and assessment of viability. The entire procedure was repeated after 3–7 days. The cyst was punctured, fluid aspirated, alcohol was injected and once again not reaspirated. Scolex viability and the presence of bilirubin were reassessed.

In the surgery group, the surgical procedure used was cystectomy, *i.e.* removal of ectocyst and endocyst. The procedure was performed by an experienced surgeon not below the grade of a professor and with at least 15 years' experience. After an abdominal incision, the operative field was meticulously packed with povidone-iodine-soaked gauzes to prevent peritoneal spillage. The liver was mobilized and adhesions to the cyst, if any, were dissected, followed by aspiration of cyst fluid by a trocar plus suction tubing and evacuation of the laminated membrane by sponge holding forceps. The pericyst was not removed except along the liver surface to permit cavity management. The pericyst-lined residual cavity was then inspected for any biliary communication, which was sutured if present. The residual cavity was managed by omentoplasty, capitonnage or tube drainage as per the preference of the operating surgeon. Patients requiring more radical procedures such as pericystectomy or lobectomy were excluded from the study.

Figure 1. (a) Membranes separating on needle insertion. (b) Hyperechoic appearance of alcohol in cyst cavity.



(a) (b)

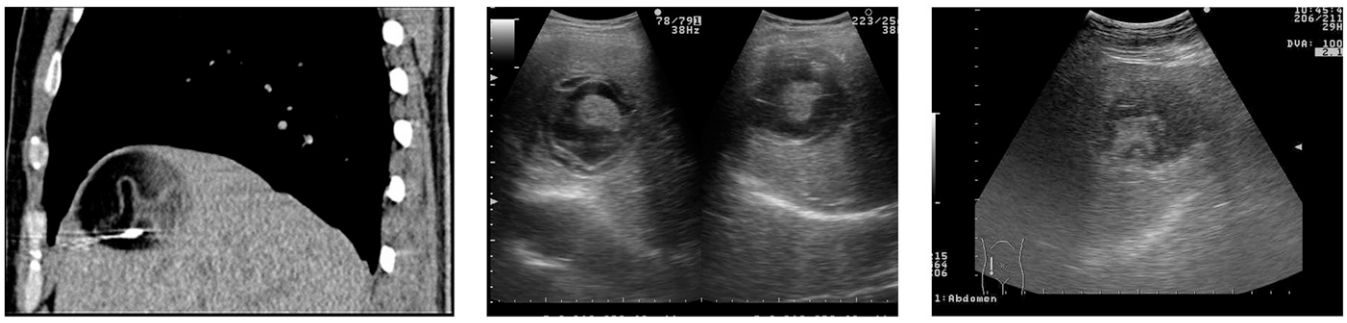
Both groups of patients received albendazole (10 mg/kg/day) in three cycles of 3 weeks each, with a 1-week break between the cycles.

After either intervention, patients were followed up on an outpatient basis with clinical, laboratory and ultrasonographic examinations performed monthly for the first 3 months, then at the sixth month and 6 monthly thereafter. Outcome variables were collected as per a predefined *pro forma* and included cyst volume, cyst appearance, Immunoglobulin G (IgG) Enzyme Linked Immunosorbent Assay (ELISA) titres, complications, hospital stay and treatment response. The outcome variable predominantly used to assess response to treatment was volume of the residual cyst cavity. In the surgery group, the residual cavity consisted of a pericyst-lined area filled with fluid and debris. In the DPAI group, the residual cavity consisted of a pericyst-lined area containing the detached laminated membrane, fluid and debris. The volume of the cavity was calculated by measuring the diameter in three dimensions. Other variables used to assess treatment response were cyst appearance and IgG ELISA titres.

In the absence of any guidelines for assessment of treatment response, definitions adapted from Smego et al[22] were used to categorize response to treatment. Successful treatment was defined as disappearance of clinical symptoms with separation of the endocyst from the pericyst and a decrease in cyst size up to 50% or less, forming either a small residual cyst cavity or a pseudotumour or no residual lesion. Incomplete response was defined as $<$50% decrease in volume after at least 12 months of follow-up. Treatment failure was defined as no change in size and appearance of cyst on serial imaging or increasing size. Recurrence was defined as increase in size of cyst after an initial decrease or development of new daughter cysts in the residual cavity.

Complications were categorized as major or minor. Major complications were defined as those which prolonged hospital stay, required readmission or posed a threat to life. In the patients from the surgery group whose cavity was managed by tube drainage, the drain was removed when the drain output decreased to $<$15 ml/day, followed by USG documentation of cavity collapse. Persistent drainage from the cavity for less than 1 month was termed as prolonged tube drainage and was considered to be a complication of the procedure.

Figure 2. A 45-year-old male treated with CT-guided double percutaneous aspiration injection: (a) hypodense appearance of alcohol on CT forming a fluid–fluid level with residual cyst fluid. (b) Same patient at 1 month after the procedure. (c) 24 months after the procedure, a heterogeneous solid residual lesion is seen.



(a) (b) (c)

RESULTS

43 patients were enrolled in the study, out of which 22 patients were randomized to the DPAI group and 21 patients were randomized to the surgery group. In one of the patients from DPAI group, the fluid aspirated at the first puncture was positive for bilirubin on the dipstick test, the procedure was abandoned and the patient was excluded from the study. Baseline characteristics of the two groups are given in Table 2, and there was no statistically significant difference between the two groups.

In the surgery group, 21 patients underwent surgery. Cystectomy with tube drainage was performed in 76.2% ($n = 16$) patients, followed by cystectomy with capitonnage in 14.3% ($n = 3$) patients and cystectomy with omentopexy in 9.5% ($n = 2$) patients. The mean operating time was 95 min.

In the DPAI group, a total of 42 punctures were performed in 21 patients. In 17 (80.95%) patients, subcostal route was used and in rest of the patients ($n = 4$), intercostal route was used. In 18 (85.71%) patients, the procedure was performed under USG guidance and in rest of the patients ($n = 3$), CT guidance was used. The mean time taken per percutaneous aspiration injection (PAI) was 20.1 min (range 15–35 min). After the first puncture of the cyst, clear fluid rushed out on withdrawal of the stylet of the spinal needle and immediate separation of endocyst occurred, which progressively increased as more fluid was aspirated (Figure 1a). Once the aspiration was complete, the absolute alcohol injected into the cyst cavity and appeared on ultrasonography as hyperechoic contents partially filling the cyst cavity (Figure 1b), and on CT as hypodense contents within the cyst cavity with fat attenuation (Figure 2a). Before the second puncture, the cyst cavity showed echogenic contents and membranes and regained most of its original volume. Upon the puncture of the cyst for the second time, aspirate was turbid and slightly orange coloured with numerous bits of membranes and debris in the aspirate.

Volume of cyst fluid aspirated in PAI-1 ranged from 45–700 ml (mean 165 ml) and in PAI-2, it ranged from 40–600 ml (mean 143.3 ml). Amount of absolute alcohol injected in PAI-1 ranged from 25 ml to 140 ml (mean 64 ml) and in PAI-2, it ranged from 20 ml to 110 ml (mean 57.6 ml) (Figure 3).

In the DPAI group at the initial puncture, staining and microscopy of the aspirate showed that scolices were viable in 19 (90.4%) patients and non-viable in 2 (9.6%) patients. At the second puncture, scolices were absent in 10 (47.6%) patients and present but non-viable in 8 (38.09%) patients. 3 (14.28%) cysts still had viable scolices at the time of second puncture.

In the DPAI group, most patients were discharged the second day. In 4 cases (8 punctures), the patients were discharged on the third day. The average hospital stay per puncture was 1.14 days. Total hospital stay per patient averaged 2.28 days in the DPAI group. In the surgery group, average hospital stay was 8.23 days (range 5–14 days) ($p = 0.00000000017$). Readmission for complications, if required, was not counted in the total hospital stay.

8 (19.04%) patients were followed for 18 months, 14 (33.33%) patients for 24 months, 12 (28.57%) patients for 30 months and 8 (19.04%) patients for 36 months. Mean follow-up period was 26 months in DPAI group and 27.71 months in the surgery group. The difference between the two groups was not statistically significant ($p = 0.35$). No patient was lost to follow-up.

In the DPAI group, response was categorized as successful in 95.3% cysts ($n = 20$) (95% CI 0.773–0.998) and incomplete in 4.7% ($n = 1$) cysts. In the surgery group, response was characterized as successful in 85.7% cysts ($n = 18$) (95% CI 0.654–0.95) and incomplete in 4.7% ($n = 1$) cysts, and recurrence was seen in 9.5% ($n = 2$) cysts. The difference between the two groups was not statistically significant ($p = 0.8269$). 90 % CI for the difference is from −0.068 to 0.265. Using a 10% margin for non-inferiority, treatment response in the DPAI group was non-inferior to that of the surgery group.

On follow-up, progressive reduction in mean cyst size was seen in both the groups. The cysts in the surgery group tended to have lower volumes than those in the DPAI group (Table 3). In

Figure 3. Amount of fluid aspirated and alcohol injected in each patient.

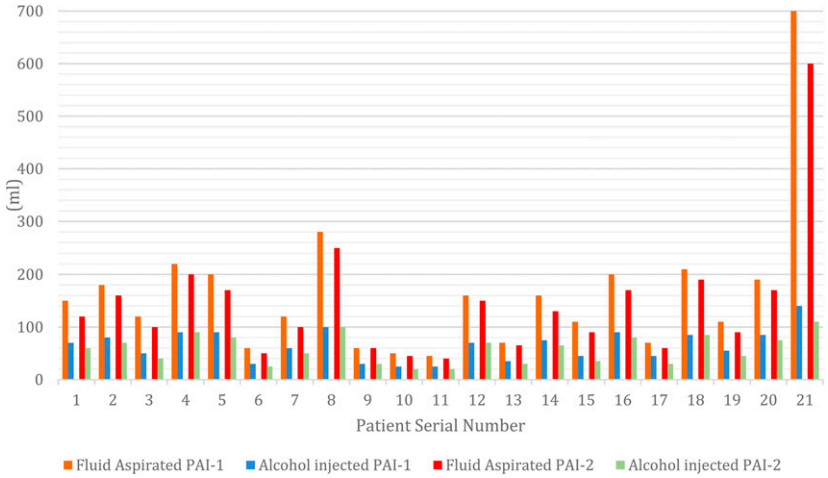


Table 3. Change in mean cyst volume with time

Group	Baseline	1 m	2 m	3 m	6 m	12 m	18 m	24 m	30 m	36 m
DPAI	192.6	126.8	113.6	99.6	84.0	74.8	68.4	67.3	46.1	33.0
Surgery	201.0	64.0	55.6	50.0	43.9	40.8	30.8	22.4	18.5	20.0
p	0.854259	0.001887	0.003706	0.010287	0.043273	0.086244	0.049211	0.039636	0.023953	0.417863

DPAI, double percutaneous aspiration injection.

the DPAI group, the most common pattern visible at the time of the last visit was that of a solid (pseudotumour) appearance seen in 12 (57.14%) cysts (Figure 2a,b and Figure 4a–c), followed by residual cavity with semi-solid contents in 5 (23.81%) cysts (Figure 5a–c), disappearance in 3 (14.29%) cysts and anechoic cavity in 1 (4.76%) cyst. In the surgery group, the most common pattern was of an anechoic residual cavity with irregular walls seen in 8 (38.1%) cysts, solid (pseudotumour) appearance in 6 (28.57%) cysts, disappearance in 6 (28.57%) cysts and semi-solid in 1 (4.76%) cyst. The difference in final appearance of the two groups was statistically significant ($p = 0.008$).

Baseline titres of the two groups showed no statistically significant difference. In both the groups, titres on IgG ELISA showed a pattern of rise after the intervention, followed by a gradual fall over 18–36 months towards pre-procedure values (Table 4). At 1 month, all patients in the DPAI group had positive titres, including the ones who were initially negative or equivocal (Table 2), whereas in the surgery group, 18 of 21 patients had positive titres. The rise in titres after either intervention reflects an increase in IgG antibodies which occurs owing to small amounts of echinococcal antigens gaining access to the blood stream during the procedure. 27 patients (17 patients from the DPAI group and 10 patients from the surgery group) continued to have positive titres at the last visit, despite sonographic features suggesting a successful response to treatment; 1 of the patients in the surgery group had a negative titre and the rest had equivocal titres. The patients who developed a recurrence after surgery showed a rise in titres with increase in size of the residual cavity. The two patients with incomplete response showed no fall in titres over the follow-up period.

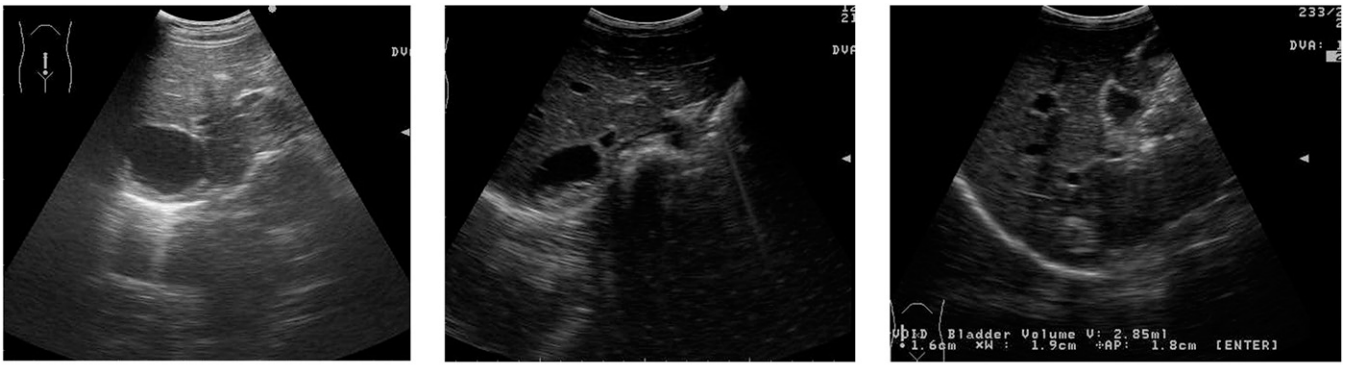
In the DPAI group, 19 patients had no complications, minor complications were seen in 4.7% ($n = 1$) patients and a major complication was seen in 4.7% ($n = 1$) patients. In the surgery group, no complications were seen in 13 patients, major complications were seen in 28.57% ($n = 6$) patients and minor complications were seen in 9.5% ($n = 2$) patients (Table 5). Complications were more common in the patients undergoing surgery ($p = 0.038$). All the major complications in the surgery group occurred in patients in whom the cavity had been managed with tube drainage.

DISCUSSION

CE is considered to be an "orphan disease" in developed countries and a neglected zoonosis overall by current standards of public health.[23,24] It is a potentially life-threatening disease found in pastural regions with an incidence as high as 220 per 100,000 inhabitants in some endemic areas.[3] A wide range of treatment modalities available at various stages with an equally wide range of resources, technological and training backgrounds are necessary for implementation and delivery of each of these modalities. This by itself becomes a big issue in developing countries such as ours, where the patient load is high and both resources and skilled manpower are limited.

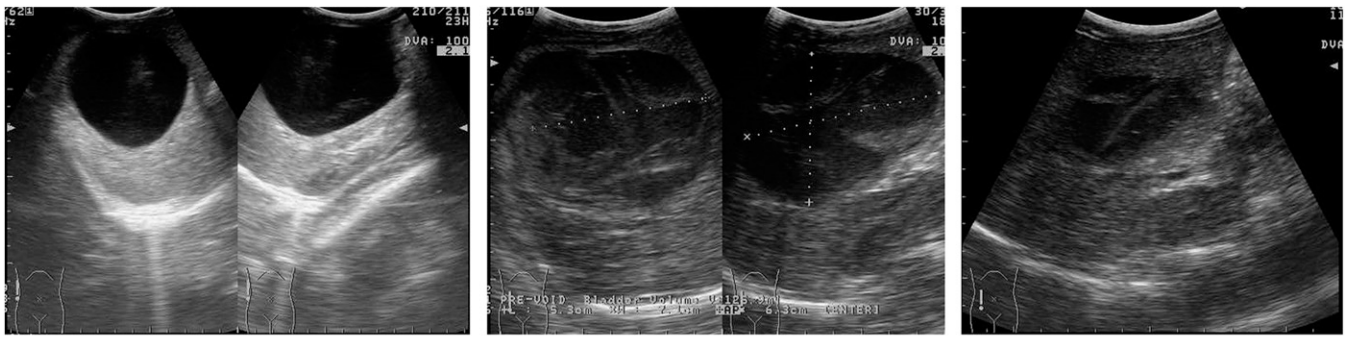
Surgery was first reported in the treatment of human CE in 1821,[25] use of benzimidazole was first reported in 1977[26] and successful percutaneous drainage was first reported in 1985.[27] Despite all three modalities of treatment being concurrently available for almost 30 years, optimal treatment for CE is yet to be fully determined. A recent study from World Health Organization Informal Working Group on Echinococcosis, which graded the quality of evidence and strength of recommendation

Figure 4. A 35-year-old female treated with Ultrasonography (USG)-guided double percutaneous aspiration injection (DPAI): (a) pre-procedure USG. (b) 6 months after DPAI. (c) 36 months after DPAI.



(a) (b) (c)

Figure 5. A 14-year-old male treated with Ultrasonography (USG)-guided double percutaneous aspiration injection (DPAI): (a) pre-procedure USG. (b) Immediately after DPAI. (c) 30 months after DPAI.



(a) (b) (c)

for various modalities in treatment of CE, gave all three of the above modalities as well as the Wait and Watch approach a strength of recommendation of B and Quality of Evidence of III, implying the paucity of evidence from well-designed trials to arrive at a consensus on the optimal treatment.[28] Our study was thus undertaken to prospectively compare DPAI with surgery in the treatment of CE of liver. To the best of our knowledge, such a study has not been undertaken till date.

Current evidence does not support medical therapy alone in the treatment of CE owing to poor response rates (60%) and long durations of therapy required especially in cysts >6 cm.[29] Of all the treatment modalities available for treatment of hepatic CE, PT appears to be best suited for routine use particularly in developing countries owing to its observed good results, short hospital stay, lesser morbidity, lower cost to the patient, the hospital as well as the state and early return to work especially when compared with the standard treatment, *i.e.* surgery.[30]

DPAI differs from other methods of PT in that the scolicide is not reaspirated from the cyst cavity at the end of the procedure. This results in a longer contact period, potentially improving the efficacy while shortening the overall duration of the procedure at the same time. Repeating the procedure after a duration of 3–7 days helps by providing a second dose of scolicide to scolices which may have survived the first session and may be a potential source of recurrence. The utility of this second PAI is highlighted by the fact that in our study, viable scolices were still detectable in 14.2% of our patients after one session of PAI. Similar findings have been reported by Giorgio et al.[20,21] Our results show that as a first-line treatment, DPAI is non-inferior to surgery in the treatment of CE while providing a much shorter hospital stay and lower complications, therefore providing a safer and more cost-effective alternative to surgery. Indeed, since the conclusion of our study, we have started the practice of performing the procedure on a day care basis and only few select patients, in whom complications are anticipated (larger volumes of alcohol used, superficial cysts or multiple passes made through liver parenchyma), are kept overnight. When compared with the case series reported by Giorgio et al,[20,21] although our treatment success rates are equivalent, our cyst disappearance rates appear to be lower. This could be attributed to our shorter follow-up period, with the presumption that more cysts might disappear if followed for a longer period. A second contributing factor could be that we restricted the amount of alcohol injected to approximately 150 ml, while Giorgio et al used volumes as high as 250 ml. Our results, however, are consistent with other reports of PT.[17,22,31–34]

In our study, both the groups showed a pattern of rise in titres on IgG ELISA 1 month after the intervention, followed by a gradual fall to baseline values. The rise in titres after either intervention reflects an increase in IgG antibody that occurs owing to small amounts of echinococcal antigens gaining access to the blood stream during the procedure. Most patients continued to have positive titres despite an adequate sonographic response, implying that serology does not have a major role in confirming successful response to treatment and monitoring of titres post-treatment should be carried out with the aim of detecting recurrences. Similar issues have been noted by Zhang and McManus[35] on the role of antibody titres in follow-up of cured individuals. Güerri et al and Lawn et al[36,37] have shown that CE-specific total IgG levels are sensitive for diagnosis, but unhelpful for follow-up of patients treated where IgG4 and IgG2

Table 4. Geometric mean titres

Group	Baseline	1 m	2 m	3 m	6 m	12 m	18 m	24 m	30 m	36 m
DPAI	1 : 131.25	1 : 280.42	1 : 262.51	1 : 237.76	1 : 230.04	1 : 222.57	1 : 185.14	1 : 160.00	1 : 160.00	1 : 126.99
Surgery	1 : 154.81	1 : 215.34	1 : 208.35	1 : 195.04	1 : 188.71	1 : 176.65	1 : 154.81	1 : 131.98	1 : 132.44	1 : 91.90
p^a	0.52	0.12	0.15	0.25	0.27	0.11	0.27	0.14	0.08	0.39

DPAI, double percutaneous aspiration injection.
[a]Geometric mean titres were compared by applying Student's unpaired *t*-test on the log-transformed value of the titres.

Table 5. Complications

Type	Complication	DPAI	Surgery
Major	High-grade fever/sepsis[a]	1	2
	Bile leak[b]	0	2
	Subphrenic collection[c]	0	1
	Prolonged tube drainage[d]	0	1
Minor	Pneumothorax[e]	1	0
	Low-grade fever	0	1
	Wound infection	0	1

DPAI, double percutaneous aspiration injection.
[a]All who responded to i.v. antibiotics did not require any surgery or image-guided intervention.
[b]Needed Endoscopic Retrograde Cholangiopancreaticography and sphincterotomy.
[c]Found to be purulent on aspiration; managed with Ultrasonography (USG)-guided catheter insertion.
[d]Persistent drainage of >15 ml/day from cavities managed by cystectomy and tube drainage for >1 month.
[e]Not requiring chest tube insertion managed conservatively.

subclasses, respectively, are useful because they become negative soon after an adequate response and remain positive in residual cysts or disease recrudescence.

Complications in general and major complications in particular were more common in the surgery group. Side effects of DPAI were noted in some of the patients in our study and included transient pain on withdrawal of needle, nausea and/or dizziness. These, however, settled on their own within a few minutes and were not included among complications. No anaphylaxis, allergic reactions or death was noted in either group. Although in the past, puncture/aspiration of CE was considered inadvisable owing to a risk of anaphylaxis, a recent study by Neumayr et al[38] reviewing literature on lethal and non-lethal anaphylactic reactions in PT of CE revealed that lethal anaphylaxis as a result of PT is extremely rare and is observed no more frequently than drug-related anaphylactic reactions. In our study, all complications in the surgery group were seen to occur in patients undergoing cystectomy with tube drainage. Although the number of patients undergoing other forms of residual cavity management is small in our study (capitonnage = 3 and omentopexy = 2), our findings are consistent with Wani et al[39] and Demirci et al,[40] who reported higher complication rates in patients undergoing tube drainage.

The major limitations of our study are the intermediate length of the follow-up period, which is long enough to demonstrate a response to treatment but not enough to detect all the recurrences, and the limited sample size, which was chosen to be enough for a non-inferiority analysis. A larger sample size may help demonstrate the superiority of one modality over the other but would significantly prolong the study duration. Further, our study does not compare the efficacy of various percutaneous methods for treatment of CE among themselves, which seems to be a topic worth investigating.

In conclusion, DPAI is non-inferior to surgery in the treatment of CE of the liver and qualifies to be popularized as first-line alternative to the surgical treatment for the definitive management of CE without undue fear of possible anaphylactic reactions, as it has advantages of shorter hospital stay, minimal invasiveness, shorter convalescence period and lower adverse effects.

ACKNOWLEDGMENTS

We thank Prof Antonio Gorgio who provided insight and expertise that greatly assisted the study.

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