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Short Communication

High-intensity focused ultrasound for the treatment of hepatic echinococcosis

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ABSTRACT

Objective of the study was to investigate the safety and effectiveness of high-intensity focused ultrasound (HIFU) to treat hepatic echinococcosis (HE). Eight HE patients treated between 2008 and 2010 were evaluated for the effectiveness of HIFU treatment; the occurrence of complications such as post treatment pain, fever, and skin burns; prognosis; and recurrence. Clinical and imaging evaluation of disease improved after treatment in all eight patients. Postoperatively, all patients experienced changes in liver function that returned to normal within 5 days. Three patients experienced low-grade fever that resolved in 6 days. Six patients complained of right upper quadrant pain that resolved in 7 days. Three patients experienced minor swelling of the skin. No unexpected complications were noted. HIFU was safe and effective for treating HE. It is non-invasive and caused no severe postoperative complications.

Keywords: Hepatic echinococcosis, Combination therapy

INTRODUCTION

Hepatic echinococcosis (HE) is a serious condition that is not easily treated, mostly affects people who reside in farming areas. Our objective was to determine whether high intensity focused ultra sound (HIFU) is a viable option in treating HE. The incidence rate of HE in China is estimated at 50 per 100,000 person-years, with about 66 million people currently affected by the disease, with the highest prevalence being in Xinjiang, Qinghai, Tibet, Gansu, Ningxia, Mongolia, and Western Sichuan.[1] Surgery is the primary treatment method, but HIFU may be a minimally invasive alternative. This study investigated the efficacy and safety of HIFU for treating HE. We evaluate the effectiveness of HIFU by comparing the imaging results of the disease and abdominal symptoms before and after treatment. We also took into account liver function and post-treatment complications.

METHODS

Patients

Eight patients diagnosed with HE by computed tomography (CT) or magnetic resonance imaging (MRI) between 2008 and 2010 were selected and treated by HIFU. Four were men and four were women between 27 and 42 years of age, in good condition, and with stable vital signs. Comorbidities included diabetes and rheumatoid arthritis in one patient, hepatitis B cirrhosis with a history of upper gastrointestinal hemorrhage in another, and previous HE treatment by surgical resection in three patients. Before HIFU treatment, all patients complained of right upper quadrant discomfort or pain, but their liver function was normal without the presence of jaundice or fever. The patient baseline characteristics are presented in Table 1.

Instruments and methods

The model used was a JC focused ultrasound tumor therapeutic system (Chongqing Haifu Medical Technology Co., Ltd., Chongqing, China), while a diagnostic ultrasound probe took real-time ultrasound imaging to monitor the treatment procedure. HIFU procedure used a therapeutic transducer of diameter 200 mm, focal length of 155 mm. The focal region was an ellipsoid with 3 mm transversally and 8mm longitudinally. Before HIFU, the colon was prepared through liquid food, catharsis, as well as using a cleaning enema to protect intestine. Skin in the Treatment area was first defatted by using 75% alcohol, and then degassed by use of vacuum extractor as reduce the risk of burn. Patients were placed either in right lateral position or prone position, according to the location of lesions. Then target area skin was immersed in degassed water. The lesions were divided into 5 mm sections, and ultrasound focus was started at deepest layer of a section. The HIFU settings were adjusted according to lesion size and patient tolerance and are presented in Table 2. The frequency was 0.85 MHz, at a power between 130 and 380 W, and a time between 907 and 8734 sec. The target region was ablated going from deep to superficial, which was repeated in every section until the lesion was fully ablated. Three patients required a second treatment after intervals of 11 days, 19 days, and 4 months because of severe symptoms and large hydatid cysts.

Table 1: Patient characteristics.

Patient	Gender	Age (years)	Infected site	Operation history	The imaging scan report before the treatment
1	Male	36	Anterior segment of the right lobe of the liver and medial segment of the left lobe of the liver	No operation history	Ultrasound shows solids lesions in the liver and abdominal cavity, consider HE.
2	Female	38	Right lobe of the liver	No operation history	MRI showed mixed signal shadows dominated by long T1 and T2 in the right lobe of the liver and multiple patchy long T1 and short T2 shadows in the lesion.
3	Male	36	Right lobe of the liver and medial segment left lobe of the liver	No operation history	MRI suggested a large number of nodular long T1 and long T2 signal shadows in the right lobe and the left medial segment of the liver.
4	Male	27	Lower end of the right lobe of the liver	No operation history	Ultrasound and CT scan show solid lesions in the posterior lower part of the right lobe of the liver with calcification.
5	Female	41	Left lobe of the liver and right lobe of the liver	No operation history	MRI shows large nodular masses, and the main mixed signals shown were slightly lower T1 and slightly higher T2 signals in the left and right lobes of the liver; T2WI shows low signal in the mass.
6	Female	42	Right lobe of the liver and medial segment left lobe of the liver	Surgical resection of liver hydatid cyst	MRI shows that intra-hepatic bile duct dilation, long T1 and long T2 signal in the gallbladder fossa, non-uniform long T1 and long T2 signals in the border area of left and right lobe of liver, and small cystic signal foci.
7	Female	33	Right lobe of the liver and caudate lobe	Surgical resection of liver hydatid cyst	MRI showed multiple cystic lesions in the right posterior lobe of the liver. There was a cystic lesion in the caudate lobe of the liver, with clear and smooth boundary and mostly long T1 and long T2 signals inside, and some of them were short T1 and long T2.
8	Male	36	Left lobe of the liver	Surgical resection of liver hydatid cyst	Magnetic resonance imaging showed reduced volume of the left lobe of the liver, irregular and long T1 mixed with T2 signal shadows in the left lobe and hilar area, unclear boundary, and disordered surrounding structure.

Table 2: HIFU parameters.

Patient	Frequency (MHz)	Power (W)	Treatment duration (s)
Patient 1			
Right liver lobe	0.85	277	2 508
Left liver lobe	0.85	288	907
Patient 2	0.85	251	4 785
Patient 3			
First treatment	0.85	360	8 459
Second treatment 19 days later	0.85	340	8 734
Patient 4	0.85	290	7 115
Patient 5	0.85		
First treatment	0.85	212	6 172
Second treatment 4 months later			
Right liver lobe	0.85	272	6 888
Left liver lobe	0.85	130	5 350
Patient 6	0.85	300	1 447
Patient 7	0.85	380	6 225
Patient 8			
First treatment	0.85	160	3 226
Second treatment 11 days later	0.85	300	2 043

Patients were given supplementary oxygen after treatment, and their electrocardiogram was monitored for 24 hours. All patients received prophylactic anti-infectives, hepatoprotective medications, fluid infusions, and nutritional support. Their vital signs, skin condition, and symptoms were monitored during the hospital stay. CT, MRI, and liver function tests were performed as appropriate.

RESULTS

Changes in imaging and liver function

Liver imaging before and after treatment confirmed decreased cyst volume, loss of distinct cyst boundaries, and decrease in the number of cysts. Representative CT and MRI images are presented in Figure 1 and 2.

Liver function tests before and after HIFU treatment (Table 3) found that alanine aminotransferase (ALT) and aspartate aminotransferase (AST) increased after HIFU treatment but returned to normal within 5 days, serum albumin (ALB) was slightly decreased following treatment, and serum bilirubin was not changed.

Complications

HIFU treatment was associated with minor complications (Table 4). Three patients experienced fever that resolved in 2 to 6 days; six reported right upper quadrant pain that resolved in 2 to 7 days; three experienced mild, localized skin swelling; and one experienced transient vomiting.

Follow-up

After 1-year of follow-up, patient symptoms were improved. One patient was given a second HIFU treatment at 4 months after experiencing abdominal discomfort, and after 4 months, he did not experience any further abdominal discomfort. One patient was hospitalized after 3 months because of upper gastrointestinal hemorrhage. None of the other patients experienced HE symptoms and had no signs of cyst recurrence.

Table 3: Changes in liver function indicators.

Patient	The second day after surgery				The fifth day after surgery			
	ALT (IU/l)	AST (IU/l)	ALB (g/l)	STB (umol/l)	ALT (IU/l)	AST (IU/l)	ALB (g/l)	STB (umol/l)
1	56	33	35.7	14.3	52	35	37.2	16.2
2	26	23	35.4	9.6	45	22	34.5	9.0
3	57	34	44.3	17.4	55	31	41.2	20.1
4	16	20	38.8	10.8	40	48	33.9	12.3
5	51	56	28.5	6.8	39	43	28.3	6.9
6	65	62	27.0	27.2	105	165	27.4	29.6
7	14	19	48.1	6.4	14	20	37.8	8.5
8	18	27	30.6	7.2	26	43	31.5	13.7

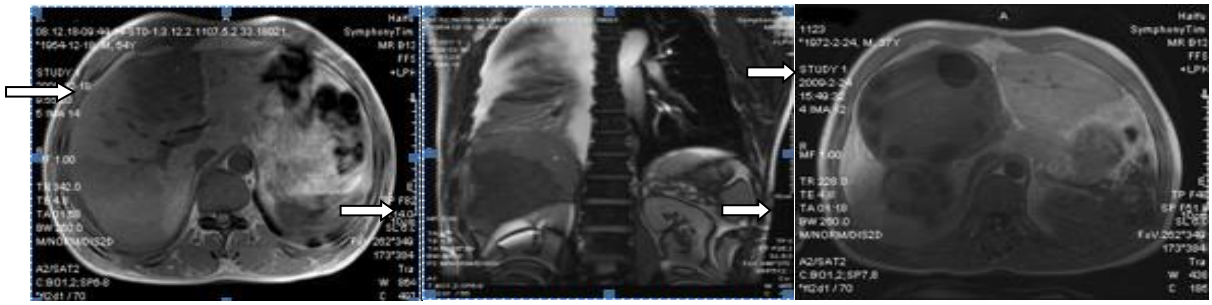

Figure 1: MRI before HIFU treatment (a) A hepatic hydatid cyst (arrow) in patient 1 with a clear boundary and mixed signal intensity within the cyst, (b) Coronal plane with a hepatic hydatid cyst (arrow) with a clear boundary and a mixed signal intensity within the cyst, and (c) a large cyst with a clear boundary in patient 3 (top arrow). Cysts with septations, and of various sizes and strength signal intensity within small vesicles, are seen. The bottom arrow indicates small vesicles within a cyst.

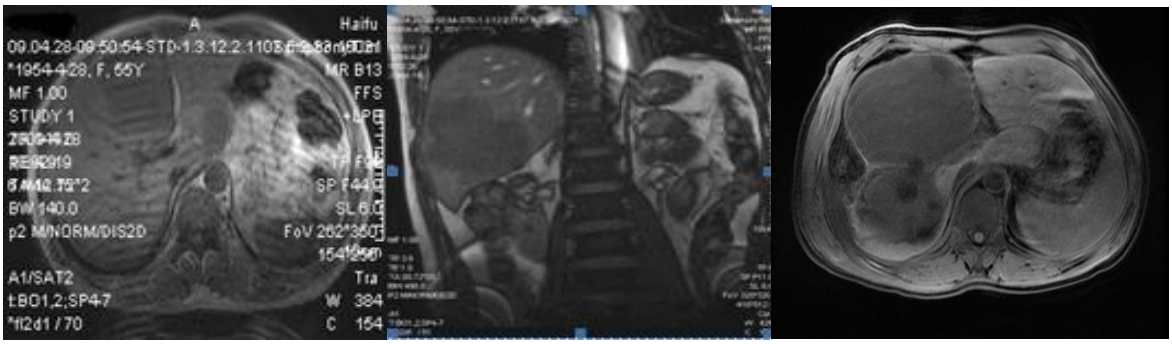

Figure 2: MRI after HIFU treatment showing the same cysts as in Figure 1, (a) the volume of the cyst (arrow) is reduced, the boundary is now indistinct, and the signal intensity has become more uniform, (b) coronal plane image showing that the cyst (arrow) volume is smaller than before treatment, and the signal intensity is increased and more uniform, and (c) the cyst (top arrow) volume has decreased, the boundary is now indistinct, the volumes and number of small vesicles (bottom arrow) are both reduced, and the number of vesicles decreased.

DISCUSSION

Most cases of HE occurs in regions of rural China where health conditions are poor.[2] The recurrence rate is high, and many patients undergo multiple surgical procedures. The prevalence of morbidity is high and has significant effects on the quality of life and income. HE is caused by a liver parasite that severely damages the liver and other involved organs. About 60% to 75% of the Echinococcus cysts are found in the liver, 15% in the lungs, and 10% in other organs.[3] Depending on the location, cyst rupture can lead to cholangitis, anaphylaxis, or peritoneal dissemination.[4] Other complications include intestinal adhesion, intestinal obstruction, and incision-nonunion.

Clinical signs and symptoms

HE can range from an asymptomatic liver infection to liver failure if not treated.[5] HE usually presents first in the liver but can spread to other organs. Abdominal pain, nausea, and vomiting are frequent, and jaundice is sometimes reported but is usually caused by bile duct obstruction due to cyst enlargement.[6] A case of HE associated with Budd–Chiari syndrome and pulmonary embolism has been reported.[7]

Diagnosis

HE is usually diagnosed by imaging and serology. About 85% to 97% of cases can be diagnosed by imaging. Intradermal injection of hydatid fluid and complement fixation can diagnose up to 90% of cases.[8,9] Polymerase chain reaction (PCR) assay, positron emission tomography–computed tomography (PET-CT), and other three-dimensional imaging modes are also useful for the diagnosis and treatment of HE.[10,11]

Treatment

Of the many methods for HE treatment, surgery is still the most frequently used.[12] The disadvantages of surgery include the relatively high cost, which makes it difficult for patients from a poor farming background to afford the expenses or the time required for surgery and recovery. In addition, as cysts cannot always be removed completely, recurrences associated with undetected residual parasites in the liver are likely. If all cysts could be completely removed, then patient benefit would be much greater.[13,14] Novel treatments, some of which can be combined with surgery, include percutaneous puncture and sclerotherapy and percutaneous transhepatic cholangial drainage.[15,16]

Liver transplantation has been used to treat HE, but mortality rate of as high as 25% to 45% has been reported.[17] Regardless of the choice of treatment, recurrence is the primary complication. The recurrence rate following surgical treatment is from 4.5% to 20.2%, and the rate following puncture drainage and alcohol injection is higher, possibly because of cyst fluid entering the abdominal cavity, implantation, and incomplete killing of the protoscoleces.[18]

Feasibility and advantages of HIFU for treating HE

HIFU is a minimally invasive treatment in which low-energy ultrasound is focused on the target tissue, resulting in high temperatures, cavitation, and other mechanical stresses that cause coagulative necrosis.[19] With sufficient intensity and time of exposure, HIFU would be expected to kill all protoscoleces while avoiding hemorrhage and vascular obstruction.[20] It can also be used to treat small vessel hemorrhages with little effect on the surrounding normal tissues. HIFU causes less trauma than surgery and is regarded as a safe method of treating HE. It can also be considered as a supplement to surgery or other treatments to increase the therapeutic effect.

Compared with surgery, HIFU is minimally invasive and less painful and is associated with faster recovery and fewer complications. Unlike HIFU, surgery also poses a risk of entry of cyst fluid into the abdominal cavity, causing anaphylactic shock or postoperative recurrence.[21] HIFU has a better kill rate than percutaneous drainage, and it causes fewer complications, such as spreading of the infection by needle tract implantation. Patients do not experience pain caused by alcohol irritation and do not require a persistent drainage tube. Through the HIFU, multiple surgeries to treat recurrences can be avoided, as well as the repeated risk of surgical complications. Elderly patients who are poor surgical risks can be treated using HIFU, which can reduce their symptoms, relieve pain, and improve the quality of life. Combining HIFU with other treatment methods improves the curative effect. HIFU can be used to kill protoscoleces in advance of surgical resection, which reduces transfer and implantation and decreases the risk of postoperative recurrence. HIFU can also be used before puncture drainage to reduce the risk of spread by needle tract implantation. Combining minimally invasive methods increases the cure and lowers recurrences, all the while retaining the advantages of minimal invasiveness.

Treatment of the study group

Abdominal distension and symptoms were absent following HIFU. One patient needed a second treatment after 4 months due to recurrence, but the other seven patients exhibited no symptoms consistent with HE recurrence. Imaging confirmed a decrease in the size of hydatid cysts, blurring of cyst boundaries, decrease in the number of small vesicles, and reduction in the volume of small vesicles. The radiographic evidence and improvement of symptoms indicate that HIFU was an effective treatment for HE. As a minimally invasive treatment, HIFU was not associated with severe complications. Patients did not experience severe pain, and all had short recovery times. HIFU kills protoscoleces and destroy cyst walls but may also cause damage to the surrounding normal liver cells. The resulting increase in serum transaminases returned to normal with time and with the help of hepatoprotective medication administered before the procedure. Liver function was affected, but the changes did not progress to hepatic failure, hepatic coma, hepatic encephalopathy, or any other serious complications. The few complications that occurred, such as fever, vomiting, and pain, all disappeared after a short period of time. The experience with these eight patients supports the safety and effectiveness of HIFU for the treatment of HE. HIFU relieved symptoms, delayed disease progression, and was associated with few short-term and no long-term complications.

CONCLUSION

HIFU was safe and effective in this group of HE patients. The symptoms disappeared in all patients following treatment. Although recurrence did occur, the rate was lower than reported following other treatment methods, and the curative effect was obvious. There were no long-term complications.

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