

# The effect of combination therapy with albendazole and praziquantel on hydatid cyst treatment

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**Abstract** The standard therapy of hydatid cyst is surgery but, in nonoperable patients and multiple organ involvement, medical therapy may be more useful. The efficacy of drugs especially in short-term treatment of hydatid cyst is unknown. This study was carried out to evaluate the effect of combination therapy with albendazole and praziquantel in the treatment of hydatid diseases. In a nonrandomized quasi-experimental study, nine patients with multiple hydatid cysts were treated with albendazole (400 mg/twice a day) and praziquantel (40 mg/kg per day) twice a week for 4 weeks. This regimen was repeated for three courses with a 2-week interval between each one. The average follow-up period after treatment was 18 months. Response to treatment was assessed through the observation of the symptoms and radiologic findings (computed axial tomography scan, sonography, X-ray). Symptoms disappeared in seven (77.8%) patients and improved partially in two

(22.2%) patients. Radiological assessment showed significant improvement in five (55.6%) and partial improvement in four (44.4%) patients. Combination therapy with albendazole and praziquantel is effective in the treatment of hydatid cyst and can be used as an alternative to surgery in disseminated and nonoperable cases.

## Introduction

The parasitic infestation with *Echinococcus* had been the world's health problem from a long time ago. Surgery is the first choice for single hydatid cyst treatment nowadays, but it is not useful for patients with several lesions in different organs or for patients without appropriate physical conditions for surgery. On the other hand, the surgery results were not always successful and surgery sometimes had been associated with local recurrence or secondary dissemination (Anadol et al. 2001; EL-On 2002). So the medical treatments are used in some patients. These drugs are from the benzimidazoles family including albendazole and mebendazole. The efficacy of these drugs has been reported as different (Yasawy et al. 2001; Nutman and Weller 2001). Praziquantel is an isoquinoline that has been used in animal models, laboratory, and human hydatid cyst recently. It has been used solely or with benzimidazole (Amir-Jahed et al. 1975; Taylor et al. 1989; Teggi et al. 1993). So the aim of this study was to investigate the efficacy of treatment with albendazole and praziquantel together in selected hydatid cyst patients.

## Materials and methods

This study was a cross-sectional quasi-experimental study with nonrandomized sampling. The study was completed

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within 3.5 years. Inclusion criteria were as follows: (1) multiple hydatid cysts diagnosed with one of the radiological methods (computed axial tomography (CT scan), sonography, or simple radiography), (2) confirmed hydatid cyst diagnosis by indirect immunofluorescent antibody (IFA) serology test, (3) single cystic lesion (only when the patient disagreed with surgery or the surgery was of high risk for the patient), (4) age over 10 years old, (5) absence of underlying hepatic disease, (6) negative beta-human chorionic gonadotropin test for women of childbearing age, and (7) agreement to participate in the study and follow-up. After completing a consent form, a questionnaire including demographic information such as age, sex, job and history, physical examination results, medical records with primary laboratory findings (hydatid cyst serology test, peripheral blood leukocytes count, and liver function tests), and radiological findings reports was filled up for each patient. Then the patients were treated with albendazole (400 mg/twice a day) and praziquantel (40 mg/kg per day) at a single dose twice a week for 4 weeks. This was repeated for three courses with 2-week interval between each one. The patients were followed up for clinical symptoms, liver function tests, and peripheral leukocytes count on the 4th, 10th, and 16th weeks. Radiological follow-up was done at the end of the treatment (16th week), 6th and 12th month, and 24th and 36th months in some cases. The clinical criteria of response to treatment were complete improvement and partial improvement. In these criteria, complete clinical improvement means 100% improvement in clinical symptoms to the end of the treatment and partial clinical improvement means at least 50% improvement in clinical symptoms. Based on the review of literature, radiological improvement also contains complete improvement (complete disappearance of the cyst or complete lesion collapse) and partial improvement (obvious cyst size decrease, parietal layers collapse, cyst layers collapse with considerable increase in density of the previous hypodense lesions and obvious calcification) (Amir-Jahed et al. 1975; Teggi et al. 1993; Taylor et al. 1989). As the follow-up period was at least 1 year after treatment and the hydatid cyst choice of treatment is surgery, only nine patients had enough criteria to be included in the study. After the data collection, the results were analyzed with Epi Info 2007 software version 3.4.1 and statistics tests including chi-square and Fisher exact test.

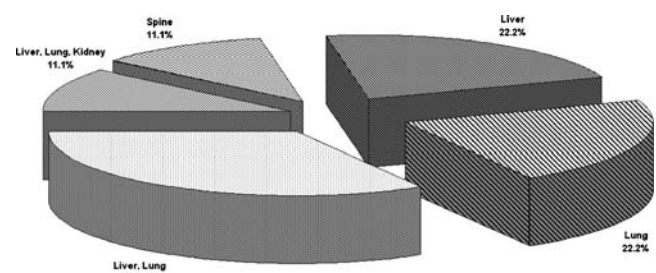
## Results

This quasi-experimental study was conducted on nine patients who met the criteria to be included in the study. The mean follow-up period was 18 months (12–36 months) after the end of treatment. Five cases were on females (55.6%) and four cases were on males (44.4%). The mean age of participants was  $32.56 \pm 16.23$  years. The organs

involved are shown in Fig. 1. The prevalence and clinical symptoms were different from one organ involved to another. In the patients with lung involvement, the symptoms were chest pain, cough, sputum, and hemoptysis in one case. In the liver and abdominal organ involvement, the symptoms were abdominal pain, nausea, and vomiting; in the spinal column involvement, symptoms included lumbago and paraplegia. The earliest response to treatment was for lung cysts that were at least 4 to 10 weeks, and the earliest radiological response was also for lung cysts that were between the 10th and 16th week. In other cases, the radiological response to treatment was between 16th weeks and 6th month. The treatment results based on the organ involved have been summarized in Table 1. Out of nine patients, complete clinical response was in seven cases (77.8%), partial clinical response was in two (22.2%), complete radiological response was in five (55.6%), and partial radiological response was in four (44.4%). In order to give more information, two cases are presented here—one with complete radiological response and one with partial radiological response. Radiological reports before and after the end of treatment are also available.

### Case 1

A 29-year-old woman (a housewife, a native of one of the Khomein's villages, and who had a known case of Hodgkin's lymphoma 6 years ago) with inactive disease was referred with pain in the right hypochondriac region, nausea, vomiting, recurrent rash, and pulmonary symptoms including cough, sputum, and chest pain 3 months ago. Sonography and CT scan showed several hypodense lesions in the liver and there were similar lesions shown in the chest X-ray. Diagnostic laparotomy was performed with suspicion of lymphoma relapse and one of the liver lesions (cysts lesion) was excised. Hydatid cyst wall with germinal layer was reported in the pathology specimen. So, considering the different organs involved (liver, lung, kidney, pancreas, spleen, etc.), she was a candidate for medical treatment and it was initiated. She was observed clinically and with laboratory tests from the initiation of the treatment



**Fig. 1** Distribution of organs involved in hydatid cyst

**Table 1** Assessment of treatment results based on the involved organs

Involved organs	Number of patients	Clinical response				Radiological response			
		Complete		Partial		Complete		Partial	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Liver and lung	3	3	100	0	0	1	33.4	2	66.6
Lung	2	2	100	0	0	2	100	0	0
Liver	2	2	100	0	0	2	100	0	0
Liver, lung, kidney, pancreas, spleen	1	0	0	1	100	0	0	1	100
Spinal column	1	0	0	1	100	0	0	1	100
Total number of patients	9	7	77.8	2	22.2	5	55.6	4	44.6

up to the 16th week (the end of treatment). Improvement was first seen in pulmonary symptoms such as cough, sputum, and chest pain. Then there was partial improvement in abdominal symptoms. When the treatment was finished, radiological and sonographical assessments showed cystic lesions with septomatic shape, decreased size, and hyperdensity. Relative to the radiological criteria, the case was classified in the partial improvement group. The recurrence symptoms were not seen within 36 months of observation (Fig. 2a and b).

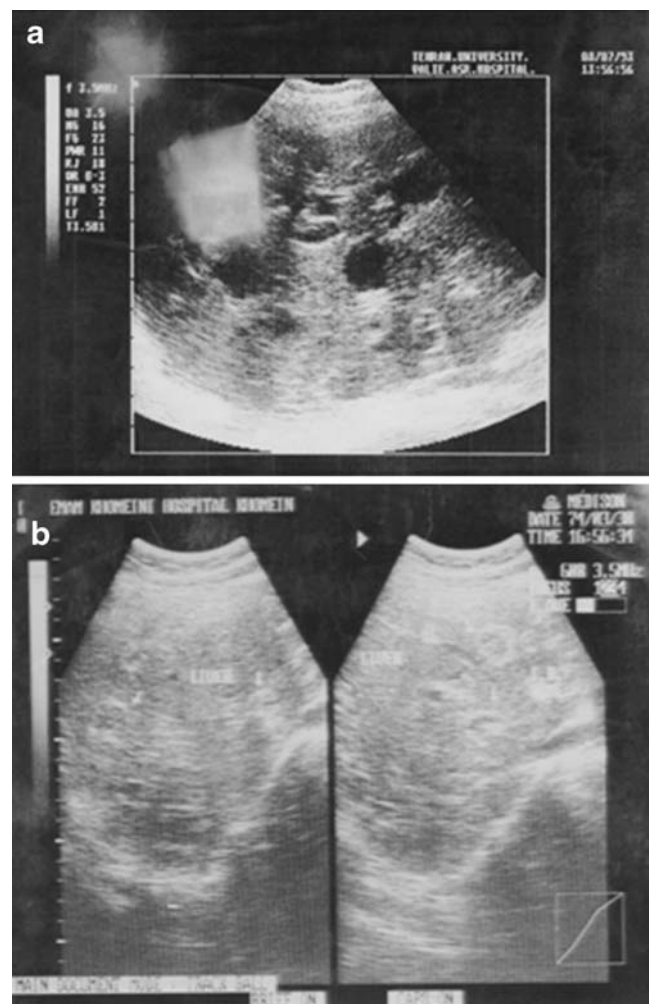
#### Case 2

A 24-year-old man (a native of Afghanistan, a resident in Tehran, and a building worker) was referred with pain in the upper right quadrant of the abdomen. Sonography results reported a thoracic wall cyst. The cyst was drained with sonography-guided drainage. After 4 months, pain appeared in the right hypochondria again; it was also a thoracic wall cyst, and it was drained with similar method but no microbial germ was detected in the sample. After 1 year, the patient was referred for abdominal pain in the right hypochondrial region. Sonography showed a cystic lesion, 2×3 cm in size, in the anterior segment of the right liver lobe (Fig. 3a). The patient's hydatid cyst serology with IFA method was positive and the patient disagreed to an operation. Because of multiple cysts (three hepatic cysts), the medical treatment was used. The patient was followed up to the 16th week (end of the treatment), the symptoms improved gradually, and sonography was reported as normal at the end of treatment (Fig. 3b). There was no recurrence after 24 months of follow-up.

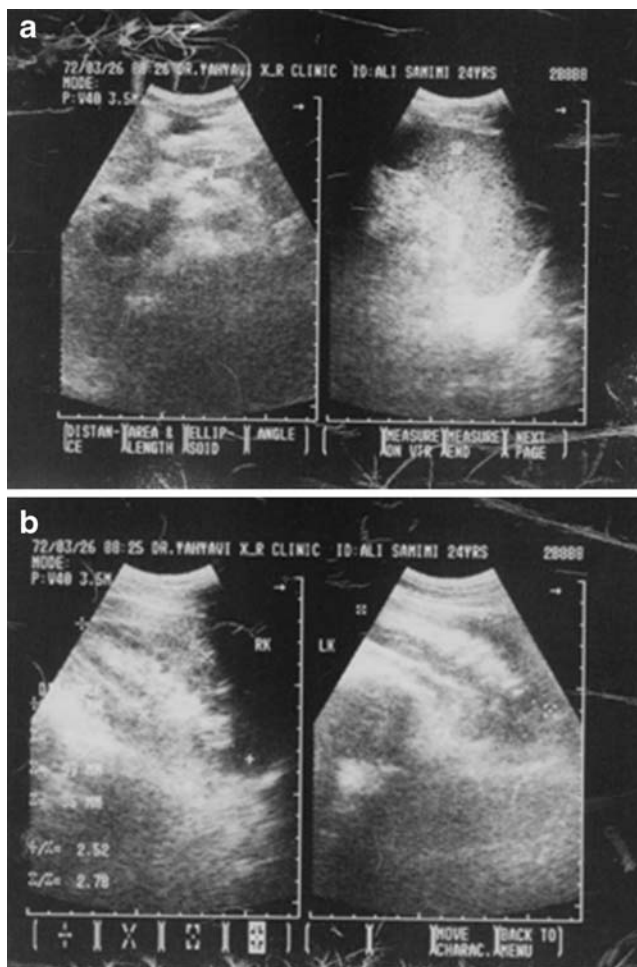
#### Discussion

There were several studies about hydatid cyst treatment from many years ago. Before the discovery of benzimidazoles in 1961, operation was the only treatment; so nonoperable patients were convicted to get into disease complications or death. When this drug family was discovered, many studies were conducted in order to use the medications in hydatid cyst treatment. Mebendazole was the first drug of this family to be used but, because of

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**Fig. 2** Case 1: sonography before (a) and after treatment (b)



**Fig. 3** Case 2: sonography before (a) and after treatment (b)

its side effects in long-term usage, albendazole was substituted in the treatment of diffused hydatid cyst (Anadol et al. 2001; Yasawy et al. 2001; EL-On 2002). Praziquantel is the other drug that is from the isoquinoline family and it is usually used for killing adult worms in dogs' gastrointestinal system; its therapeutic effect on protoscolices in larval stage has been reported recently. Although it does not have much inhibitory effect on the cysts' growth, albendazole is the most effective drug for inhibition of cyst growth. Several studies have assessed combination therapy with albendazole and praziquantel on in vitro animal models and humans in some cases, which had hopeful results (King 2000; Urrea-Paris et al. 2000; Moreno et al. 2001). So the aim of this study was to investigate the efficacy of the combination therapy with albendazole and praziquantel in hydatid cyst disease. Out of nine patients, seven cases had complete clinical improvement (77.8%) and two cases had partial clinical improvement (22.2%). In these two cases, one had paraplegia. This paraplegic condition improved after treatment, but the long-term paraplegic complications were present. The other case with diffuse cysts in abdomen and lungs complained of

abdominal and chest pain. The gastrointestinal department has done a research on ten patients with gastrointestinal hydatid cyst; this study showed 100% clinical improvement with using a combination of albendazole and praziquantel for treatment (Yasawy et al. 1993). In our study, radiological assessment was also done after treatment. Complete radiological improvement was seen in five cases (55.6%). It was from the disappearance of lesions to complete lesion collapse based on the mentioned criteria, and partial radiological improvement was seen in four cases (44.4%). Complete improvement was also seen in lung cysts such that there was no radiological recurrence at follow-up on the 12th, 24th, and 36th month. In the study, albendazole therapy for 6 to 24 months caused the disappearance of cysts in eight cases (34.4%), and albendazole and praziquantel combination therapy for 2 to 6 months in 19 hydatid cyst patients caused complete disappearance of cysts in nine cases (47.4%) and 50% decrease in cyst size upon radiology assessment in five cases (36.84%; Moreno et al. 2001). Other studies have shown 100% radiological improvement in ten patients with hepatic hydatid cyst after 3 months of combination therapy with albendazole and praziquantel, and there was not any relapsing symptom after 1-year follow-up (Yasawy et al. 1993). Also, the combination therapy with albendazole and praziquantel caused 50% radiological improvement after the treatment in another research (Yasawy et al. 2001). The other research mentioned that albendazole is more effective than mebendazole and the combination therapy with albendazole and praziquantel has a more therapeutic effect than using each of them solely (EL-On 2002). The studies on animal models or larval stage of hydatid cyst (protoscolices) have showed good therapeutic effect in albendazole and praziquantel combination therapy in comparison with using them solely (Morris et al. 1990; Urrea-Paris et al. 2000; Moreno et al. 2001). Other studies implied that the albendazole and praziquantel combination therapy for hydatid cyst treatment or preoperational chemoprophylaxis is more effective than using them solely and it decreases the treatment period (Yasawy et al. 2001). So, in our study, nine patients with several cysts received a combination therapy of those drugs, and clinical and radiological improvements were seen from partial to complete responses. Regarding the absence of recurrence, it seems that medications may be used as a good alternative to surgery in these patients. On the other hand, because there are some cases with postoperational recurrence or secondary diffusion, using a combination of scolicidal drugs before and after surgery may prevent postoperational recurrence. Further clinical studies (case-control) are needed in the field of combination therapy and prevention with these combinations to declare the effectiveness of this treatment.



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