



Drug Treatment of *Hydatid Cyst* With Albendazole and Praziquantel in Humans

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Abstract

Introduction: The standard treatment for hydatid cyst is surgery, but in cases where there are multiple cysts in vital organs, treatment with drugs such as those of benzimidazole family (albendazole-mebendazole) will be substituted if the patient is at high risk for surgery. In this study, concomitant treatment of hydatid cyst with albendazole and an effective drug on protoscolices from the isoquinoline family called praziquantel was assessed in humans.

Methods: In this study, 10 patients with multiple cysts were treated with albendazole 400 mg twice daily and praziquantel 40 mg twice daily for 3 months. Patients were followed for recurrence of lesions for an average of 18 months after the end of treatment.

Results: A complete clinical improvement and a partial clinical improvement were observed in 7 cases (70%) and 3 cases (30%), respectively. Radiologically, there was a complete improvement in 6 cases (60%) and partial improvement in 4 cases (40%). Further, one of the patients underwent histopathological examination after the end of treatment, indicating the complete disappearance of the germ layer.

Conclusion: The combined use of albendazole and praziquantel can be used as an alternative treatment in patients with hydatid cysts disseminated in vital organs or patients at high risk of surgery.

Keywords: Hydatid cyst, Albendazole, Praziquantel, Human

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Introduction

Human infection with the parasitic infections of *Echinococcus* has long been a far cry from the world's health problems. At present, surgery is the treatment alternative for a single hydatid cyst. However, some patients cannot be candidates for surgery due to the presence of multiple lesions in different organs or due to special physical conditions (1). On the other hand, the results of surgeries have not always been successful and have been accompanied by secondary diffusion and local recurrences in some cases (2). In these cases, drug treatments are used. Commonly used drugs of the benzimidazole family include albendazole and mebendazole, which have been studied in various studies, reporting diverse efficiencies (3). Praziquantel is an isoquinoline that has recently been used in animal models, laboratory, as well as in human hydatid cyst alone or in combination with a benzimidazole (4). This study aimed to evaluate the combined therapeutic effect

of albendazole and praziquantel in patients with hydatid cysts.

Materials and Methods

This study is a quasi-experimental interventional clinical trial with a non-probability sampling method. The inclusion criteria were diagnosis of multiple hydatid cysts by one of the radiological methods (i.e., CT scan, sonography, or plain radiography and confirmation of hydatid cyst disease by indirect immunofluorescence antibody (IFA) serological testing. Further, the other criteria included the presence of a single cystic lesion only in cases where the patient has not consented to surgery or surgery has a high risk for the patient, age over 10 years, absence of underlying liver disease, beta-hCG negative test for women of childbearing age, and acceptance of participation in the study and cooperation for follow-up. Moreover, information form includes demographic information, occupation, history, physical examination, medical history, results of initial laboratory tests (hydatid



cyst serology, peripheral blood leukocyte count, and liver function tests), and report of radiological examinations for each patient.

Albendazole at 400 mg twice daily and praziquantel at 40 mg/kg body weight were applied in a single dose twice a week for 4 weeks followed by two weeks of drug rest were repeated for 3 full cycles. Then, the patients were checked in terms of clinical symptoms (using liver function tests, and peripheral blood leukocyte count) at weeks 4, 10, and 16, as well as radiological symptoms at the end of the treatment (at week 16), 6 and 12 months, and in some cases, at 24 and 36 (average 18 months). During the treatment period, in weeks 4 and 12, liver function tests and peripheral blood cell counts were performed to evaluate drug side effects. Complete clinical recovery refers to cases in which 100% of clinical symptoms improved by the end of treatment, and partial clinical improvement refers to cases in which at least 50% of symptoms improved (5). Radiologically, complete recovery includes complete disappearance of the cyst or complete collapse of the lesion, while partial recovery involves the marked reduction in cyst size, shedding of the wall layers, and shrinkage of the cyst layers with a significant increase in the density of previous hypoplastic lesions and a full calcification (6). Considering that patients needed follow-up for at least one year after the end of treatment, and on the other hand, the treatment of choice is hydatid cyst surgery, the number of patients who met the inclusion criteria was only 10 cases (7). Statistical analysis was performed by Epi Info statistical software, and chi-square and Fisher's exact test were used to analyze the data.

Results

Ten patients (5 females and 5 males) with a mean age of 16-32 years were examined. The mean duration of follow-up was 18 months (minimum 12 and maximum 36 months). The involved organs were liver and lung in 3 cases (30%), liver and lung alone in 2 cases (20% each), spine in 1 case (10%), and liver, lung, spleen, and pancreas, respectively. There was 1 case (10%) with 6 cases of liver and 6 cases of lung involvement, but other organs had one case each. In patients with pulmonary involvement, the symptoms were chest pain, cough, and sputum, and there were liver and intra-abdominal involvement in one case of hemoptysis with abdominal pain, nausea, and vomiting symptoms, and spinal involvement exhibited symptoms of back pain and paraplegia. The earliest clinical response was related to lung cysts with the minimum response time between weeks 4-10, and the earliest radiological response was for lung cysts between weeks 10-16. In other cases, the radiological response was between 16 weeks and 6 months after the end of treatment.

Out of 10 patients undergoing treatment, 7 (70%) had complete clinical response, 3 (30%) had partial

clinical response, 6 (60%) showed complete radiological response, and 4 (40%) exhibited partial radiological response. Moreover, out of 3 cases (30%) of relative clinical improvement, one case was presented with paraplegia which was out of paraplegic state after the end of treatment but had symptoms due to long-term paraplegia. The other patient had diffuse abdominal and lung cysts that sometimes reported abdominal and chest pain. In one case, a histological examination was performed in which the complete disappearance of the germ layer and its inactivity were reported. The results of treatment based on the affected organs are summarized in Table 1. During the follow-up of patients, no clinical or laboratory complications resulting from treatment and drug side effects were observed.

Discussion

Extensive studies on the treatment of hydatid cyst have been conducted for decades. Before 1961, the discovery of benzimidazoles was the only cure for the surgery, but many patients who could not undergo surgery for any reason were doomed to complications and even death. With the discovery of benzimidazoles, extensive studies have been performed on drug treatments for hydatid cyst (8,9). The first drug used was mebendazole, which due to its side effects in long-term use, was replaced by another drug of this family called albendazole used in the treatment of diffuse hydatid cyst. Another drug for the treatment of hydatid cysts is praziquantel from the group of isoquinoline. It is most commonly used in the treatment of adult canine and canine gastrointestinal worms, but its therapeutic effects on superficial protoscolices have also been reported recently, although it has had a little inhibitory effect on cyst growth (10,11). Albendazole, on the other hand, is the most effective drug in treating cyst growth. Therefore, several studies have been conducted on the combined use of albendazole and praziquantel in animal models, in vitro, and in human cases, yielding promising results (12). The aim of this study was to evaluate the therapeutic effects of the combined use of albendazole and praziquantel in the treatment of hydatid cyst. In this study, out of 10 evaluated patients, 7 (70%)

Table 1. Results of Treatment Based on the Affected Organ

	Clinical Response		Radiological Response	
	Complete	Partial	Complete	Partial
Liver and lung (n=4)	4 (100)	0	2 (50)	2 (50)
Lung (n=2)	1 (50)	0	2 (100)	0
Liver (n=2)	2 (100)	0	2 (100)	0
Liver, lung, kidney, pancreas, and spleen (n=1)	0	2 (100)	0	1 (100)
Spinal cord (n=1)	0	1 (100)	0	1 (100)
Total patients (n=10)	7 (70)	3 (30)	6 (60)	4 (40)

Note. The numbers in parentheses represent the percentage.

had complete clinical improvement and 3 (30%) had partial clinical improvement. In a study of 10 patients with gastrointestinal hydatid cyst, albendazole and praziquantel led to 100% clinical improvement.

In addition, 6 cases (60%) and 4 cases (40%) indicated a complete radiological improvement and partial radiological improvement in our patients, respectively. Further complete recovery was observed in pulmonary cysts and during follow-up at 12, 24, and 36 months, and no radiological signs of recurrence of the lesion were observed. In other studies, almost the same results were observed; for example, in a study, the use of albendazole for 6 to 24 months caused the complete disappearance of cysts in 8 cases, and the combined use of albendazole and praziquantel with a treatment period of 2 to 6 months completely eliminated 19 cases of cysts. Completely eliminated cystic lesions in 9 cases and a 50% reduction in cyst size in 5 cases on radiological examination. In another study, administration of albendazole and praziquantel in 10 patients with hepatic hydatid cyst was associated with 100% radiological improvement after 3 months of treatment, and no recurrence of lesions was observed after one year of follow-up. In another study, the combined use of albendazole and praziquantel resulted in a 50% improvement in radiological criteria after the termination of treatment. One study found that the use of albendazole was more effective than mebendazole, and the combined use of albendazole and praziquantel was more effective than either alone. In studies performed on animal models or in the larval stage of hydatid cysts (protoscolices), appropriate therapeutic effects have been observed with the combined use of albendazole and praziquantel compared to their separate use (13-15).

In general, co-administration of albendazole and praziquantel as a drug treatment for hydatid cyst or chemoprophylaxis before cyst surgery is considered to be more effective than their application alone and shortens the treatment period (16-18). In the present study, a clinical and radiological improvement from partial to complete was observed, suggesting that the clinical response was higher than radiological. Due to the lack of recurrence of lesions during follow-up, it seems that drug treatment of hydatid cyst may be one of the appropriate alternatives to surgery in these patients. On the other hand, due to cases of recurrence of the disease and its secondary spread after surgery, concomitant use of drugs that have scolicedal effects, before and during surgery, can be effective in preventing the recurrence of lesions (19, 20).

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Authors' Contribution

All listed author(s) have made a substantial, direct, and intellectual

contribution to the work, and approved it for publication.

Conflict of Interests

The listed author(s) declare no conflict of interests in any capacity, including competing or financial.

Ethical Issues

All ethical principles are fully observed in this study.

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