

Effect of Albendazole and Mebendazole on Hydatid Cyst of Mice

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How to cite this paper: Fagiree, E.I., Saad, B.M. and Elsadig, A.A. (2017) Effect of Albendazole and Mebendazole on Hydatid Cyst of Mice. *Open Journal of Epidemiology*, 7, 307-316.

<https://doi.org/10.4236/ojepi.2017.74025>

Received: April 11, 2017

Accepted: October 14, 2017

Published: October 17, 2017

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Abstract

In the current study, hydatid cysts from livers and lungs of camels were obtained from Tambool slaughter house and protoscoleces were separated aseptically. 36-weeks-old Swiss mice (25 - 30 gram body weight males and females) were divided into two groups of 6 each: a prophylactic group dosed with 150 ml/kg of albendazole and mebendazole was given directly after injection with 2000 protoscoleces intraperitoneally for 10 consecutive days. The treated group was given a dose of 300 ml/kg of albendazole and mebendazole for 24 days with 4 days interval separated by 2 days and after 6 months of inoculation with protoscoleces, the two groups in addition to the control group were sacrificed and necropsied. The results revealed a significant difference in the development of hydatid cyst ($p < 0.01$). Inside the mice, small number of cysts was noticed in the group treated with albendazole and mebendazole compared to the control group, however, albendazole was highly efficacious than the mebendazole where the efficiency of albendazole reached 97% while the mebendazole efficiency rate was almost 50% which indicates that albendazole could be considered the drug of choice in the treatment of hydatid cyst.

Keywords

Hydatid Cyst, Mebendazole, Albendazole

1. Introduction

Cystic echinococcosis (CE) caused by the metacestode (larval) stage of *Echinococcus granulosus* is still an important public health concern in many countries of the world, such as the Mediterranean and South American countries as the disease affects humans and domestic livestock including cattle, sheep, camels,

pigs, horses and others [1]. In the early 1970s, benzimidazole methylcarbamates derivatives (BZD) were proved to be effective against *E. granulosus*, and since then, many investigators have used albendazole (ABZ) and mebendazole (MBZ) for the treatment of human hydatidosis [2]. Albendazole and mebendazole are considered to be equally effective. When evaluated up to 12 months after initiation of benzimidazole treatment, 10% - 30% of patients show cyst disappearance, 50% - 70% show degeneration of cysts and 20% - 30% show no morphological changes in the cyst appearance. Continuous or intermittent treatment with albendazole is recommended for a period of 6 months [3]. At present time, benzimidazole methylcarbamate compounds such as albendazole and mebendazole have been used to treat CE in humans [4]. Mebendazole was the first compound widely used [5]. Although effective, the main disadvantage was the extremely high doses and prolonged administration period required to achieve a satisfactory clinical efficacy. Albendazole was therefore a major breakthrough because, while absorption of the parent compound remained poor, its metabolite, albendazole-sulphoxide (ABZSO) was shown to be an active anthelmintic agent [6]. Both ABZ and ABZSO have been shown to be active against protoscolices of *E. granulosus* in *in vitro* culture systems. However, the *in vitro* protoscolicidal action of ABZ and ABZSO is very slow and requires a longer incubation period compared to that observed for MBZ [7]. *In vitro* and *in vivo* differences in the protoscolicidal activity of BZD anthelmintics have been observed. The significance of the effects of albendazole, mebendazole has been discussed by a few researchers [8] [9] [10]. [11] had concluded that albendazole and povidoneiodine are effective for the killing of hydatid protoscoleces and inhibit hydatid cyst development.

Long term daily albendazole treatment after surgical resection of the cyst masses, has suppressed parasite growth in some dogs with *Echinococcus multilocularis* cysts [12].

2. Materials and Methods

The field work was conducted in Tambool area (Central Eastern Sudan) where slaughtered camels were checked for hydatid cysts. Laboratory work was performed at the laboratories of the Faculty of Education, Alzaem Alazhari University and the Faculty of Education, University of Khartoum.

The study included camels slaughtered at Tambool market using white mice (25 - 30 gram body weight males and females) which were obtained from Veterinary Research Center, Soba, Khartoum for experimental purposes.

One hundred fifty slaughtered camels in Tambool market were thoroughly inspected for the presence of hydatid cysts in different organs. Hydatid cysts, when found were counted. The size of the cysts was measured using an ordinary ruler [13]. Aspiration of cyst fluid was made for detection of fertility or sterility status of the cysts.

Three parasitological parameters were considered when a cyst was found.

These were measuring the cyst size, status of cyst fluid, and viability of the cyst.

Protoscoleces were collected under aseptic conditions from hydatid cysts obtained from camels. Viability of the protoscoleces was confirmed by visual inspection through inverted microscope. The protoscoleces were resuspended with water and 2000 of protoscoleces were inoculated intraperitoneally in each mice (30 weeks of age). Male and female mice weighing 25 - 30 g were used. Thirty mice were inoculated with protoscoleces of hydatid cyst and divided into 5 groups of 6 mice each. Two prophylactic groups, immediately after being inoculated with protoscoleces, received 150 mg/kg bw/day albendazole (group 1) and mebendazole (group 2) orally for 10 days. Two other groups (treatment groups) received oral treatment 6 months after inoculation with protoscoleces with 300 mg/kg of albendazole (group 3) and mebendazole (group 4) every 4 days with an interval of 2 days for totally 24 treatment days (six times). The fifth group of mice remained as the untreated control. All mice were scarified after 7 months and internal organs were observed for the presence of hydatid cyst.

The efficacy rate was determined using the formula:

$$\frac{\text{Number of cyst in the control group} - \text{Number of cyst in the treated group}}{\text{Number of cyst in the control group}} \times 100$$

Statistical Analysis: The data were analyzed using SPSS program (version10) and Excel application. Results were considered, Non significant at $p > 0.05$, significant at $p < 0.05$, highly significant at $p < 0.01$.

3. Results

It is to be revealed that all mice were sacrificed 7 month after inoculation for all groups (prophylactic, treated and control group). In group one (prophylactic), which received 150 mg albendazole for 10 days, 8 cysts were counted for all the mice showing an efficiency rate of 70% compared to that of the control group. All the cysts encountered were of the small size and located either in the liver or peritoneal cavity (**Table 1(a)** and **Table 1(b)**, **Figure 1**). In group 2 (prophylactic) which received 150 mg mebendazole for 10 days, 19 cysts were counted for all the mice showing an efficiency rate of 42% compared to that of the control group. All cysts encountered were of the small size and located either in the liver or peritoneal cavity (**Table 1(a)** and **Table 1(b)**, **Figures 2-4**). In group 3 (treated) which received treatment with 300 mg albendazole for 24 days, only one small cyst in the peritoneal cavity was encountered showing an efficiency rate of 97% (**Table 2(a)** and **Table 2(b)**, **Figure 5**). In Group 4 (treated) which received 300 mg mebendazole for 24 days, 9 cysts were counted showing an efficiency rate of 73% (**Table 2(a)** and **Table 2(b)**, **Figures 6-8**). All of the cysts were small size and located in the liver or peritoneal cavity, 3 cyst were observed in the lung and subcutaneous tissues. In the control group, 33 cysts were counted, all of the medium size. As expected, the majority of cysts were fertile (**Table 3** and **Figure 9** and **Figure 10**).

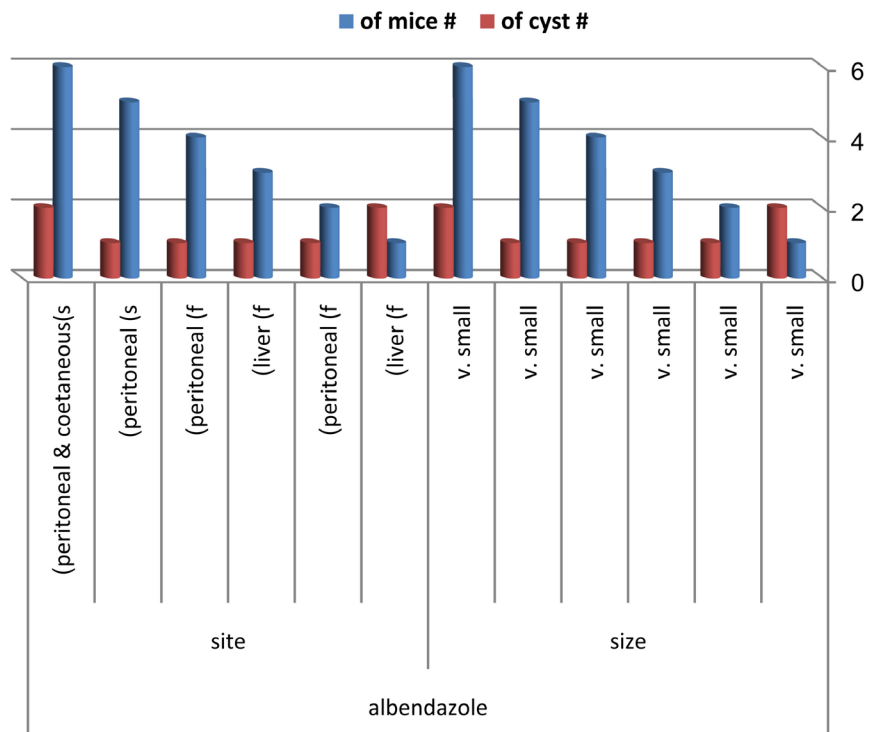


Figure 1. *In vivo* effect of albendazole on hydatid cyst of mice (prophylactic group).

Table 1. (a) *In vivo* effect of albendazole and mebendazole on hydatid cyst of mice (prophylactic group); (b) The efficiency rate of albendazole and mebendazole in prophylactic group.

(a)

Mice No.	Albendazole			Mebendazole		
	No. of cyst	site	size	No. of cyst	site	size
1	2	liver	v small	3	liver & peritoneal (f)	Small
2	1	peritoneal (f)	v small	1	peritoneal (f)	Small
3	1	liver	v small	5	liver & peritoneal (f)	Small
4	1	peritoneal (f)	v small	5	liver & peritoneal (f)	Small
5	1	peritoneal (f)	v small	4	liver & peritoneal (f)	Small
6	2	peritoneal & coetaneous (s)	v small	1	liver (f)	Small
Total	8			19		

V: Very. F: Fertile. S: Sterile.

(b)

Groups	No. of cyst	Size	Efficiency %
Albendazole	8	small	70%
Mebendazole	19	small	42%
Control	33		100%

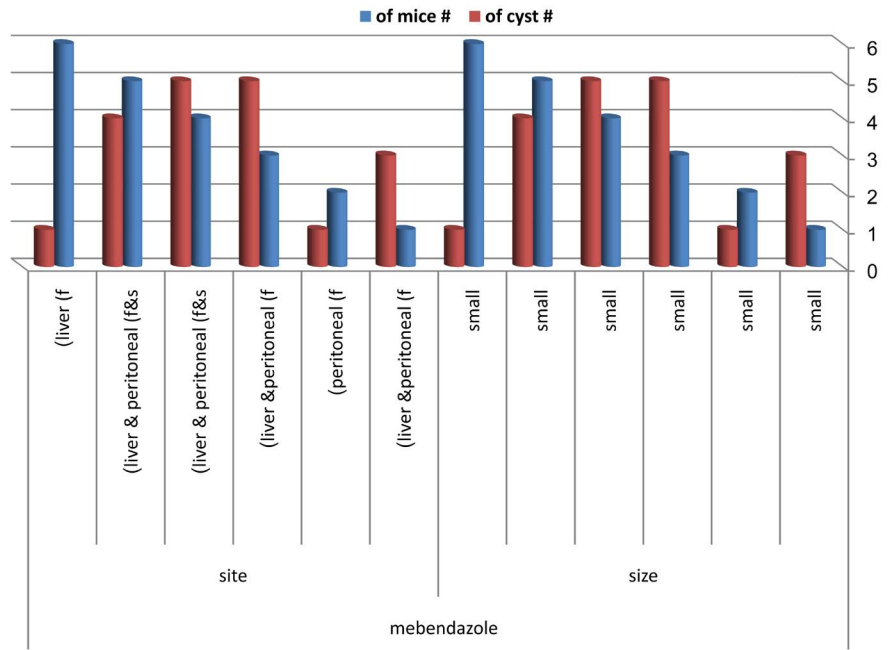


Figure 2. *In vivo* effect of mebendazole on hydatid cyst of mice (prophylactic group).

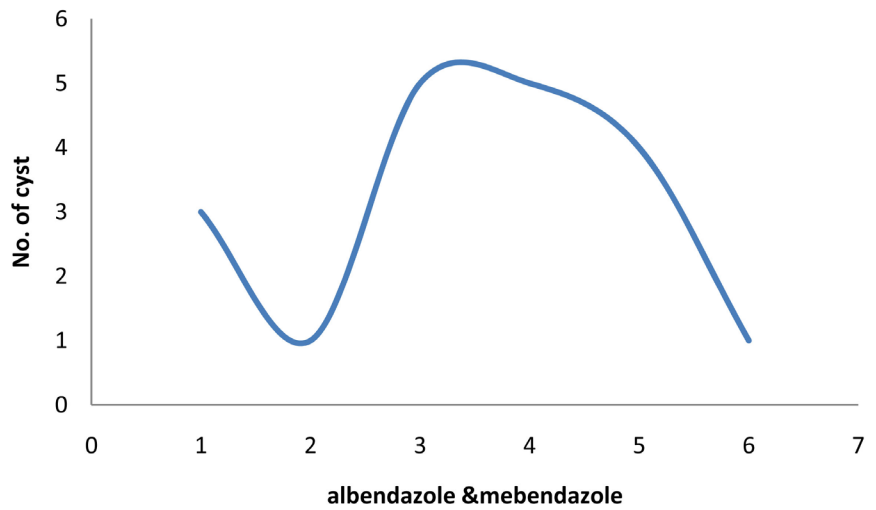


Figure 3. Prophylactic group.

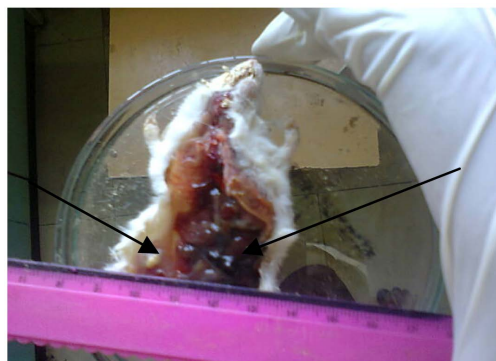


Figure 4. Cysts in prophylactic group (Mebendazole).

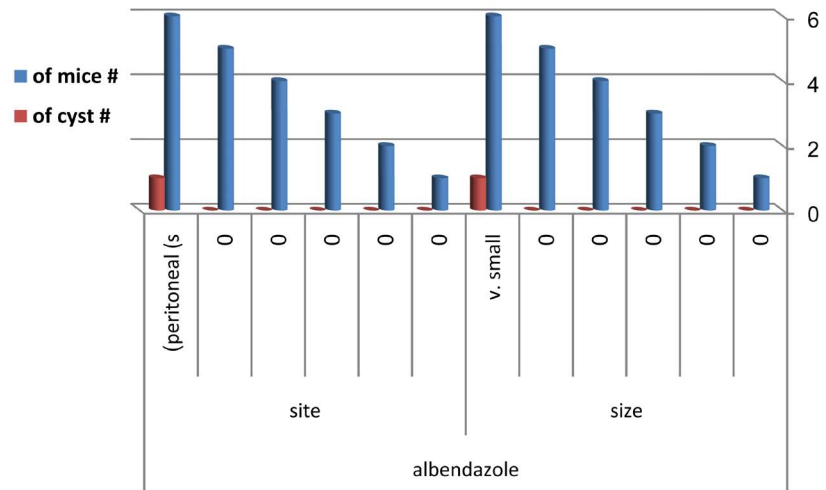


Figure 5. *In vivo* effect of albendazole on hydatid cyst of mice (treated group).

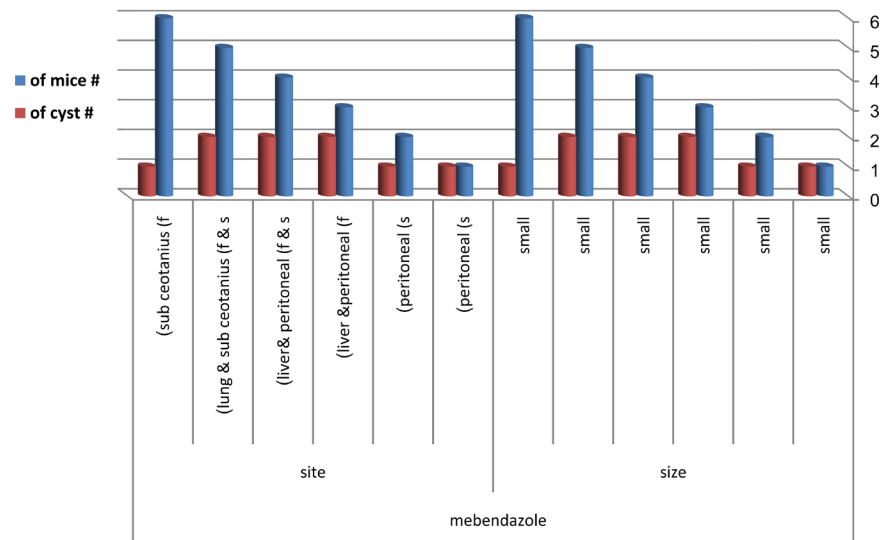


Figure 6. *In vivo* effect of mebendazole on hydatid cyst of mice (treated group).

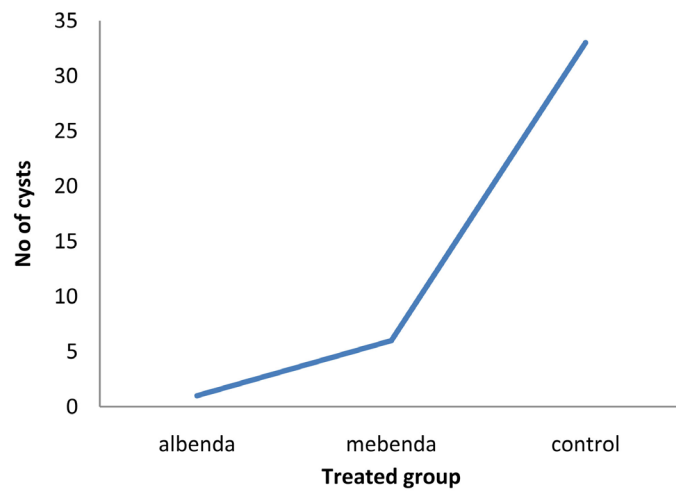


Figure 7. Treated groups.

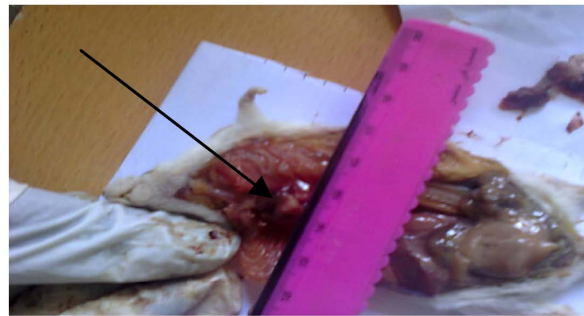


Figure 8. Cysts in treated group with mebendazole.

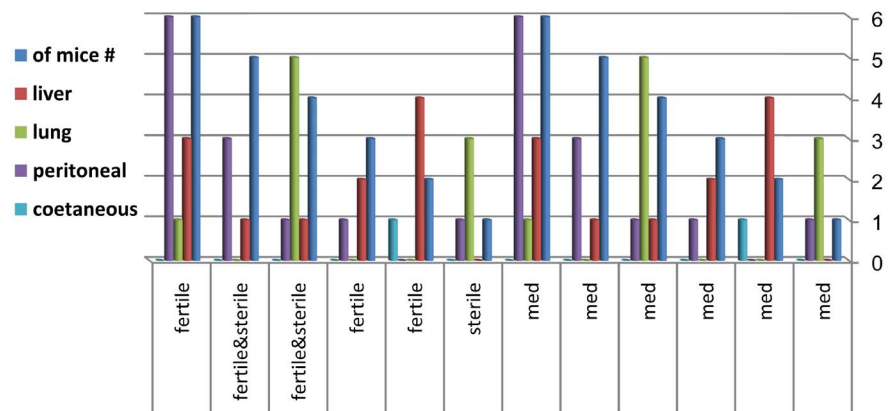


Figure 9. *In vivo* effect of albendazole and mebendazole on hydatid cyst of mice (control group).

Table 2. (a) *In vivo* effect of albendazole and mebendazole on hydatid cyst of mice (treated group); (b) The efficiency rate of albendazole and mebendazole in treated group.

(a)

No of mice	Albendazole			Mebendazole		
	No. of cyst	site	size	No of cyst	site	size
1	0	-	-	1	peritoneal (s)	Small
2	0	-	-	1	peritoneal (s)	Small
3	0	-	-	2	liver & peritoneal (f)	Small
4	0	-	-	2	liver & peritoneal (f)	Small
5	0	-	-	2	lung & sub (f & s)	Small
6	1	peritoneal (s)	v small	1	sub ceotanius (f)	Small
Total	1			9		

V: Very. F: Fertile. S: Sterile.

(b)

Groups	No. of cyst	Size	Efficiency %
Albendazole	1	Small	97%
Mebendazole	9	Small	73%
Control	33	Medium	100%



Figure 10. Cysts in control group.

Table 3. *In vivo* effect of albendazole and mebendazole on hydatid cyst of mice (control group).

No of Mice	size	liver	lung	peritoneal	coetaneous	case
1	medium	0	3	1	0	sterile
2	medium	4	0	0	1	fertile
3	medium	2	0	1	0	fertile
4	medium	1	5	1	0	fertile & sterile
5	medium	1	0	3	0	fertile & sterile
6	medium	3	1	6	0	fertile
Total	medium	11	9	12	1	

4. Discussion

In the present study, the efficacy of albendazole and mebendazole in the treatment of hydatid cyst in mice was investigated. The results showed that when mice were treated with albendazole, no cysts were found in internal organs, while treatment with mebendazole showed many cysts in internal organs, which indicates that albendazole, is more effective than mebendazole. Our finding was consistent with the finding of [14] [15] [16] who reported that continuous long term albendazole therapy in animal models is parasitocidal against larval stage of *E. multilocularis* especially in the early stages of infection. Our findings are also in line with the work of [17] who evaluated the effect of albendazole on hydatid cysts of human. Twenty-nine patients with 240 cysts received albendazole (400 mg twice a day, in 3 cycles of 6 weeks long with 2 weeks off between cycles). Some patients with liver cysts after treatment showed increasing heterogeneity and density suggestive of inactive cysts. Patients with larger cysts and those with pulmonary involvement were better responders. The observed results are encouraging, showing high efficacy of albendazole for the treatment of hydatidosis

and should be offered to patients as an alternative before surgical treatment is considered. Another experiment by Daniel, M. *et al.* [18] compared two different preparations (solution and suspension) of three benzimidazole carbamate drugs (mebendazole, albendazole & ricobendazole) were compared by analyzing their activities against *Echinococcus granulosus* cysts in mice. The effect was more prominent on mebendazole-treated mice, at doses of 25 - 50 mg/kg. It has been reported by [14] that although mebendazole, the first benzimidazole used, has some beneficial effects on the disease in selected patients, it has also been associated with treatment failure in some cases, perhaps because of its poor absorption. It has been shown by [19] that hydatid cysts were severely damaged in mice treated with mebendazole and new vesicles did not develop around the damaged ones. In another experiment by [20], indicated that the postoperative prophylactic course of mebendazole is reliable, safe and with minor side effects and the recurrence rate of the disease was reduced to the lowest possible levels. The results of the above experiments with mebendazole were not consistent with our results which proved high efficiency rate of elbendazole compared with that of mebendazole.

Acknowledgements

The authors wish to thank Mr. Sofian Albasheer for providing help in statistics of the study, thank Miss Suad Fagiry for supply and thanks are extended to Mr. Mohammed Osman and Mr. Abdorahman Dahees. Our thanks are also extended to the technical staff of the department of histopathology, faculty of Medical Laboratory sciences, Al Zaeim Al Azhari University for their technical assistance.

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