

EFFECT OF BENZIMIDAZOL ON THE VIABILITY DEVELOPMENT AND SIZES OF *ECHINOCOCCUS GRANULOSUS* PROTOSCOLICIES IN MICE

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ABSTRACT

This study was designed on to show the effect of albendazol and mebendazol alone and their combination on survival, development and size of *Echinococcus granulosus* protoscolices of (10 mg/ml) intraperitoneal in mice. The study shows that the mebendazol and combination drugs were greater than the albendazol during on the first four days nor effect on the five day in vivo intraperitoneal administration of combination drugs were greater than albendazol and mebendazol alone on the development and size of cysts which about (5.2 ± 2.17) , (7.0 ± 1.0) , (10.0 ± 3.16) for the development and (1.13 ± 0.38) , (1.18 ± 0.54) , (1.20 ± 0.49) for the cysts size.

INTRODUCTION

Benzimidazol derivatives such as albendazol and mebendazol are currently used for the long – term chemotherapy of alveolar echinococcosis^(1,2,3), albendazol is poorly resorbed and is rapidly metabolized. Alveolar echinococcus is prevalent in many regions where the disease is endemic it is well known as a public health hazard to humans⁽⁴⁾. Recently several drugs have been reported to be effective against human hydatidosis. It has been reported that mebendazol and benzimidazol compounds are effective against the growth of hydatidosis in man^(5,6) and laboratory animals⁽⁷⁾. It also shown that albendazol reduces the development of hydatid cysts in gerbil⁽⁸⁾. This study was carried out to compare the protoscolicidal effect of albendazol and mebendazol and its combination in mice.

MATERIALS AND METHODS

The hydatid cysts were obtained from Al-basrah slaughter. Protoscolices were collected and washed three times in physiological saline, then sedimented by gravity and uniform suspension of protoscolices was prepared in physiological saline (2ml) of each solution was temperature equilibrated in a test tube at (37°C) of the viable protoscolices about (800) protoscol. The

exposed surface of the cysts was painted with (1%) iodine solution in (95%) ethanol, the viability of protoscolices was determined by (0.1%) eosin solution⁽⁹⁾ when examined. The number of protoscolices were counted by ⁽¹⁰⁾.

Antihelminthics:- Albendazol from (Smith Kline of French laboratories) mebendazol from (Janseen pharmaceutical – 10ug/ml) suspension in distilled water were made for in vitro experiment and for intraperitoneal inoculation of mice.

In vivo experiments: Twenty mice within age (25 days) were injected intraperitoneally with (0.1 ml) protoscolices, first group was inoculated with (10 ug/mg) body weight albendazol, second group with (10 ug/gm) body weight mebendazol, third group inoculated with combination for ten days. Mice were killed and examined for size and number of cysts.

RESULTS

In vitro, the effect of mebendazol and combination of drugs on viability of protoscolices on the first three days after incubation were greater albendazol but on four and five day there was no significant differences table (1). The total number of (cysts/mouse) treated with combination of drug were lower than those treated with either albendazol or mebendazol and control table (2). Table (3) show that combination of albendazol and mebendazol reduce size of cysts more than using albendazol or mebendazol alone.

Table (1):- effect of albendazol , mebendazol and their combination on the viability of protoscolices

Treatment	Mean of four samples \pm SD Days after incubation				
	1	2	3	4	5
Albendazo + mebendazol	40 \pm 16	36 \pm 0.2	10 \pm 0.1	4 \pm 0.8	-
Albendazol	50 \pm 23	30 \pm 24	20 \pm 0.8	4 \pm 0.8	-
Mebendazol	40 \pm 31	35 \pm 2.4	10 \pm 0.8	4 \pm 0.8	-
Control	60 \pm 2.4	50 \pm 1.6	30 \pm 1.3	10 \pm 1.3	few

Table (2):- Numbers of hydatid cysts in liver and lung of mice treated with albendazol, mebendazol and combination

Treatment	Mean of cysts \pm SD		Mean number of cysts / mouse
	Liver	lung	
Albendazol+mebendazol	2.6 \pm 0.55	0.6 \pm 0.55	5.2 \pm 2.1
Albendazol	2.6 \pm 0.89	18 \pm 0.84	7.0 \pm 1.0
Mebendazol	2.75 \pm 0.95	1.5 \pm 0.58	7.0 \pm 1.0
Control	4.0 \pm 2.45	2.0 \pm 0.0	10.0 \pm 3.16

Table (3):- Size of hydatid cysts in liver and lung of mice treated with bendazol mebendazol and combination

Treatment	Mean size of cysts \pm SD		Mean size of cysts / mouse
	Liver	lung	
Albendazol+mebendazol	1.25 \pm 0.32	0.67 \pm 0.29	1.13 \pm 0.38
Albendazol	1.41 \pm 0.46	0.67 \pm 0.25	1.18 \pm 0.54
Mebendazol	1.36 \pm 0.25	0.75 \pm 0.27	1.20 \pm 0.49
Control	1.96 \pm 0.46	0.81 \pm 0.26	1.69 \pm 0.65

DISCUSSION

A parasitocidal effect of treatment with various concentration of benzimidazol was reported by⁽¹¹⁾ in that study in vitro model of *Echinococcus multilocularis* with parasites grown the parasitocidal effect of mebendazol treatment was determined by observing the loss of cysts and by reduce the parasite proliferation. In present study effect of albendazol, mebendazol and combination on the viability of protoscolices reduce the survival of protoscolices were marked on the first three days post infection this due to lack of supply of nutrient required for parasite metabolism⁽¹²⁾ this result agree with ⁽¹³⁾ who confirmed that the earlier results that the main

metabolites present in vesicle fluid are succinate acetate, alanine and Lactate these compounds are all end products of the accepted pathway of glucose metabolism. Mebendazole and combination of drugs seems to affect this reduction earlier than albendazole alone this effect of these drugs might be due to interference with glucose uptake by this parasite and this agreed with the result of⁽¹⁴⁾ who confirmed that benzimidazole induce the blockage of glucose absorption and lead to glycogen depletion. In the present study also a dose of (10 ug/gm) of benzimidazole reduce the number and size of hydatid cysts in albino mice and the effect of combination were greater than either treatment alone where this could be explained by synergistic effect of combination drugs by more damage to the parasite⁽¹⁵⁾. Also in the present study neither mebendazole or bendazole prevent the development of hydatid cysts and this may due to low doses of both treatments and the delay in administration of treatment after intraperitoneal inoculation of protoscolices, showed⁽¹⁶⁾ that daily administration of 50 mg/kg body weight of mebendazole for (10) days in mice prevents the development of cysts also the⁽¹⁷⁾ found complete prevention of development of cysts in gerbils using (10mg/kg) for (15) days. Finally the present study suggest using a combination drugs as prophylaxis for hydatidosis also the treatment should be administered in high dose in order to maintain effective level of the drug.

تأثير مركبات البنزيميدازول على حيوية وتطور واحجام رؤيسات الاكياس المائية في الفئران

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الخلاصة

صممت هذه الدراسة الى بيان تأثير كل من البنزيميدازول والمبندازول كلا على حده أو بأستخدامها معاً على حيوية، وتطور واحجام رؤيسات الاكياس المائية بأستخدام جرعة مقدارها (10 ملغم/مل) داخل الخلب في الفئران. أظهرت الدراسة ان تأثير المبندازول بالاضافة الى العقارين معاً كان اكبر من تأثير البندازول خلال الأربعة أيام الأولى من التجربة ولم يلاحظ أي تأثير في اليوم الخامس مقارنة مع مجموعة السيطرة. كذلك فقد كان تأثير العقارين معاً أكبر على تطور الرؤيسات حيث بلغ اعداد الاكياس لكل فئه (5.2±2.1) بينما بلغ تأثير البندازول والمبندازول (0.7±1) مقارنة مع مجموعة السيطرة والبالغة (10.0±3.1) أما تأثيرهما على حجم الأكياس المائية فقد كان تأثير العقارين سوية اكبر من تأثير البندازول والمبندازول كلاً على حدة حيث بلغ معدل حجم الأكياس لكل فأر (1.13±0.38) و (18±0.5) و (1.20±0.49) على التوالي مقارنة مع حيوانات مجموعة السيطرة والتي بلغت (1.69±0.65).

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