ORIGINAL ARTICLE

Liver enzymes derangement and the influence of diet in animals given oral albendazole

Gabriel Olaiya Omotoso, Bernard Ufuoma Enaibe, Adeoye Oyetunji Oyewopo, Ismail Olashile Onanuga

Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Ilorin, Ilorin, Nigeria

ABSTRACT

Background: Albendazole is used as an anthelmintic in the treatment of some parasitic infections. This study determined how the effects of albendazole on liver enzymes are influenced by diet. **Materials and Method:** Thirty adult male Wistar rats of mean weight 304.12 ± 11.34 g were randomly grouped into five: Group A: Control, was given rat pellets and water only; Group B received 15 mg/kg/d of albendazole while fasting; Group C received 15 mg/kg/d of albendazole with fatty meal; Group D received 15 mg/kg/d of albendazole with normal diet (rat pellets); and, Group E received 30 mg/kg/d of albendazole with normal diet (rat pellets); they were given orally for 3 consecutive days. The animals were sacrificed thereafter and blood samples obtained for quantitative study of the serum activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP). **Results:** Significant elevation in the serum levels of the transaminases especially in animals which were on their normal diet (rat pellets), while ALP was either reduced or increased based on dietary factors. **Conclusions:** Oral administration of albendazole before meal or with a fatty diet could help limit severe elevation of liver enzymes associated with its use, while still ensuring optimal efficacy.

Key words: Albendazole, fasting, fatty meal, liver enzymes

Address for correspondence:
Dr. Gabriel Olaiya Omotoso,
Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Ilorin, P.M.B. 1515, Ilorin, Nigeria.
E-mail: gabrielolaiya@yahoo.com

INTRODUCTION

Albendazole is a benzimidazole carbamate used in the treatment of cysticercosis, hydatid disease, larva migrans, strongyloidiasis, toxicariasis, and many other parasitic infections,[1-3] as a broad-spectrum anthelmintic drug.[4] When used orally, it is rapidly metabolised in the liver to its active metabolite-albendazole sulfoxide. To ensure a maximal drug effect, albendazole is administered either with a fatty meal for tissue infection, or on an empty stomach, in case of intraluminal infection.[1] It could also be used in combination with other anthelminthics, such as ivermectin.[5,6] The dosage of drug administration varies, depending on clinical indication; it could be as low as 15 mg/kg/d for 3 consecutive days, or for one or more week(s).

Access this article online	
Quick Response Code:	Website: www.nigeriamedj.com
	DOI: 10.4103/0300-1652.122333

As the site of the first-pass metabolism, the liver is subject to certain deleterious effects of the drug that could adversely affect hepatic functions, although albendazole is said to have no pharmacologic effect in human. The use of albendazole has been linked to various degrees of derangement in liver enzymes and hepatic function parameters.[7] Chronic administration of ivermectin and albendazole could compromise the integrity of the kidney and the liver.[5]

The elevation in serum levels of liver enzymes could be used in assessing the degree of liver injury. Enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) are commonly used markers of hepatocellular injuries. They are capable of inducing alterations in membrane permeability properties of the liver. Serum elevation of ALP could occur due to blockage of bile ducts or impairment of bile production in the liver.[8]

The current study aimed at determining the effect of albendazole on serum levels of liver enzymes when administered with a fatty diet and when used on an empty stomach.

MATERIALS AND METHODS

Thirty (30) adult male Wistar rats of mean weight 304.12 ± 11.34 g were used for the experiment. The animals were housed in individual cages and allowed to acclimatize prior to commencement of the experiment. They were kept under hygienic and favourable condition, and maintained under a 12 h light/12 h dark cycle, with feeds and water available *ad libitum.*

The animals were randomly grouped into five (5), with six (6) rats in each group, as follows:

Group A: Control, fed with rat pellets and water only

Group B: received 15 mg/kg/d of albendazole while fasting

Group C: received 15 mg/kg/d of albendazole with fatty meal

Group D: received 15 mg/kg/d of albendazole with normal diet (rat pellets)

Group E: received 30 mg/kg/d of albendazole with normal diet (rat pellets)

The pelletised feed (rat pellets) was procured from UAC Vital Feeds®, and contains 15% crude protein, 7% fat, 10% crude fibre, 1% calcium, 0.35% phosphorus, 2550 kcal/kg of metabolised energy. The absolute fatty meal was prepared by mixing groundnut cake, butter and egg yolk together.

Group A animals were given rat pellets and water only. All animals in the Treatment Groups B, C and D received 15 mg/kg/d of albendazole each, while animals in Group E received 30 mg/kg/d albendazole. Group B animals were made to abstain from feeds and water about one hour prior to administration of drug; Group C animals were fed with fatty meal from about 30 min onwards before administration of albendazole; and Groups D and E received the drug while on their regular feeds (rat pellets) and water. The mode of administration was oral, with the aid of a feeding tube and syringe, for 3 consecutive days.

About 24 hours after the last day of drug administration, the animals were sacrificed by cervical dislocation. Intracardial blood was collected into lithium heparinised bottles for liver enzyme studies.

Quantitative study of the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) was done using appropriate biochemical kits from Randox® (Antrim, UK).

Statistical analysis of data

The data obtained were expressed as means ± SEM, and analysed using the Student's t-test. The level of significance was taken at *P*-values < 0.05.

RESULTS

The activities of ALT, AST and ALP following a 3-day administration of albendazole increased virtually in all the groups compared with the Control Group. Animals in Group D which received the lower dose (15 mg/kg/d) of the drug with normal diet (rat pellets) had the highest levels of ALT, AST and ALP, while Group E animals on normal diet which received the higher dose (30 mg/kg/d) of the drug had lower levels of serum ALT, AST and ALP compared with animals in Group D; the difference in serum ALT between Groups D and E was statistically significant ($P < 0.05$), but not for AST and ALP ($P > 0.05$), [Table 1].

Among the low dose groups B, C and D, which received same dose of albendazole (15 mg/kg/d) under different dietary conditions, Group B animals had the lowest serum level of ALT (21.0 ± 2.27 IU/L), while Group D had the highest (28.8 ± 0.85 IU/L), and in most cases, the differences between the three groups were statistically significant ($P < 0.05$) [Table 1].

Serum activity of AST also increased in all the groups compared with the Control, being highest in rats given 15 mg/kg/d albendazole on normal rat pellets, but the increase was only statistically significant in Group C ($P < 0.05$) that received 15 mg/kg/d albendazole with fatty diet, compared to the Control. When placed on rat pellets, Group D that got a lower dose (15 mg/kg/d) of the drug had a higher serum AST (36.75 ± 2.14 IU/L) compared with Group E given a higher dose (30 mg/kg/d; 35.00 ± 3.16 IU/L); this difference was however not statistically significant ($P > 0.05$). Animals given the low dose with rat pellets (36.75 ± 2.14 IU/L) had a statistically significant higher level of AST compared with those animals that fasted (29.00 ± 1.83 IU/L), [Table 1].

Activities of serum ALP was highest in Group D (23.25 ± 2.84 IU/L), but lowest in Group C (18.00 ± 2.42 IU/L)

Table 1: Serum levels of liver enzymes

Enzymes	A: vontrol	B: 15 mg/kg/d+fasting	C: 15 mg/kg/d+fatty diet	D: 15 mg/kg/d+rat pellets	E: 30 mg/kg/d+rat pellets
ALT (IU/L)	15.5±1.19	21.0±2.27*	24.5±0.96†≠	28.8±0.85*†≠§	20.3±0.85§
AST (IU/L)	26.75±2.39	29.00±1.83*	33.75±1.49†	36.75±2.14*	35.00±3.16
ALP (IU/L)	20.75±0.95	20.25±2.93	18.00±2.42	23.25±2.84	21.50±2.40

*Statistically significant difference between Groups B and D, †Statistically significant difference compared with Control, ≠Statistically significant difference between Groups C and D, §Statistically significant difference between Groups D and E, ALT – Alanine aminotransferase, AST – Aspartate aminotransferase, ALP – Alkaline phosphatase

compared with the Control (20.75 ± 0.95 IU/L). ALP levels in both Groups B (20.25 ± 2.93 IU/L) and C (18.00 ± 2.42 IU/L) were lower than that of the Control too. These differences in between groups, and in comparison with the Control were however not statistically significant ($P > 0.05$), [Table 1].

DISCUSSION

Various studies, especially in experimental animals, have demonstrated some of the untoward effects associated with the use of albendazole, including teratogenic, embryotoxic, and other organ-specific adverse effects.[5,7] Different forms of bony abnormalities and resorption have been noted when administered to experimental animals during specific gestational period.[2,9] Liver enzymes such as alanine aminotransferase and aspartate aminotransferase are involved in protein metabolism and are commonly used markers of hepatocellular injury, although other clinical conditions could result in increased levels of these enzymes. The degree of elevation of these enzymes including, alkaline phosphatase, in many instances is directly proportional to the damage done. A subtle derangement in the serum level of these enzymes could be a pointer to an ongoing liver pathology even in the absence of apparent histomorphological abnormalities.

Studies by Lange *et al*.,[10] showed that use of albendazole in patients with echinococcosis resulted in an increased bioavailability of the drug when taken with a fatty breakfast meal than when taken on an empty stomach. However, in intraluminal involvement, it is more appropriate to administer the drug on an empty stomach.[10] The current study observed that the aminotransferases were elevated in the animals irrespective of their dietary consideration. However, when administered on an empty stomach or with fatty meal, the serum levels of these enzymes were, significantly, not as high as in the animals that received the drug with their regular meal.

The alteration seen in the serum level of alkaline phosphatase is such that elevation of the enzyme occurred only when albendazole was used with the regular diet. Serum ALP was observed to reduce, though not significantly, in animals fed on fatty diet and those that abstained from food and water, compared to the Control animals.

These show that whatever damage is caused to the liver by albendazole, it could be minimised by administering the drug on an empty stomach or with a fatty diet, and the former would probably give a better outcome.

Conclusively, in order to minimise the hepatocellular damage that accompanies the use of albendazole, it is preferable to administer the drug with a fatty meal, or better still, on an empty stomach, and this also enhances a maximal drug effect.

REFERENCES

1. Kamgno J, Boussinesq M. Effect of a single dose (600 mg) of albendazole on Loa loa microfilaraemia. Parasite 2002;9: 59-63.
2. Teruel M, García, V, Catalano R. Effects of albendazole sulphoxide on embryonic, foetal and placental parameters in Wistar Rats. Int J Morphol 2009;27:1147-53.
3. Chaurasia RN, Garg RK, Agarwall A, Kohli N, Verma R, Singh MK, *et al*. Three day albendazole therapy in patients with a solitary cysticercus granuloma: A randomized double blind placebo controlled study. Southeast Asian J Trop Med Public Health 2010;41:517-25.
4. Gurram SP, Kollu NR, Sivadevuni G, Solipuram MR. Biotransformation of albendazole by Cunninghamella blakesleeana: Influence of incubation time, media, vitamins and solvents. Iran J Biotechnol 2009;7:205-15.
5. Arise RO, Malomo SO. Effects of ivermectin and albendazole on some liver and kidney function indices in rats. Afr J Biochem Res 2009;3:190-7.
6. Awadzi K, Edwards G, Duke BO, Opoku NO, Attah SK, Addy ET, *et al*. The co-administration of ivermectin and albendazole-safety, pharmacokinetics and efficacy against Onchocerca volvulus. Ann Trop Med Parasitol 2003;97:165-78.
7. Yarsan E, Altinsaat Ç, Ayçiçek H, Sahindokuyucu F, Kalkan F. Effects of albendazole treatment on haematological and biochemical parameters in healthy and toxocara canisinfected mice. Turk J Vet Anim Sci 2003;27:1057-63.
8. Johnston DE. Special considerations in interpreting liver function tests. Am Fam Physician 1999;59:2223-30.
9. Lak E, Ranjbar R, Najafzadeh H, Morovvati H, Khaksary M. Protective effect of sambucus elbus extract on teratogenicity of albendazole. Middle-East J Sci Res 2011;8:606-10.
10. Lange H, Eggers R, Bircher J. Increased systemic availability of albendazole when taken with a fatty meal. Eur J Clin Pharmacol 1988;34:315-7.

How to cite this article: Omotoso GO, Enaibe BU, Oyewopo AO, Onanuga IO. Liver enzymes derangement and the influence of diet in animals given oral albendazole. Niger Med J 2013;54:310-2.

Source of Support: Nil, **Conflict of Interest:** None declared.