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EFFECT OF ALBENDAZOLE ON SOME HORMONAL, HAEMATOLOGICAL AND BIOCHEMICAL PROFILES IN SHEEP

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ABSTRACT

In this study, the effects of albendazole (10 mg/kg b.wt.) on some hormonal, haematological and biochemical profiles of 20 mature sheep of both sex were studied after its oral administration as 2.5 % suspension.Albendazole exerted a significant increase in the levels of serum globulins, alanine aminotransferase (ALT),aspartate aminotransferase (AST), superoxide dismutase (SOD), total leukocytic count (WBCs) and their differential count, particularly lymphocytes and neutrophils. Moreover, it evoked a significant decrease in serum testosterone of rams. Meanwhile, it demonstrated no significant effect on the levels of estradiol and progesterone in ewes.

INTRODUCTION

Although anthelmintics are of great importance because helminthiasis is very common allover the world, only a few therapeutic agents are available for mass eradication programs.The need for an anthelmintic with a wide range of antiparasitic action and high degree of efficacy, necessitate a good margin of safety and versatility of administration.

Albendazole {Methyl (propylthio -1H- benzimi - dazole -2- yl) carbamate } is a potent member of the benzimidazole group of anthelmintics with a broad spectrum activity against gastrointestinal roundworms including larval stages of tapeworms, liver flukes and lungworms in many species [1-4]. It is absorbed to a much greater degree than other benzimidazoles because 47 % of the administered dose is recovered in urine over a 9-day period [5].

The benzimidazoles act agianst helminths by inhibiting the uptake of glycogen in the gut of the parasites [6] or by inhibiting the enzyme fumarate reductase [7] or by both actions.

The aim of the present study is to investigate the effects of albendazole on some hormonal, haematological and biochemical profiles of sheep. These parameters were selected and assested in their importance on the reproductive state and general health condition of sheep.

MATERIAL AND METHODS

Drug :

Albendazole (Anthel-All® 2.5 % suspension, Amoun Pharmaceutical Co., Egypt.

Animals :

A total of 20 clinically healthy adult sheep of both sex, weighing 53-58 kg , were used throughout this experiment. The animals were housed in open yards under a relatively good environmental conditions as far as possible and fed *ad-libitum* on hay and formulated diet.

Experimental :

The animals were classified into 2 main groups (each of 5 males and 5 females).The 1st group served as control and orally administered normal saline solution. Meanwhile the 2nd group was administered a single oral dose of albendazole (2.5 % suspension) at a rate of 10 mg/kg b.wt. [8], given as a drench.

Sampling and analysis :

After 1 and 2 week post dosing, two blood samples were collected from the jugular vein of each animal.One in a clean dry centrifuge tube (for serum collection)and the other in clean heparinized tube (for whole blood).The sera were separated by centrifugation at 3000 r.p.m for 15 minutes and kept frozen at -20°C until assayed.

The whole blood samples were used for determination of superoxide dismutase [9], haemoglobin content [10], total red blood cells and total leukocytic count [11], while the differential leukocytic count was performed using Giemsa stained blood films [12].

On the otherhand, the serum samples were assayed for testosterone [13], estradiol [14], progesterone [15], total proteins [16], Albumen [17], urea [18], creatinine [19], alkaline phosphatase [20], alanine aminotransferase and aspartate aminotransferase levels [21].

Statistical analysis of the present data was carried out using Students "t" test [22].

RESULTS AND DISCUSSION

It is probable that much of the anthelmintic activity of albendazole in sheep is due to the

metabolically formed sulfoxide and sulfone [23], which are considered responsible for its ongoing side effects [24].

The evaluation of haematological profile in sheep administered albendazole (Table 1) indicates a statistically significant increase in superoxide dismutase level ($P<0.05$) after 1 week post dosing, and a significant decrease ($P<0.05$) in total leukocytic count (leukopenia) after 1st and 2nd week post treatment in rams and ewes, particularly lymphocytes and neutrophils (neutropenia). The significant increase in superoxide dismutase in sheep may be attributed to the high concentration of superoxide radical, that had been removed by dismutation reactions, to minimize the damage effect which may be induced by the radical [25,26].

The increase in superoxide dismutase level may be also due to the effect of albendazole on the blood [27] who reported that administration of thiabendazole leads to transient anemia in dogs.

The effect of albendazole on leukocytes was compatible with that reported before [28, 29] who found that, albendazole has tendency to induce leukopenia and neutropenia in man.Moreover, it was found that, thiabendazole induces also leukopenia in dogs [27].

Concerning the serum biochemical studies as seen in (Table 2), no significant changes were observed in the levels of total proteins, albumin, urea, creatinine and alkaline phosphatase. Whereas, a significant increase ($P<0.05$) in serum globulins was recorded one week post treatment in both sexes. Furthermore, the drug evoked also a significant increase in the levels of

Table (1): Effects of the orally administered albendazole (10 mg/kg b.wt) on some haematological profile in sheep. (M ± S.E) n = 5

Sex / Parameter	Males (Rams)			Females (Ewes)		
	Control	1st week	2nd week	Control	1st week	2nd week
Superoxide dismutase Ug/100 ml	63 ± 2.3	70± 2.1*	65± 4.1	60± 5.7	81± 5.2*	64± 2.2
Haemoglobin (g/100 ml)	8.1 ± 0.3	7.8± 0.37	7.3± 0.32	8.3± 0.45	6.9± 0.64	7.1± 0.42
W.B.Cs (10 x6 /ml)	6.1± 0.3	6.5± 0.16	5.9± 0.48	5.31± 1.03	5.2± 0.25	5.3± 1.04
Differential leukocytic count (%)	10.14± 0.9	7.38± 0.7*	6.26± 0.8*	9.32± 0.6	6.96± 0.7*	7.9± 0.2*
Neutrophils	32.2± 1.2	30.± 2.3	29.4±0.27*	34.2± 0.47	33.0± 0.12*	34.6± 0.9
Lymphocytes	59.3± 1.98	53.4± 1.6*	54.2±0.26*	56.3± 1.35	52.3± 1.24*	54.8± 0.6
Eosinophils	4.4± 1.27	4.2± 1.31	4.8± 1.18	6.1± 0.8	5.8± 0.73	4.6± 1.2
Monocytes	3.2± 0.6	2.9± 0.7	3.4± 0.3	3.16± 1.2	3.75± 0.8	3.3± 0.5
Basophils	0.3± 0.1	0.2± 0.06	0.4± 0.12	0.2± 0.02	0.3± 0.1	--

* Significnat at $P<0.05$

Table (2): Effects of the orally administered albendazole (10 mg/kg b.wt) on some serum biochemical parameters in sheep. (M ± S.E) n = 5

Sex / Parameter	Males (Rams)			Females (Ewes)		
	Control	1st week	2nd week	Control	1st week	2nd week
Total proteins (gm/L)	69.3 ± 5.4	78.4 ± 9.6	73.2 ± 3.5	66.4 ± 3.6	68.2 ± 6.1	69.3 ± 5.4
Albumin (gm/L)	39.6 ± 1.3	39.5 ± 2.4	41.3 ± 2.4	37.3 ± 1.9	35.2 ± 1.2	42.0 ± 1.5
Globulins (gm/L)	29.7± 1.4	36.9 ± 1.9*	31.9 ± 1.8	29.6 ± 1.8	33.9 ± 1.9*	31.2 ± 1.6
Urea (mg/dl)	43.8± 3.2	45.5 ± 2.7	43.6 ± 3.1	42.4 ± 2.9	44.6 ± 3.6	41.8 ± 1.5
Creatinine (mg/dl)	0.68± 0.07	0.66 ± 0.01	1.4 ± 0.9	0.7 ± 0.12	0.8 ± 0.08	1.2 ± 0.1
Alk. phosphatase (mg/dl)	13.1± 0.3	14.6 ± 0.8	15.4 ± 0.7	14.1 ± 0.6	13.8 ± 0.5	16.1 ± 0.9
ALT (U/L)	13.8± 3.4	18.6 ± 4.9	39.0 ± 8.8*	14.4 ± 5.9	33.4 ± 4.8*	36.8 ± 6.3*
AST (U/L)	27.6± 6.2	72 ± 4.6**	60 ± 3.1**	41.6 ± 5.3	70.4 ±3.6**	67.9±2.1**

* Significnat at P<0.05 ** Significnat at P<0.005

serum ALT (P<0.05) and AST (P<0.005) up to 2 weeks post dosing in the treated group when compared with the control group.

These findings may indicate that, albendazole administration results in liver function disturbance.Our results coincides with the results reported before [28], who found that albendazole caused liver function abnormalities in man.

The major side effects of albendazole in man are hepato-toxicity and increasing transaminase levels [29]. In addition, administration of mebendazole to foals, elicited a significant increase in ALT & AST and a significant drop in total proteins [30]. Moreover, albendazole results in acute hepatitis with jaundice in dogs [3].

As regards, the hormonal level of serum testosterone in rams revealed a significant decrease after 1st (P<0.05) and 2nd (P<0.005) week of treatment (Table 3). Whereas, no marked alterations were detected in both estradiol and progesterone levels in ewes, although albendazole has embryotoxic and teratogenic effects in pregnant ewes [8].

The decreased level of testosterone hormone in rams may be attributed to the effect of metabolically formed sulfoxide [24] which may cause testicular damage.On the otherhand, it has been reported that testosterone level in serum reaches 5.22 ± 0.55 ng/ml in rams but the difference in its level may be attributed to the animal's age, metabolic clearance rate, season of year, time of the day, frequency, and condition of the sampling [31].

Thus, it could be concluded from this study that,the hepatic enzymology and hormonal profiles revealed hepatic disorder associated with some hormonal disturbance, which necessitate close therapeutic monitoring of patient animals who are given albendazole.

Table (3) : Effect of the orally administered albendazole (10 mg/kg b.wt) on some reproductive hormones in sheep. (M± S.E) n = 5

Sex / Parameter	Males (Rams)			Females (Ewes)		
	Control	1st week	2nd week	Control	1st week	2nd week
Testosterone (ng/ml)	2.78 ± 0.2	0.9 ± 0.2**	0.17±0.04**	-	-	-
Estradiol (pg/ml)	-	-	-	128.6 ± 2.4	132. ± 3.2	134.1 ± 3.9
Progesterone (ng/ml)	-	-	-	2.42 ± 0.1	2.76 ± 0.84	2.1 ± 0.65

** Significnat at P<0.005

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تأثير دواء البندازول علي بعض الأوجة الهرمونية ، الدموية والبيوكيميائية في الأغنام

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تناولت هذه الدراسة معرفة تأثير عقار البندازول (٥ر٢٪ معلق) والمستخدم بكثرة كمركب واسع الأنتشار ضد الديدان على الأغنام . قسمت الأغنام (عدد ٢٠ من الجنسين) إلى مجموعتين بواقع ١٠ أغنام لكل (٥ ذكور ، ٥ إناث) ، واستخدمت المجموعة الأولى كمجموعة ضابطة ، بينما تم اعطاء المجموعة الثانية جرعة واحده من الدواء (١٠ مجم / كجم) عن طريق الفم .

تم أخذ عينات دم ومصل بعد أسبوع وأسبوعين من اعطاء الدواء وذلك لإجراء بعض القياسات فيهما للوقوف على الاثار الناتجة من استخدامه فى الأغنام .

هذا وقد أظهرت النتائج وجود زيادة معنوية فى نسبة كل من الجلوبيولين ، انزيم الألانين أمينو ترانس فيريز ، انزيم اسبرتات امينو ترانس فيريز ، انزيم سوبر اوكسيد ديسميوتيز ، وكذلك زيادة معنوية فى عدد كرات الدم البيضاء .

كما وجد أن العقار قد سبب نقصاً معنوياً فى منسوب هرمون التستوستيرون فى الذكور ، بينما لم يحدث تغيرات معنوية فى منسوب كل من هرمونى الاستروجين والبروجيستيرون فى الإناث .

مما سبق نستنتج أن استخدام عقار البندازول يصاحبه بعض اضطرابات فى وظائف الكبد وفى بعض مكونات الدم ، وقد يحدث خلل فى بعض هرمونات التناسل خاصة عند الذكور مما يستدعى الحذر عند استخدامه .