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THE EFFECT OF FEEDING SYSTEM AND TREATMENT BY TRICLABENDAZOLE (FASINEX®) ON BLOOD PICTURE AND METABOLIC PROFILE CHANGES IN SHEEP FASCIOLIASIS IN ASSIUT GOVERNORATE

(With One Table and One Figure)

By

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تأثير نظام التغذية والعلاج بالترايكلابندازول (فازينكس) على تغيرات صورة الدم والأيض في الأغنام المصابة بالديدان الكبدية في محافظة أسيوط.

مصطفى أحمد صالح ، حسن زكي راتب

أجريت هذه الدراسة لمعرفة تأثير التغذية بالنظام التقليدي (الرعي) والنظام المكثف على التغيرات في صورة الدم والأيض في الأغنام المصابة بالديدان الكبدية وتأثير العلاج بالترايكلابندازول (الفازينكس) عليها. تم اختيار عدد ٤٠ نعجة بلدي (٢-٣ أعوام) من قطيعين أحدهما يعتمد في تغذيته على الرعي (عدد٢٠ ، مجموعة أ) والآخر يعتمد على التربية المكثفة داخل الحظائر(عدد ٢٠، مجموعة ب) بإحدى المناطق (عرب المدابغ) الموبوءة بالديدان الكبدية بمدينة أسيوط. وطبقاً للأعراض الإكلينيكية وفحص البراز قسمت كل مجموعة إلى مجموعتين فرعيتين متساويتين (١٠ في كل منها) إحداهما مصابة إكلينيكيا بالديدان الكبدية (٢٠٠-٣٠٠ بويضة/ جم) والأخرى سليمة حيث استخدمت الأخيرة كمجموعة ضابطة لكل قطيع. تم أخذ عينات الدم قبل وبعد أربعة أسابيع من العلاج بالفازينكس. أظهرت النتائج أن نظام التغذية له تأثير واضح على كل القياسات الهيماتولوجية والبيوكيميائية في دم الحيوانات السليمة باستثناء صورة كريات الدم البيضاء والبليروبين ومستوى نشاط الأمينوترانزفيريزات. بينما لوحظ أن التغيرات في البروتين الكلي والألبومين والبليروبين والأمينوترانزفيريزات والنحاس والزنك الناتجة من الإصابة بالديدان الكبدية كانت لا تختلف بنظام التغذية ولكن كان هناك اختلاف في نسب الجلوكوز والحديد في مصل الدم. كما أوضحت الدراسة أن العلاج بالفازينكس ذو كفاءة عالية في علاج الديدان الكبدية دون النظر إلى نوع التغذية.

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SUMMARY

The effect of feeding and treatment by Fasinex on the behavior of cellular and metabolic profile in Fasciola hepatica infested sheep was monitored. For this purpose, a total number of 40 Balady ewes (2-3 years) were selected (grouped equally, 20 each) from 2 private herds in a known Fasciola hepatica endemic area (Arab-El-Madabegh), Assiut City. One of the herds was depending on free grazing and the other was depending on indoor-feeding system. Each group was sub-classified according to clinical symptoms and fecal examination into 2 sub-groups (10 ewes each), clinical fascioliasis (200-300 epg) and healthy (control) groups. Blood was drained just before and 4 weeks after treatment by triclabendazole (Fasinex®) for hematological and biochemical studies. In both control groups, feeding system had significant effect on all studied parameters except leukocyte profile, bilirubin, and aminotransferases activities of blood serum. The nutritional factor did not affect the changes in total protein, albumin, AST, ALT, bilirubin, Cu and Zn that caused by fascioliasis in both infested groups, while the changes in glucose and iron differed by the two planes of nutrition. It seems that feeding system has a non-neglected effect on the pathogenesis of fascioliasis. In addition, the study declared that Fasinex at the commercially recommended dose is highly effective against adult Fasciola hepatica irrespective of feeding system.

Key words: *Fascioliasis, feeding, triclabendazole, metabolism.*

INTRODUCTION

Fascioliasis is a parasitic disease infects several species of domestic animals and wildlife, but it considered to be of primary economic importance in cattle and sheep (Malone, 1997). Anemia, esinophelia, hypo-albuminemia and hyper-activity of the liver enzymes are considered the basic features of fascioliasis (Urquhart et al., 1996 and Boray, 1997b). Hope Cawdery et al. (1977) and Mehra et al. (1999) studied the adverse effect of fascioliasis on appetite, dry matter intake and food conversion efficacy in ruminants. The effective strategies for the control of fascioliasis, based largely on drug (fasciolicide) use, epidemiological data, rotation of pasture, snail control, breeding of resistant hosts, dietary condition and pathophysiological data (Boray, 1997_b, Malone, 1997 and Fairweather and Boray, 1999).

On the base of epidemiological data, triclabendazole (Fasinex) showed 100% efficacy against adult sheep fascioliasis in Egypt (Ezzat et al., 1994). This study aimed to evaluate the effects of two feeding systems on the blood composition of sheep, and to illustrate the effect of feeding systems on the cellular and metabolic profile changes in sheep infested by fascioliasis, as well as the effect of treatment by Fasinex on these changes.

MATERIALS and METHODS

A total number of 40 Balady ewes (2-3 years) were selected equally (20 each) from 2 private herds in a known Fasciola hepatica endemic area (Arab-El-Madabegh), Assiut City. The first herd was depending on free grazing on the spontaneously miscellaneous grown grasses on the banks of irrigation channels, pasture residues, straw and chaffs (conventional rearing system). The second herd was reared in indoors (condensed rearing system) depending on concentrate mixture (40% wheat bran, 32% maize, 25% decorticated cotton seed meal, 2% limestone and 1% NaCl) and Barseem (Medicago sativa) *ad-lib*. Each group was sub-classified according to clinical symptoms (Radostits et al., 1994) and fecal examination (Coles, 1986) into 2 sub-groups (10 ewes each), i.e., clinical fascioliasis and healthy (control) groups. The infested groups showed depressed appetite, pale mucus membrane, emaciation, dullness and sub-mandibular edema. These groups were proved to be positive for Fasciola hepatica egg in feces (200-300 epg) and free from other internal parasites. Two blood samples were drained from each ewe just before and four weeks after treatment by triclabendazole (Fasinex 10%, Novartis Inc. Basle, Switzerland) which was orally administrated at a commercial dose of 12 mg/kg (Boray et al., 1983) for the diseased groups. The first blood sample contained anti-coagulant, used for hematological studies (Schalm et al., 1979). The second one used to obtain serum for biochemical determination of total protein, albumin, glucose, total bilirubin (Henry et al., 1974), Aspartate and Alanine amino-transferases (Reitman and Frankel, 1957). In addition, blood serum Fe, Cu, and Zn were determined by acetylene type computerized atomic absorption technique (GBC, 932 AA). Fecal examination was carried-out 4 weeks after treatment. The results were subjected to anova and expressed as mean ± se to differentiate between the two control groups in the two systems, also to differentiate between

pre and post-treatment values within groups and the healthy control animals of each group using software program (Prism, 1996).

RESULTS

Mean values of investigated parameters are illustrated in Table 1 and Figure 1. Metabolic and cellular profiles (in both control groups) were affected by the dietary factor. Conventional fed animals showed lower values in RBC, Hb, PCV, total protein, albumin, glucose, Fe, Cu and Zn if compared by the indoor-fed healthy group. MCV, MCH leukocytic picture, bilirubin, AST and ALT were not affected by the dietary regime.

On the other hand, the results showed that the dietary system did not affect the metabolic and cellular changes that caused by fascioliasis. Both the two infested groups showed nearly the same variations in the hematological and biochemical parameters if compared by the corresponding control animals in each group except serum glucose and Fe levels. The last two parameters showed non-significant changes under the effect of facioliasis in indoor-fed animals, while they reduced significantly in grazing group.

Four weeks after treatment by Fasinex, the clinical signs of fascioliasis disappeared, the animals restored their normal vitality and fecal examination was negative for Fasciola hepatica eggs. In addition, hematological and biochemical values in both treated groups were not significantly differing than those in the corresponding control groups.

DISCUSSION

The blood cellular and metabolic profiles are widely used to identify herd problems and dietary causes of low production in addition to disease diagnosis (Lee et al., 1978). It had been established that the concentrate mixture and Barseem (*Medicago sativa*) are rich in crude proteins, crude fat and nitrogen free extract, while the miscellaneous grasses, pasture residues, straw and chaffs are extremely fibrous and of low nutritive value (McDonald et al., 1982 and Payne, 1990). Under conventional system, the hematological and biochemical values of healthy animals were lower than the corresponding group reared indoors, and lies in the lower normal ranges cited by Schalm et al. (1979) and Coles (1986). In fact, there is unanimity of view regarding the effect of type of nutrition on blood parameters (Jain, 1993 and Kaneko et. al., 1997).

Blood abnormalities are a common complication of liver disease and depend on the nature of hepatic dysfunction (Spivak, 2000). Anemia is one of the hallmarks of ovine fascioliasis (Urquhart et al., 1996). Our results showed that the dietary factor had no effect on the progressing of anemia during ovine fascioliasis. Both diseased groups showed reduction in RBC, PCV and Hb if compared with healthy animals. The MCV and MCH values revealed normocytic normochromic anemia in both affected groups. These results differ than the hypochromic anemia obtained by Shalaby et al. (1990) but coincide with those reported by Ogunrinade (1984) and Nwiyi and Chaudrai(1996). In the opinion of Sinclar (1964 & 1965), dishaemopoiesis and reticulo-endothelial function disorders were the major aetiological factors of anemia in fascioliasis because of decreased erythrocyte production and increased erythrocyte destruction. Holmes et al. (1968) attributed such condition to the feeding habit of the flukes or the haemolysis factor produced by the parasite. On the other hand, Berry and Dargie (1978) and Karram, et al. (1988) noticed that anemia in fascioliasis may be hemorrhagic in origin through out direct loss of whole blood either by ingestion or by physical damage of the liver during fluke penetration. Urquhart et al. (1996) reported that more than 0.5-ml blood per fluke could be lost into the bile ducts each day. In addition, it had been reported that erythropoietic dysfunction may be incriminated in similar disorders (Spivak 2000).
Leukocytosis accompanied by lymphocytosis and eosinophilia are common features of fascioliasis (Sykes et al., 1980 and Urquhart et al., 1996). These changes were evident in both groups as a reaction of the host against the heavily invading parasite (Jain, 1993).

In despite of the extensive studies on the pathogenesis of fascioliasis, trace elements had received a little attention. The present work showed that the nutritional factor affects the behavior of Fe during Fasciola hepatica infestation but not affect Cu and Zn. The reduction of Fe in the first group is similar to those early reported by Sinclar (1965). The author interpreted his results by the probability of simple loss of iron, disturbances in Fe metabolism or the storage Fe was inadequate to maintain the metabolic needs, which may accepted with the low plane of nutrition in the present work. Fascioliasis had no effect on serum copper in the present work. Our results in this respect agree with Gadzhiev and Garaev (1986). The authors reported that fascioliasis stimulates ceruloplasmin synthesis in the liver without changes in serum copper level. The reduction of zinc in both infested groups is directly related to the reduction of albumin. Circulating zinc is bound to albumin, therefor,

zinc concentration will be reduced when albumin concentration decreased (Galloway et al., 2000).

In the present study, serum total protein, and albumin levels were reduced in both infested groups. Many authors (Urquhart et al., 1996 and Waweru et al., 1999) previously accepted these results. It seems that the dietary factor has no role, and this reduction reflects the impairment of the liver synthesis function. Schalm et al. (1979), Karram et al. (1988) and Kaneko (1997) suggested that the liver damage during the migratory phase of the parasite interfere with albumin synthesis. The authors added that albumin may be lost with the inflammatory exudate of the damaged liver. Our obtained data are in agreement with the previous suggestions.

As in trace elements, the work on glucose behavior during fascioliasis is very rare. In despite, Roshdy (1977) noticed hypoglycemia during ovine fascioliasis under Egyptian condition. On the other hand, Rowlands and Clampitt (1979) failed to obtain hypoglycemia in Fasciola hepatica infested sheep under laboratory conditions. Our results suggest that this difference may be related to dietetic factors. The type of diet had a significant effect on glucose behavior during fascioliasis in the current work. Glucose level was reduced in conventional fed sheep while it did not affected in condensed fed group if compared by control animals for each group. Lenton et al. (1996) noticed reduction in glycogen content, cytochrome P_{450} and mitochondrial respiration of the Fasciola hepatica infested liver in sheep. Since ruminants are highly dependent on gluconeogenesis or glycogen stores for the maintenance of blood glucose, the reduction of serum glucose in this work is due to the low-grade nutrient intake.

Recorded results in this work revealed absence of the dietary effect on the behavior of aminotransferases and bilirubin during Fasciola hepatica infection. It seems that the changes in these indices are directly related to the hepatic damage and biliary obstruction. Our obtained data concerning higher serum aminotransferases and bilirubin are in agreement with those previously reported by Coles (1986), Urquhart et al. (1996), Tenant (1997) and Waweru et al. (1999). These authors reported necrotic degeneration of the liver, periductal fibrosis and blockage of the bile ducts during fluke migration. They added that higher serum aminotransferases level used as index of liver damage caused by fascioliasis.

Four weeks after treatment by Fasinex, both the infested groups showed absence of Fasciola hepatica eggs in feces, disappearance of clinical signs, and absence of significant variations in the hematological

and biochemical indices between the both infested groups and the corresponding controls. Ferre et al. (1997) obtained a significant interaction between diet and disposition of oral benzimidazole anthelmintics such as triclabendazole and suggested that changes in ruminal pH caused by diet changes could modify the fate of these drugs with possible consequences on their therapeutic effectiveness. However, our results clinically support the fact that triclabendazole at the commercially recommended dose is 100% effective against adult Fasciola hepatica (Turner et al., 1984, Boray, 1997a and Fairweather and Boray, 1999) in both conventional and condensed fed groups.

Finally, it seems that feeding system has a non-neglected effect on the pathogenesis of fascioliasis specially Fe and glucose metabolism. In addition, it proved that Fasinex at the commercially recommended dose is highly effective against adult Fasciola hepatica irrespective of feeding system.

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Table 1: Blood picture and metabolic profile (value ± SE, N=10) in Fasciola hepatica infested sheep under two planes of nutrition pre and post-treatment by Fasinex.

		CONVENTIONAL FED GROUP			CONDENSED FED GROUP		
Parameter	Unit	Pre-treat	Post-treat	Control	Pre-treat	Post-treat	Control
RBC	10^6/µl	04.4±0.16^a	07.8±0.21^b	08.1±0.23^b	06.3±0.17^c	09.9±0.25^{bd}	11.3±0.51^d
PCV	%	17.3±1.11^a	30.7±0.98^b	32.9±0.89^b	25.1±1.08^c	37.8±0.96^d	41.9±0.63^d
HB	g/dl	04.8±0.47^a	09.1±0.54^b	09.6±0.53^b	07.1±0.39^c	11.1±0.43^e	12.4±0.54^d
MCV	fl	39.3±0.91^a	39.3±1.21^a	40.6±0.98^a	39.8±.1.1^a	38.2±01.3^a	37.1±01.6^a
MCH	pg	10.9±0.41^a	11.6±0.69^a	11.8±0.56^a	11.3±0.51^a	11.2±0.37^a	10.8±0.61^a
WBC	10^3/µl	08.9±0.31^a	07.4±0.42^b	07.2±0.37^b	09.4±0.51^a	07.5±0.46^b	06.9±0.51^b
Lymphoc.	10^3/µl	06.1±0.29^a	05.1±0.31^b	04.8±0.37^b	06.6±0.32^a	04.9±0.41^b	4.52±0.39^b
Neutroph.	10^3/µl	01.7±0.16^a	01.8±0.09^a	01.9±0.14^a	02.1±0.16^a	02.1±0.21^a	01.9±0.23^a
Monocyt.	10^3/µl	0.23±0.08^a	0.20±0.04^a	0.21±0.04^a	0.19±0.04^a	0.23±0.05^a	0.21±0.04^a
Esinophil	10^3/µl	0.87±0.09^a	0.29±0.04^b	0.26±0.07^b	0.48±0.05^c	0.29±0.06^b	0.27±0.05^b
T. protein	g/dl	5.24±0.31^a	7.22±0.27^b	7.18±0.39^b	6.62±0.31^b	8.27±0.31^c	8.49±0.29^c
Albumin	g/dl	2.18±0.17^a	3.61±0.38^b	3.76±0.29^b	2.49±0.21^a	4.51±0.37^{bc}	4.61±0.31^c
Glucose	mg/dl	37.1±01.2^a	49.7±0.99^b	51.8±01.6^b	61.8±01.8^c	59.6±01.1^c	63.1±01.7^c
T.bilirubin	mg/dl	0.52±0.05^a	0.31±0.04^b	0.25±0.02^b	0.49±0.03^a	0.26±0.03^b	0.27±0.04^b
AST	iu/l	112.6±8.5^a	61.8±05.4^b	52.1±7.23^b	97.4±05.9^a	54.3±04.1^b	49.9±05.8^b
ALT	iu/l	98.5±6.25^a	53.2±06.1^b	41.2±4.99^b	94.1±07.5^a	49.8±5.17^b	43.7±06.3^b
Iron	g/dl	89.7±06.4^a	116.1±6.1^b	121.2±7.1^b	139.9±9.1^{bc}	147.2±8.8^c	151.8±8.4^c
Copper	g/dl	89.1±05.8^a	91.3±04.2^a	086.8±5.3^a	111.2±6.2^b	106.8±3.9^b	109.1±5.1^b
Zinc	g/dl	51.3±03.6^a	68.7±05.2^b	071.3±3.9^b	072.2±3.9^b	096.7±4.1^c	091.8±4.8^c

Values in the same row with unlike superscripts are significantly differing at P<0.05

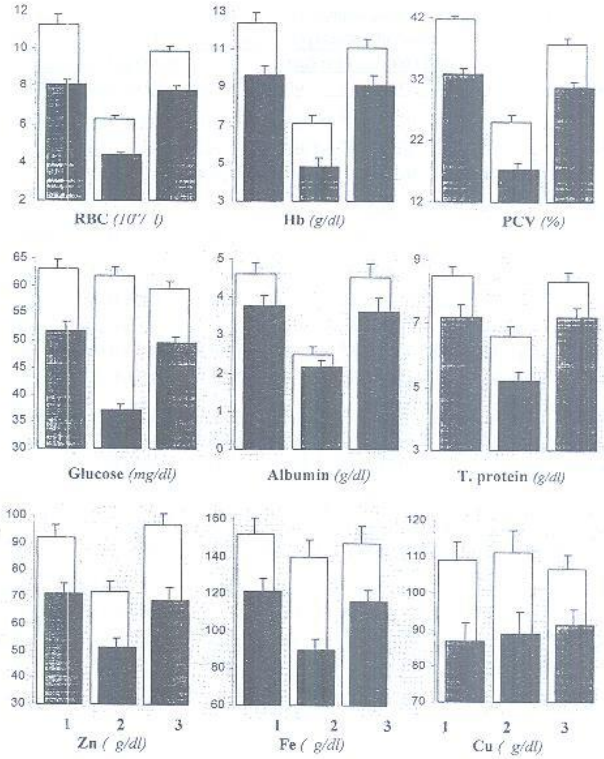

Fig (1): The effect of conventional (dark bars) and condensed (white bars) feeding on the metabolic profile in healthy sheep (**1**) and infested sheep with fasciola pre (**2**) and post-treatment (**3**) by Fasinex.