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SOME STUDIES ON THE ANTIPARASITIC DRUGS, MOXIDECTIN AND DORAMECTIN IN CATTLE INFESTED WITH SOME PARASITES

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SUMMARY

Fifty cow heiffers (Balady), 1-2 years age, at Sarnga, Dakahlia Governorate were examined for infestation with ecto and endoparasites and classified into three groups. Group I infested with ectoparasites, group II infested with endoparasites and group III those free from any infestation. Parasitized animals were treated with a single subcutaneous dose of moxidectin or doramectin at dose level of 200 ug/kg. B. Wt. Parasitological examinations using a hand lens and microscopically were performed every five days for five weeks post-treatment with moxidectin or doramectin. The study revealed that both drugs were highly effective (more than 90 %) on the 5th day post-treatment against *Oesphagostomum radiatum, Haemonchus sp* and *Strongyloide papillosus*, whereas, the effectiveness against *Nematodirus sp.* and *Trichuris sp.* were less than 90 %. Moxidectin was more effective than doramectin in reduction of egg counts of most tested endoparasites. Administration of moxidectin or doramectin resulted in an elimination of most sucking lice and mites from animal body on 5th day post-treatment. Haematological and biochemical parameters in infested animals were improved after treatment with both drugs.

INTRODUCTION

Infestation of cattle with internal and external parasites are a common problem leading to economic losses due to productivity reduction of infested animals. The introduction of avermectins for veterinary use represented a

major advance in the treatment and prophylaxis of many parasitic diseases (Campbell, 1985), However resistant strains may be developed as a consequence to continuous use of a certain antiparasitic drug (Waller, 1986 and Barton and Mc Lausland, 1987). Hence, the use of an alternative antiparasitic drug to keep the parasite population under control is recommended (Uriate et al., 1994). Recently, moxidectin and doramectin have been introduced as new members of avermectins family. These products are macrocyclic lactones derived from *Streptomyces spp.* With broad spectrum of antiparasitic activity (William et al., 1992; Yazwinski et al., 1994 and Selim, 1997).

Moxidectin has been shown to be active against *Hypoderma lineatum, Chorioptes bovis, Sarcoptes scabiei* and several species of cattle nematodes (Scholl et al., 1992; William et al., 1992 and Losson and Lonneux, 1993). On the other hand, several studies referred to efficacy of doramectin against cattle gastro-intestinal nematodes, however, a little is known about its effect on ectoparasites (Jones et al., 1993; Vercraysse et al., 1993 and Yazwinski et al., 1994). The present work was carried out to compare efficacy of moxidectin and doramectin against prevalent parasites in naturally infested cattle. Moreover, the study aims to assess safety of both drugs by studying the haematological and biochemical alterations in blood of treated cattle.

MATERIAL AND METHODS

Drugs:

1- Doramectin (Dectomax ®, Pfizer, Egypt)

2- Moxidectin (Cydectin ®, cynamid, U. S. A).

Animals & grouping

Fifty cow heiffers (Balady), 1-2 years age at Sarnga, Dakahlia Governorate were examined for ecto and endoparasites and classified into 3 main groups. Group I, animals infested with ectoparasites, group II, animals infested with endoparasites each of these two groups are consisted of 20 cow heiffers and group III, 10 animals were free from both ecto and endoparasites this group was kept as control. The animals were divided after skin and faecal examination. Those of group I were selected on the basis of confirmed active infestation of lice, mites or ticks. Identification of lice and ticks species was done by hand lens. Skin scrapings were collected from periphery of mite lesions, taking about 10% of the total area of any lesion at any sampling time and examined according to Lonneux and Losson, (1992). Samples were counted and examined microscopically according to Solusby, (1982), Faecal samples were collected individually from the rectum or immediately after defaecation in clean plastic containers, examined macroscopically for any gross parasites and microscopically for nematodes eggs using the concentration floatation technique, denoting the infested group

(Group II) and the non infested group (Group III). Degree of infestation has been determined by egg counting using the modified Mc. Master technique and faecal culture with larval differentiation was conducted (Solusby, 1982).

Treatment

Each infested group was divided into three subrgoups. Subgroup I was taken as positive control, 10 cow heiffers injected subcutaneously with saline.

Subgroups 2 and 3, each consists of 5 cow heiffers were injected subcutaneously with moxidectin and doramectin respectively at a dose level of 200 ug/kg. B. wt., while group III, 10 animals was used as a negative control (non infested, non treated).

Examination and Sampling

Skin and faecal examination were done before and every five days for five weeks after treatment. Heparinized blood and serum were collected from every animal for haematological and biochemical studies at 7^{th} and 14^{th} days after treatment..

Haematological Studies

Total erythrocytic count (RBCs), haemoglobin percent (Hb%), packed cell volume percent (PCV %), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH, mean corpuscular haemoglobin concentration (MCHC), total leucocytic count (TLC) and differential leucocytic count were estimated according to Coles, (1986).

Biochemical Studies

Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined according to Reitman and Frankel (1957). Serum total proteins (T. P.) and albumin after Doumas (1975) and Doumas et al., (1971) respectively. Globulins were calculated. Serum urea (Fawcett and Scott, 1960), creatinine (Husdan and Rapoport, 1968), calcium (Ca) (Gindler and King, (1972), inorganic phosphorus (Pi) (El-Merzabani et al., 1977) and magnesium (Mg) (Bohuon, 1962) were also estimated.

Statistical analysis was carried out using student "t" test and Chi square as described by Snedecor and Cochran (1980).

RESULTS

Moxidectin application resulted in an elimination of most sucking lice and mites from animal body on 5^{th} day post-treatment, whereas, on 10^{th} day it compeletely disappeared (table 1).

In animals treated with doramectin, most of sucking lice were eliminated on 5^{th} day post-treatment and on 10^{th} day it completely disappeared (Table, 2) Large poroportion of mites were died within five days post-treatment

Table (1): Efficacy of moxidectin at therapeutic dose level (one subcutaneous dose, 200 ug/kg. B.Wt.) against ectoparasites in infested cow heiffers.

Ectoparasites	Number of parasites after treatment						
	0 day	5 days	Reduction %	10 days	Reduction %	15-35 days	Reduction %
A- Sucking Lice							
1- *Haematopinus eurysternus*	10-10	1-4	90	0	100	0	100
2- *Linognathus vituli*	15-30	2-5	88.3	0	100	0	100
B- Mite							
1- *Sarcoptic scabiei var bovis*	10-19	2-4	79.5	0	100	0	100
2- *Psoroptes communis var bovis*	5-15	2-3	70	0	100	0	100
C- Ticks							
Boophilus microplus	10-10	2-3	68.3	2	73	0	100

Table (2): Efficacy of doramectin at therapeutic dose level (one subcutaneous dose, 200 ug/kg. B.Wt.) against ectoparasites in infested cow heiffers.

Ectoparasites / Day of treatment	Number of parasites after treatment						
	0 day	5 days	Reduction %	10 days	Reduction %	15-35 days	Reduction %
A- Sucking Lice							
1- *Haematopinus eurysternus*	15-39	6-16	59-5	0	100	0	100
2- *Linognathus vituli*	13-30	6-17	48.6	0	100	0	100
B- Mite							
1- *Sarcoptic scabiei var bovis*	8-19	2-6	71.7	1	94.7	0	100
2- *Psoroptes communis var bovis*	9-17	3-5	68.6	1	94.1	0	100
C- Ticks							
Boophilus microplus	7-9	2-4	63.5	2-3	62.5	1	88.9

Table (3): Efficacy of moxidectin at therapeutic dose level (one subcutaneous dose, 200 ug/kg. B.Wt.) on reduction of faecal egg count of nematodes in infested cow heiffers.

Nematodes species / Day of treatment	Egg per gram of faeces (EPG)						
	0 day	5 days	Reduction %	10 days	Reduction %	15-35 days	Reduction %
Trichostrongylus oxei	500-2500	20-165	95	10-117	96.5	4-40	99.2
Oesphagostomum radiatum	600-3500	38-320	92.3	27-163	95.5	9-54	98.5
Haemonchus sp.	320-2100	20-188	93.4	10-94	96.2	5-37	98.4
Strongyloide papillosus	400-3600	50-450	86.5	37-462	88.9	16-93	93.5
Nematodirus sp.	200-1900	34-324	83.1	31-296	84.5	23-219	88.5
Trichuris sp.	400-2200	81-438	79.9	75-405	81.4	50-270	86.6

Table (4): Efficacy of doramectin at therapeutic dose level (one subcutaneous dose, 200 ug/kg. B.Wt.) on reduction of faecal egg counts of nematodes in infested cow heiffers.

Nematodes species / Day of treatment	Egg per gram of faeces (EPG)						
	0 day	5 days	Reduction %	10 days	Reduction %	15-35 days	Reduction %
Trichostrongylus oxei	250-3500	58-816	76.8	27-139	88.4	9-146	96.2
Oesphagostomum radiatum	400-3200	37-300	89.7	25-200	93.8	18-150	95.5
Haemonchus sp.	600-1800	75-225	86.5	55-168	89.8	18-56	96.6
Strongyloide papillosus	220-2100	30-590	79.6	21-490	83.6	18-425	85.5
Nematodirus sp.	300-1600	64-350	76.1	55-300	81.5	16-250	84.5
Trichuris sp.	200-2400	46-562	76.8	40-468	80.2	30-355	85.1

Table (5): Efficacy of moxidectin and doramectin on haemogram pattern in cow heiffers infested with ectoparasites at 7th and 14th days post-treatment with the therapeutic dose (one subcutaneous dose 200 ug/kg B. Wt.).

Parameter / Group	Days after treatment	RBCs 10^6/ul	PCV %	Hb gm%	MCV FL	MCH pg	MCHC %	TLC 10^3/ul	Absol. Dif. Count 10^3 / ul				
									N	L	E	B	M
Positive control (Infested non treated) N = 10	0	6.95±0.20	34.68±2.06	8.95±0.27	49.91±3.12	12.73±0.41	25.52±1.93	7.18±0.39	2.69±0.17	3.40±0.23	0.58±0.05	0.04±0.002	0.79±0.05
Negative control (non infested. non treated) N = 10	0	7.59±0.90*	38.02±1.84*	10.48±0.28**	51.80±2.88	14.23±0.98	27.62±2.66	5.37±0.49*	2.23±0.19*	2.43±0.15*	0.27±0.02***	0.03±0.004	0.41±0.05
Infested. treated with moxidectin (N = 5)	7	7.40±0.11	34.91±1.83	10.30±0.30**	47.18±1.85	13.91±0.31	29.50±1.91	6.29±0.32*	2.46±0.10	3.00±0.25	0.37±0.03*	0.03±0.002	0.32±0.04***
	14	7.92±0.19**	36.30±2.69	11.06±0.43***	44.61±2.93	14.48±0.57	30.46±3.04	5.73±0.41**	2.23±0.09*	2.75±0.18*	0.23±0.01***	0.03±0.003*	0.31±0.06
Infested. treated with Doramectin (N = 5)	7	7.10±0.19	34.75±1.90	9.91±0.24***	48.94±1.45	13.96±0.48	28.51±1.84	6.51±0.29	2.54±0.20	3.15±0.23	0.29±0.02***	0.04±0.004	0.4±0.03***
	14	7.52±0.14*	35.00±2.00	10.63±0.36***	46.54±1.60	14.14±0.32	30.37±1.43	5.93±0.37*	2.30±0.18	2.90±0.19	0.25±0.03***	0.03±0.003*	0.34±0.03***

*P < 0.05 **P < 0.01 ***P < 0.001

Table (6): Effect of moxidectin and doramectin on some liver and kidneys function tests and levels of some minerals in cow heiffers infested with ectoparasites at 7th days post-treatment with the therapeutic dose (one subcutaneous dose. 200 ug/kg. B. Wt.).

Parameter / Group	Days after treatment	Serum Enzymes (u/ml)		Serum Proteins (gm/dl)			Urea (Mg/dl)	Creatnine (Mg/dl)	Ca (Mg/dl)	Pi (Mg/dl)	Mg (Mg/dl)
		AST	ALT	T.P.	Alb	Glob.					
Positive control (Infested non treated) N = 10	0	19.61±1.02	32.10±1.41	6.32±0.15	3.41±0.11	2.91±0.13	23.12±2.15	0.39±0.15	10.6±1.0	5.49±0.58	3.01±0.29
Negative control (non infested. non treated) N = 10	0	16.80±0.97	29.20±1.62	6.72±0.19	3.69±0.18	3.03±0.24	22.6±2.11	0.38±0.08	12.10±1.19	6.42±0.16	3.15±0.35
Infested. treated with moxidectin (N = 5)	7	18.91±0.96	30.90±1.79	6.59±0.19	3.56±0.09	3.03±0.15	22.50±2.09	0.38±0.09	10.90±1.09	5.6±0.41	3.02±0.16
	14	16.45±1.32*	29.10±2.30	6.71±0.13*	3.64±0.13	3.07±0.12	21.90±2.18	0.39±0.03	11.10±11.06	6.20±0.50	3.15±0.26
Infested. treated with Doramectin (N = 5)	7	19.01±2.0	30.80±1.96	6.20±0.20	3.34±0.12	2.86±0.10	22.86±1.89	0.39±0.01	10.30±0.99	5.83±0.35	3.04±0.12
	14	16.89±1.06*	29.90±2.46	6.61±0.15	3.60±0.16	3.01±0.19	22.01±2.23	0.38±0.06	10.86±0.86	6.00±0.37	3.20±0.21

*P < 0.05 **P < 0.01 ***P < 0.001

Table (7): Effects of moxidectin and doramectin on haemogram pattern in cow heiffers infested with endoparasites at 7th and 14th days post-treatment with the therapeutic dose (one subcutaneous dose. 200 ug/Kg. B.Wt).

Parameter / Group	Days after treatment	RBCs 10^6/ul	PCV %	Hb gm%	MCV FL	MCH pg	MCHC %	TLC 10^3/ul	Absol. Dif. Count 10^3 / ul			
									N	L	E	B
Positive control (Infested non treated) N = 10	0	6.62±0.25	35.78±1.25	8.35±0.33	54.04±1.94	12.56±0.48	23.33±1.85	6.79±0.45	2.72±0.18	2.81±0.17	0.63±0.03	0.03±0.001
Negative control (non infested, non treated) N = 10	0	7.59±0.19**	38.02±1.84*	10.48±0.28***	51.8±2.88	14.23±0.98	27.62±2.66	5.37±0.49*	2.23±0.19	2.43±0.15	0.27±0.02***	0.03±0.004
Infested, treated with moxidectin (N = 5)	7	7.36±0.3*	37.18±1.66	10.00±0.12***	50.51±2.16	13.59±0.54	26.90±1.21	6.21±0.21	2.61±0.09	2.76±0.18	0.48±0.01***	0.03±0.002
	14	7.98±0.4**	38.73±2.23*	11.04±0.32***	48.53±2.56	13.86±0.99	28.51±2.66	5.89±0.21*	2.50±0.16	2.73±0.15	0.33±0.02***	0.02±0.001
Infested, treated with Doramectin (N = 5)	7	7.10±0.08	36.93±2.22	9.38±0.46*	52.03±1.86	13.23±0.35	25.54±1.23	6.58±0.36	2.79±0.21	3.2±0.19	0.39±0.04***	0.04±0.002**
	14	7.64±0.22**	37.79±1.59	10.6±0.36***	49.46±2.57	13.87±0.69	28.05±2.92	5.97±0.19*	2.41±0.15	2.92±0.22	0.28±0.02***	0.02±0.001***

*P < 0.05 **P < 0.01 ***P < 0.001

Table (8). Effects of moxidectin and doramectin on some liver and kidneys function tests and levels of some minerals in cow heifers infested with endoparasites at 7th and 14th days post treatment with the therapeutic dose (one subcutaneous dose, 200 ug/Kg. B. Wt).

Parameter / Group	Days after treatment	Serum Enzymes (u/ml)		Serum Proteins (gm/dl)			Urea (Mg/dl)	Creatinine (Mg/dl)	Ca (Mg/dl)	P (Mg/dl)	Mg (Mg/dl)
		AST	ALT	T.P.	Alb	Glob.					
Positive control (Infested non treated) N = 10	0	24.45±1.41	41.71±2.21	6.35±0.21	3.05±0.12	3.31±0.18	22.85±2.76	0.37±0.03	10.30±2.37	6.00±0.39	2.4±0.4
Negative control (non infested, non treated) N = 10	0	16.80±0.97***	29.20±1.62*	6.27±0.19	3.69±0.18	3.03±0.24	22.6±2.11	0.38±0.08	12.10±1.19	6.42±0.61	3.15±0.35
Infested, treated with moxidectin (N = 5)	7	18.4±0.96**	40.50±2.64	6.38±0.29	3.27±0.22	3.11±0.16	21.46±2.15	0.32±0.03	11.45±1.33	6.3±0.12	3.37±0.28
	14	15.7±0.18***	37.00±1.42*	6.87±0.13*	3.75±0.16**	3.12±0.12	21.91±2.31	0.34±0.02	12.31±2.39	7.04±0.36*	3.79±0.36*
Infested, treated with Doramectin (N = 5)	7	18.32±1.41**	42.50±3.97	6.53±0.09	3.15±0.07	3.38±0.18	24.31±2.39	0.35±0.01	12.19±1.21	6.4±0.32	3.01±0.15
	14	16.20±0.86***	35.00±2.28*	6.67±0.11	3.62±0.12**	3.04±0.16	22.62±2.42	0.38±0.01	11.38±2.45	6.9±0.27*	3.45±0.39*

*P < 0.05 **P < 0.01 ***P < 0.001

and no live mites or ticks were detected after 15 days of treatment with doramectin (Table, 2). Moxidectin and doramectin showed no effect on larvae of ticks.

The study revealed that *Trichostrongylus axie, Oephagostomum radiatum, Haemonchus* sp., *Strongyloide papillosus, Nematodirus sp.* and *Trichuris sP.* were the main endoparasites in infested animals. The results showed that moxidectin and doramectin were highly effective against most gastrointestinal nematodes in treated animals. A significant reduction in nematode egg counts was proved (Table, 3 and 4). On 10th day post-treatment, moxidectin achieved a higher efficacy percent against most nematodes than doramectin in treated animals. (Table, 3 and 4).

Effects of moxidectin and doramectin on some haematological and biochemical parameters of treated cow heiffers were illustrated in tables 5, 6, 7 and 8.

DISCUSSION

The present study revealed that *Trichostrongylus axaei, Oesphagostomum radiatum, Haemonchus contortus, Strongyloide papillosus, Nematodirus sp. and Trichuris sp.* were the most common endoparasites in cattle at Sarnga, Dakahlia Governorate. In addition, *Haematopinus eursternus, Linognathus vituli, Sarcoptic scabiei var bovis, Psorptes communis and Boophilus microplus* were common prevalent ectoparasites. The study confirmed a major advantage of moxidectin and doramectin as being effective agents against most endoparasites and

ectoparasites by a single dose. The study revealed that both drugs were highly effective (more than 90%) on the 5th day post-treatment against *Oesphagostomum radiatum*, *Haemonchus sp.* and *Strongyloide papillosus*, however, the effectiveness against *Nematodirus sp.* and *Trichuris sp.* were less than 90%. The same findings were achieved by Bassano et al., (1995), Selim (1997) and Balmer et al., (1998). The results showed a good therapeutic efficacy of moxidectin and doramectin against many species of cattle endoparasites and ectoparasites. Moreover, Jones et al., (1993) reported that doramectin was at least 99.6 % effective in eliminating the immature and adult stages of 14 species of nematodes. In addition, Yazwinski et al., (1994) reported that doramectin was less effective against *Nematodirus helvetianus* and *Trichuris ovis*, a result that coincides with the present findings.

A reduction in nematode egg counts was exceded 90% in the present data even on the 35th day post-treatment with moxidectin or doramectin indicating a residual effect of both drugs. Similar results were obtained by Vercruysse et al., (1993) and Whang et al., (1994). The extended protection evoked by administration of macrocyclic lactones is consistent with the extended half-life of these products in the plasma. For example, moxidectin and the related metabolites in serum of cattle had a half-life of 3 days (Goudie et al., 1993 and Zulalian et al. 1994). The mechanism of action of the macrocyclic lactones, which include moxidectin, nemadectin, ivermectin, doramectin and milbemycin, involves receptors of gated Cl- channels (Conder et al., 1993).

The obtainted data showed that moxidectin was more effective in reduction of various species of ectoparaites. The slight variation in efficacy of both drugs could be attributed to development of a degree of resistance toward doramectin as it is a new drug recently used in Egypt in comparison to moxidectin. This view was partly supported by report of Conder et al. (1993). The author demonstrated that moxidectin was more potent than a macrocylic lactone (ivermectin) against *Haemonchus contortus* in sheep.

On the other hand, both tested drugs alleviated the normocytic normochromic anaemia produced by endo or ectoparasites where red blood cells count and haemoglobin percent in treated animals were improved. The forementioned effect was more pronounced in moxidectin than doramectin-treated cattle. In addition, the increased total leucocytic count due to eosinophilia and monocytosis in infested animals was returned to its normal level at the 14th day in endoparasites and ectoparasites infested cattle after moxidectin or doramectin administration. The same findings were achieved by Selim, (197) who reported an improvement in the level of red cell counts, PCV%, Hb concentration and

total leucocytic counts in gastrointestinal parasitized buffalo-calves towards the normal level after treatment with doramectin or moxidectin. It must be mentioned that reduction in TRBCs count, Hb concentration, and elevation of total leucocytic, monocytic and eosinophilic counts in animals infested with ecto or endoparasites were reported by Harness et al., (1971), Coles, (1986), Williams (1983) and Lowenstein et al., (1996). They attributed this effect to the excreted toxins & histamines and inability of the gut in parasitized animals to assimilate and absorb haemopoietic principal and nutrients in addition to the nuxious effect of the ectoparasites on the animal rather than the blood sucking. Accordingly, effectiveness of moxidectin and doramectin in elimination of ecto and endoparasites in the present study resulted in normalization of blood picture in treated animals.

Keeping with these lines, an improvement towards the normal in the level of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT, total proteins, albumin, phosphorous and magnesium in parasitized animals after treatment with moxidectin or doramectin was observed. These results confirmed the data obtained by Selim, (1997), who demonstrated an improvement in blood and serum parameters towards the normal level in buffalo calves infested with gastrointestinal nematodes and treated with moxidectin or doramectin.

In conculsion, moxidectin or doramectin in a single subcutanous dose was highly effective antiparasitic with a broad spectrum of activity against internal and external parasites of cattle. On the other hand, both drugs did not cause deleterious effects on biochemical and haematological parameters of treated cattle.

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