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Short Communication

THE EFFICACY OF CLOSANTEL AND RAFOXANIDE AGAINST FENBENDAZOLE- AND LEVAMISOLE-RESISTANT *HAEMONCHUS CONTORTUS* IN SMALL RUMINANTS

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Abbreviations: BZ, benzimidazole; CLO, closantel; epg, eggs per gram of faeces; FBZ, fenbendazole; FECR, faecal egg count reduction; L_3, third-stage infective larvae; LEV, levamisole; RAF, rafoxanide

INTRODUCTION

Nematode infections are ubiquitous in sheep and goats and cause heavy economic losses in meat and wool production (Gordon, 1974). Young lambs and kids are very susceptible to these infections. *Haemonchus contortus*, the most common gastrointestinal nematode in small ruminants in Kenya (Allonby and Urquhart, 1975), is responsible for most production losses in these animals (Preston and Allonby, 1979). The control of this parasite has been based on the use of conventional anthelmintics (benzimidazoles and levamisole). However, there have been increasing reports from all parts of the world of the occurrence of anthelmintic resistance in trichostrongyle nematodes in small ruminants (Prichard, 1994). Resistance has been described to all groups of anthelmintics including the latest broad-spectrum anthelmintic, ivermectin (Van Wyk and Malan, 1988; Miller and Barras, 1994).

Recent reports of strains of *H. contortus* in small ruminants in Kenya which are resistant to broad-spectrum anthelmintics (Njanja *et al.*, 1987; Waruiru, 1994; Mwamachi *et al.*, 1995; Wanyangu *et al.*, 1996) suggest that there is a need to use an alternative class of anthelmintics with a different mode of action.

Salicylanilides, such as closantel (CLO) and rafoxanide (RAF) have a narrow spectrum of activity against blood-sucking nematodes. CLO has been reported to be very effective against benzimidazole (BZ)-resistant *H. contortus* in sheep in Australia (Hall *et al.*, 1981) and Zimbabwe (Vassilev, 1995) and in goats in Malaysia (Dorny *et al.*, 1994). RAF has been shown to be effective against adult BZ-resistant *H. contortus* (Campbell and Hotson, 1971) but, although it is effective against normally developing

fourth-stage larvae at 8 days after infection (Egerton *et al.*, 1970), it is ineffective against inhibited non-BZ-resistant *H. contortus* (Le Jambre and Barger, 1979). CLO and RAF were highly effective against levamisole (LEV)-resistant *H. contortus* in sheep in India (Yadav and Kumar, 1994). The high efficacies of CLO and RAF were attributed to the long half-lives of the drugs in plasma (Maes *et al.*, 1988) and the consequently prolonged activity against blood-feeding parasites.

Resistance by *H. contortus* to CLO has been reported in South Africa (Van Wyk and Malan, 1988) and on a farm used extensively for small ruminant research in Kenya (Mwamachi *et al.*, 1995). Field strains of *H. contortus* showing resistance to RAF have also been reported in South Africa (Van Wyk and Malan, 1988).

The aim of this study was to evaluate the efficacy of CLO and RAF as alternative anthelmintics to control BZ- and LEV-resistant *H. contortus* in sheep and goats, respectively.

MATERIALS AND METHODS

The experimental animals were 24 sheep and 24 indigenous goats of mixed breeds and sexes, aged between 9 and 12 months. The animals were parasitologically negative on faecal examination before the start of the experiment. They were maintained indoors on standard feed and water was provided *ad libitum*.

Each sheep was infected with 5000 third-stage larvae (L_3) of a strain of *H. contortus* resistant to fenbendazole (FBZ) (Waruiru, 1994), while the goats received the same number of larvae suspected to be resistant to levamisole. Twenty-one days later, the numbers of strongyle-type eggs per gram of faeces in each animal were counted by a modified McMaster technique (MAFF, 1986). On the same day, the sheep and goats were both randomly divided into four groups of 6 and were dosed orally. The sheep in group I were treated with fenbendazole (Panacur, Hoechst, Munich, Germany; 5 mg/kg body weight); those in group II were treated with closantel (Flukiver, Janssen Pharmaceutica, Beerse, Belgium; 5 mg/kg body weight); and those in group III received rafoxanide (Ranide, MSD Agvet, Rahway, NJ, USA; 7.5 mg/kg body weight). The goats in group I received levamisole (Wormicid, Cosmos, Kenya; 15 mg/kg body weight), while those in group II and III were treated with CLO and RAF at the same dose rates as the sheep, as the manufacturers in Kenya do not specify dose rates for goats. In each case, the animals in group IV served as untreated controls.

All the animals were slaughtered on day 31 after infection, 10 days after treatment. At slaughter, in addition to faecal egg counts, the abomasum was removed and the worms were recovered from the contents and a mucosal digest (1% pepsin solution containing 2% concentrated HCl at 37°C for 4–6 h). The numbers of *H. contortus* were counted in four aliquots representing 4% of the total volume (MAFF, 1986). The faecal egg counts for each animal were transformed according to the expression $y = \log_{10}(\text{count}+20)$ to calculate geometric means. The faecal egg count reduction (FECR) percentage was calculated according to Presidente (1985). The efficacies of the drugs were determined on the basis of the FECR and worm count reduction in the treated groups.

TABLE I
Geometric means (and range in parentheses) of faecal egg and worm counts of sheep and goats infected with resistant strains of *Haemonchus contortus*

Host group	Treatment	Faecal egg count (epg)		FECR (%)[a]	Worm count post-treatment (day 31)	Worm reduction (WR (%))
		Pre-treatment (day 21)	Post-treatment (day 31)			
Sheep						
I	Fenbendazole (5 mg/kg)	1660 (500–3000)	1116 (400–1600)	46.9	1060 (46–2475)	51.8
II	Closantel (5 mg/kg)	1800 (1100–2500)	0	100	0	100
III	Rafoxanide (7.5 mg/kg)	1100 (300–2300)	0	100	0	100
IV	Untreated control	1500 (400–2600)	1900 (700–3300)	–	2200 (191–3354)	–
Goats						
I	Levamisole (15 mg/kg)	1775 (900–4000)	575 (100–1500)	75.6	955 (62–1862)	66.9
II	Closantel (5 mg/kg)	900 (300–2000)	0	100	0	100
III	Rafoxanide (7.5 mg/kg)	1650 (100–4000)	0	100	0	100
IV	Untreated control	2050 (1100–3500)	2725 (2000–4000)	–	2883 (791–3423)	–

[a]FECR(%) = $[1\text{-}(T_2/T_1) \times (C_1/C_2) \times 100]$ where T is treated, C is control, 1 is pre- and 2 is post-treatment means of the epg

[b]WR(%) = $[C\text{-}T/C) \times 100]$ where C is control and T is treated geometric worm count

RESULTS

CLO and RAF were completely effective against the FBZ-resistant strain of *H. contortus* in sheep while FBZ was only partially effective (Table I). CLO and RAF were also completely effective against the suspected LEV-resistant strain of *H. contortus* in goats, while LEV was only partially effective (Table I).

DISCUSSION

The ovine strain of *H. contortus* was resistant to FBZ, confirming the earlier report by Waruiru (1994). The results also confirmed that the caprine *H. contortus* showed LEV resistance.

The complete efficacy of CLO and RAF against FBZ-resistant *H. contortus* is in agreement with the findings of Campbell and Hotson (1971), Hall and colleagues (1981) and Taylor and Hunt (1993). These drugs were also very effective against LEV-resistant *H. contortus* in goats, as has previously been reported for ovine nematodes (Yadav and Kumar, 1994). Although CLO and RAF are not efficacious against other gastrointestinal nematodes in small ruminants, they may be useful in areas where *H. contortus* is a major problem. Moreover, the prolonged activity of these salicylanilides may reduce pasture contamination, resulting in better control of this parasite (Dash, 1986).

Treatment with CLO and RAF would have the additional advantage of being effective against *Fasciola gigantica* and some ectoparasites such as *Oestrus ovis* larvae (Maes *et al.*, 1988) and face lice *Linognatus ovillus* (Butler, 1986). However, these drugs should not be used in animals scheduled for slaughter within 4 weeks, as they present tissue residue problems owing to their ability to bind strongly with plasma proteins; there is lack of sufficient data on the depletion rate of such residues in domestic animals (Anonymous, 1990).

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