

## A study to evaluate the field efficacy of ivermectin, fenbendazole and pyrantel pamoate, with preliminary observations on the efficacy of doramectin, as anthelmintics in horses

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### ABSTRACT

The efficacy of ivermectin, fenbendazole, pyrantel pamoate and doramectin was evaluated under field conditions at 2 sites in the Free State Province of South Africa. The study involved 25 horses at each site, divided into 5 groups of equal size. Ivermectin, fenbendazole and pyrantel pamoate were administered orally at doses of 0.2, 10 and 19 mg/kg respectively. Doramectin was administered by intramuscular injection at a dose of 0.2 mg/kg. Treatment efficacy was based on the mean faecal egg count reduction 14 days post treatment. At site A a faecal egg count reduction of 100 % was found after treatment with ivermectin, fenbendazole and doramectin. A 96.1 % reduction was found after treatment with pyrantel pamoate. At site B ivermectin and doramectin produced a 100 % reduction in faecal egg counts, fenbendazole produced an 80.8 % reduction and pyrantel pamoate a 94.1 % reduction. Doramectin produced a 100 % reduction in faecal egg counts at both sites, despite not being registered for use in horses. In addition, the results indicated reduced efficacy of fenbendazole at site B, which suggested benzimidazole resistance. Larval cultures showed that cyathostomes accounted for between 86 and 96 % of pre-treatment parasite burdens at both sites. Other helminths identified in the faecal samples were *Strongylus* spp. and *Trichostrongylus axei*.

**Key words:** anthelmintic, cyathostomes, doramectin, equine, fenbendazole, horse, ivermectin, pyrantel, resistance.

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### INTRODUCTION

Intestinal parasites are important factors in the aetiology of gastrointestinal disease and are also of economic importance in horses throughout the world. It is not yet certain to what extent immunity is acquired either with age or exposure<sup>16,17,29</sup>, and as a result, for many years, the control of equine parasites has depended largely on the administration of anthelmintics, to remove adult parasites and prevent egg production with a subsequent reduction in infective larvae on pastures.

Intensive anthelmintic usage appears to select for those nematodes that can survive treatment. The reproduction of these individuals and the further treatment of their progeny with the same type of anthelmintic progressively selects for resistance<sup>26</sup>. Resistance in horses appears

to be restricted to the cyathostomes and most commonly involves the benzimidazole anthelmintics, although resistance to pyrantel has also been detected<sup>2,3,5,7,9,13</sup>. Anthelmintic resistance in cyathostomes of horses has become widely documented over the last 3 decades and has been reported in most countries of the world<sup>1</sup>. In South Africa only a single study in which benzimidazole resistance was reported has been documented<sup>34</sup>.

Cyathostomes commonly produce 75–100 % of eggs passed in the faeces of naturally infected, adult, grazing horses<sup>1</sup>. In contrast to previously held beliefs, it has now been established that cyathostomes can be highly pathogenic or even fatal<sup>10,24</sup>. Their clinical effects range from poor performance and colic to fatal enteritis<sup>5,18</sup>. They are also responsible for the potentially fatal larval cyathostomiasis caused by mass emergence of hypobiotic larvae usually seen in spring. These observations illustrate the need for effective cyathostome control.

The development of anthelmintic resis-

tance has indicated the need for alternative or complementary methods of parasite control and additional effective drugs. An example of the more recently developed drugs is doramectin, an avermectin currently registered for use in sheep, cattle and swine in South Africa (Dectomax, Pfizer). Although not registered for use in horses, doramectin is currently used by many horse owners who are claiming excellent results and no adverse side-effects.

The aim of this study was to investigate the efficacy of the main groups of anthelmintics in South Africa, where limited studies have been conducted to date, and to assess the efficacy of doramectin as an anthelmintic for horses.

### MATERIALS AND METHODS

This study involved 50 horses, 25 at each of 2 sites (sites A and B) in the eastern Free State Province. The trial was conducted between December and January, when day temperatures averaged 28 °C and there had been no rain for approximately 4 months. All horses included had not received anthelmintic treatment for at least 3 months and had at least 100 eggs per gram (EPG) at the beginning of the trial. The horses were predominantly Arabians, part-bred Arabians, Appaloosas and Basutho ponies.

*Site A:* horses were aged from 2 to 22 years. All horses were kept on grass although some received supplementary concentrates. Only 4 of these horses received regular treatment (every 6 months) with ivermectin (Ivomec liquid, Logos Agvet), the last treatment having been administered approximately 6 months before the study. No other method of parasite control was implemented. The pastures were grazed only by horses.

*Site B:* horses were aged from 3 months to 33 years. Two horses were stabled at night, receiving supplementary hay and concentrates. Of the others, which were kept on grass, some also received supplementary hay and/or concentrates. The horses received anthelmintics at fixed

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Table 1: Mean faecal egg counts ( $\pm$  standard deviations) and reductions for each group at sites A and B.

Group	Site A			Site B		
	Arithmetic mean (Day 0)	Arithmetic mean (Day 14)	Mean % reduction	Arithmetic mean (Day 0)	Arithmetic mean (Day 14)	Mean % reduction
IVM	2210 $\pm$ 1166	0**	100	1650 $\pm$ 823	0**	100
DRM	2220 $\pm$ 1324	0**	100	1580 $\pm$ 974	0**	100
FBZ	2200 $\pm$ 1226	0**	100	1510 $\pm$ 917	290* $\pm$ 139	80.8
PYR	2290 $\pm$ 1088	90** $\pm$ 49	96.1	1530 $\pm$ 884	90** $\pm$ 58	94.1
Control	2140 $\pm$ 1466	1670 $\pm$ 1105	22	1720 $\pm$ 820	1400 $\pm$ 683	18.6

\* $P < 0.05$ ; \*\* $P < 0.01$ .

3-monthly intervals. The drugs used included fenbendazole (Panacur liquid, Hoechst), ivermectin (Ivomec liquid, Logos Agvet) and doramectin (Dectomax liquid, Pfizer). No particular rotation was used. Fenbendazole (Panacur liquid, Hoechst) was the most recent treatment administered, having been given approximately 3 months before the study. No other management practices were employed as methods of parasite control. Mixed grazing with cattle and sheep occurred periodically.

#### Design of study

Faecal samples were collected from all horses and analysed the same day using a modified McMaster technique with a sensitivity of 50 EPG. Horses were allocated to 1 of 5 equal-sized groups according to the EPG and, where possible, sex and age. Anthelmintic treatment was carried out the following day. On Day 14 post treatment, faecal samples were again collected from each horse and faecal egg counts performed. Post-treatment samples were processed blind so that there was no knowledge of the treatment group. Before and after treatment, bulk faecal samples from each site were kept at room temperature (approx. 28 °C). Third-stage larvae were recovered using a variation of the Baermann technique and identified according to the number of intestinal cells.

Group 1 received ivermectin (Ivomec liquid, Logos Agvet), 0.2 mg/kg; group 2 received doramectin (Dectomax liquid, Pfizer), 0.2 mg/kg; group 3 received fenbendazole (Panacur liquid, Hoechst), 10 mg/kg; group 4 received pyrantel pamoate (Nemex-H powder, Pfizer), 19 mg/kg, and group 5 was an untreated control. Ivermectin (IVM), fenbendazole (FBZ) and pyrantel (PYR) were given orally, doramectin (DRM) was given by intramuscular injection. The body-weights were estimated using a weigh-band, based on heart girth measurements, and the weights were rounded up to the nearest 50 kg for dose determination.

#### Statistical methods

The effects of the different anthelmintics were estimated using the faecal egg count reduction test. Arithmetic means of the day 0 and day 14 egg counts were calculated to determine the mean percentage reductions within each group. Two-way analysis of variance was performed to evaluate the effect of day of sampling and treatment administered on mean faecal egg counts. Multiple comparisons were then made using the Tukey-HSD interval. Analysis was carried out on logarithmic transformed data ( $\log_{10}$  faecal egg count + 1), as the sample size was small and the data could not be assumed to be normally distributed.

## RESULTS

#### Faecal egg count reductions

The results of the day 0 and day 14 mean EPG values from both sites are presented in Table 1, together with the mean faecal egg count reductions. Ivermectin and doramectin produced 100 % reductions at both sites. Pyrantel pamoate showed 96.1 % efficacy at site A and 94.1 % at site B. Fenbendazole was 100 % effective at site A and 80.8 % effective at site B.

On day 0 all horses had positive egg counts with a range of 100–4000 EPG at site A and a range of 250–3200 EPG at site B. On day 14, at site A all horses in the control and pyrantel pamoate-treated group had positive egg counts, ranging from 50–2850 and 50–150 eggs per gram respectively. All horses in the ivermectin-, doramectin- and fenbendazole-treated groups had egg counts of zero. At site B all horses in the control, fenbendazole- and pyrantel pamoate-treated groups had positive egg counts, with a range of 450–2300, 100–400 and 50–200 eggs per gram respectively. All horses treated with ivermectin or doramectin had egg counts of zero. Resistance was defined as a faecal egg count reduction of less than 90 % after anthelmintic treatment<sup>2</sup>. According to this definition resistance to fenbendazole was found at site B.

At both sites significant differences ( $P <$

0.01) were found between mean faecal egg counts on day 0 and day 14 for all treated groups except the fenbendazole-treated group at site B, which showed a less significant reduction ( $P < 0.05$ ). At site A, significant differences ( $P < 0.01$ ) were found between the mean EPGs of the control and all the treatment groups on day 14. At site B the mean EPG of the control and the treated groups were also significantly different on day 14 ( $P < 0.01$ , for ivermectin, doramectin and pyrantel pamoate and  $P < 0.05$ , for the fenbendazole-treated group). It was not appropriate to pool the results from the 2 sites for statistical analysis, as it was apparent that there were between-site variations in the faecal egg count reductions in the fenbendazole-treated groups ( $P < 0.01$ ).

#### Larval identification

The pre-treatment larval cultures yielded 86 % cyathostomes and 14 % *Strongylus* spp. at site A and 96 % cyathostomes, 3 % *Strongylus* spp. and 1 % *Trichostrongylus axei* at site B.

Third-stage larvae from the pyrantel pamoate-treated group at site A were 98 % cyathostomes and 2 % *Strongylus* spp. From site B, 98 % were cyathostomes, 1 % *Strongylus* spp. and 1 % *Trichostrongylus axei*. At site B larval cultures from the fenbendazole-treated group showed 99 % cyathostomes and 1 % *Trichostrongylus axei*.

## DISCUSSION

Ivermectin produced 100 % faecal egg count reductions at both sites. Resistance to ivermectin has not been reported in horses to date, possibly owing to the longer treatment interval compared to that in anthelmintic treatment programmes of sheep, where resistance to ivermectin is a widespread problem<sup>33,35</sup>. Ivermectin is also a more recently introduced equine anthelmintic than the benzimidazoles.

A 100 % reduction in faecal egg counts was shown at both sites after administration of doramectin by intramuscular injection. These findings indicate that doramectin appears to be effective

against adult cyathostomes, *Strongylus* spp. and *Trichostrongylus axei* in horses. No adverse reactions were observed and no irritation or swelling was seen at the injection site in any of the horses. Obviously further testing with a larger sample size would be required to extend these observations.

Fenbendazole was 100% effective at site A, but reduced efficacy was apparent at site B, suggesting benzimidazole resistance. It would be incorrect to assume that this finding is representative of the area, or country as a whole, as the sample size was small, but the fact that resistance appears to have developed in the parasite population of these horses is likely to indicate a more widespread problem. Fenbendazole was reported as being highly effective in equines in South Africa in 1979 and 1981, but since then benzimidazole resistance has been reported in the only similar study<sup>22,23,34</sup>. The mean faecal egg count reduction of 80.8% in the present study is higher than that reported by Van Wyk and Van Wijk in 1992<sup>34</sup>.

The faecal egg count reductions of 96.1% and 94.1% recorded after administration of pyrantel pamoate, at sites A and B respectively, are consistent with those found by other authors<sup>7,13</sup>. These results provide no evidence of resistance. Pyrantel pamoate is not claimed to be 100% effective against cyathostomes or *Strongylus* spp.

The slight reductions seen in the control groups confirm that the considerably higher reductions in the other groups resulted from the effect of anthelmintics, not from natural factors. These reductions may have been due to a number of factors, but the most likely are that climatic conditions were unfavourable for development of infective larvae<sup>11,12,25,27,29</sup>, both before and during the study, and/or the egg-producing worms were aged (Fisher, pers. comm.). There is no reason to suspect that any between-site variation in results, in any groups, is due to errors in the experimental design as procedures were consistent at both sites. Although weighbands may not be accurate, the weights of all horses at both sites were estimated in the same way and the dose per horse determined by the same method.

It has been found that the prevalence of *Strongylus vulgaris* has decreased owing to extensive use of anthelmintics, while the proportion of cyathostomes has increased<sup>9,15,18,21</sup>. At site A, the relatively high percentage (14%) of *Strongylus* spp. found before treatment is probably due to the fact that anthelmintics are used only on 4 horses, and only every 6 months. At site B, the more frequent use of anthelmintics could account for the

lower percentage of *Strongylus* spp. *Trichostrongylus axei* accounted for 1% of the total burden, which may result from occasional mixed grazing and pasture rotation between ruminants and horses.

As previously reported, the present investigation only shows benzimidazole resistance in cyathostomes<sup>7,13,34</sup>. The relatively short life cycle of cyathostomes, when compared to *Strongylus* spp., and the fact that cyathostomes can become hypobiotic in the host, allows generations of cyathostomes to be exposed to anthelmintics more frequently, thus hastening the development of resistance<sup>4,6,28</sup>. Unconfirmed reports have also suggested resistance in *Strongylus* spp.<sup>8,31</sup>. The results of the present study do not support this. The presence of *Trichostrongylus axei* larvae after treatment with fenbendazole and pyrantel pamoate is to be expected, as these drugs are not registered for control of this parasite.

Other studies have found increased levels of benzimidazole resistance in horses treated with benzimidazoles alone or treated with benzimidazoles and non-benzimidazoles alternately<sup>14,15,20,32</sup>. The results of the present study were, therefore, as anticipated. Van Wyk and Van Wijk<sup>34</sup> mentioned that mebendazole had been used before the study, but made no further reference to previous anthelmintic usage or treatment strategies, thus making comparison difficult.

Further and more widespread studies with a larger sample size are needed to ascertain the extent of benzimidazole resistance, as the lack of studies in South Africa may conceal a problem that has not been recognised. *In-vitro* techniques may be appropriate to further assess the extent of the problem, but their use is complicated by the multiplicity of cyathostome species with which horses are infected and the lack of standard reference strains<sup>7,30</sup>. It is apparent that measures should be taken to delay further development of resistance, and that merely relying on different drugs will not be sufficient, as resistance to other anthelmintics can also develop. The rate of development of new drugs is unlikely to exceed the rate of development of resistance, therefore the efficacy of management techniques should be explored further. A number of alternative strategies have been described. Attempts should be made to decrease treatment frequency, while retaining parasite control, and thus reduce selection pressure for resistance.

In the present study, ivermectin, doramectin and pyrantel pamoate were effective against benzimidazole-resistant parasites. These findings suggest that further research into the use of dora-

mectin as an equine anthelmintic might be warranted. The fact that doramectin may be administered by intramuscular injection ensures that no anthelmintic is wasted and hence no under-dosing occurs, providing the animals' mass is accurately calculated. Under-dosing has been suggested as an important factor in hastening the development of resistance<sup>26</sup> and this is often a risk associated with oral dosing, as spillage frequently occurs. Similar results were, however, reported for cyathostominae in horses in Brazil after oral administration of doramectin at 0.2 mg/kg<sup>19</sup>. Doramectin is registered for prolonged activity over a broad spectrum of internal and external parasites in cattle, sheep and swine. This would also make doramectin usage advantageous if such claims could be substantiated in horses. Investigation of these claims was beyond the scope of this study. Considerable additional data would be required before such conclusions could be drawn.

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