

STUDIES ON THE EFFICACY OF FOUR ANTHELMINTICS AGAINST STRONGYLE INFECTIONS OF SHEEP IN NORTH SUMATRA, INDONESIA

P. Dorny¹, E. Ronjali², K. Feldman³, A. Batubara² and V. S. Pandey

Department of Animal Production and Health, Institute of Tropical Medicine,
Nationalestraat 155, B-2000 Antwerp, Belgium

Summary

Studies on anthelmintic efficacy in sheep were carried out on a large breeding farm and on 7 smallholder farms in the North-Sumatra province, Indonesia. The efficacy in reducing strongyle infections in sheep, of albendazole on all farms and of febantel, levamisole and ivermectin on the breeding farm, was estimated by means of faecal egg count reduction tests. High efficacy (> 95%) was found with all the anthelmintics tested and on all farms. The results are discussed in relation to the current parasite control programme.

(Key Words : Sheep, Strongyles, Anthelmintic Efficacy, Parasitic Control, Indonesia)

Introduction

Parasitic gastroenteritis is among the most important factors causing production losses, disease and mortality in sheep and goats in South-East Asia. *Haemonchus contortus* and *Trichostrongylus colubriformis* are most encountered and associated with disease (Carmichael, 1993; Daud-Ahmad et al., 1991; Dorny et al., 1995; Kochapakdee et al., 1991). Parasite control can dramatically increase small ruminant production in the humid tropics (Handayani and Gatenby, 1988). Control is generally based on suppressive anthelmintic treatments although alternative strategies including pasture rotation and breeding for resistance have also received attention (Carmichael, 1993; Pandey et al., 1994). However the frequent use of anthelmintics increases the risk of selection for resistant populations of nematodes (Waller, 1994). The development of anthelmintic resistance in trichostrongyle nematodes of small ruminants is of increasing concern throughout the world. The majority

of the reported cases involved not only resistance to the benzimidazole group of compounds, but also levamisole- and ivermectin-resistance. Multiple drug resistance is being reported at an increasing frequency (Bjorn, 1994). Reports on the occurrence of anthelmintic resistance in South-East Asia are also increasing. Recently benzimidazole, levamisole and ivermectin resistance in sheep (Pandey and Sivaraj, 1994a; Sivaraj and Pandey, 1994; Sivaraj et al., 1994) and benzimidazole and levamisole resistance in goats have been reported from peninsular Malaysia (Dorny et al., 1993, 1994; Rahman, 1993). In Fiji, benzimidazole resistance was also found to be common in small ruminants (Walkden-Brown and Banks, 1986) and a case of benzimidazole resistance was reported in goats in Southern Thailand (Kochapakdee et al., 1995). In all these reports, resistance involved mainly *H. contortus* but resistance of *T. colubriformis* was also shown (Dorny et al., 1994; Sivaraj et al., 1994).

In Indonesia, or parts there of, anthelmintics have been used so infrequently that resistance to them is believed to be absent (Carmichael, 1993). However intensification of the production systems and larger flock sizes are likely to increase the risk for parasitic gastroenteritis and consequently extend the use of anthelmintics to control these infections.

This paper describes studies on anthelmintic efficacy in sheep in a large sheep breeding farm and on 7 smallholder farms in the North-Sumatra province, Indonesia.

¹Address reprint requests to Dr. P. Dorny, Department of Animal Production and Health, Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium.

²Sub-Central Research Institute for Animal Production, Sungai Putih, P.O. Box, Galang, 20585, North-Sumatra, Indonesia.

³School of Veterinary Medicine, Cornell University, New York, United States of America.

Received January 9, 1995

Accepted March 29, 1995

Materials and Methods

Study site and background information

The study was carried out in the Deli Serdang district (3° 24' N, 98° 53' E) North Sumatra, Indonesia. This area has a hot humid climate with an annual rainfall of about 1,700 mm and no distinct wet and dry seasons. One large farm (Farm 1) and seven small farms (Farms 2-8) were involved in the study. The large farm (Farm 1) was a research and breeding farm comprising of about 500 ewes of various tropical breeds, including the local Sumatra Thin-tail, and crosses with St. Croix, Java Fat-tail and Barbados Blackbelly. Animals grazed from 08 to 16 h each day in a rubber plantation, and at night were confined in a sheep house with a raised slatted floor. Grass cut from an ungrazed area and concentrate were selectively administered. All sheep on the farm were given anthelmintic treatments every 3 months and moved to a pasture that had been spelled for three months. Benzimidazoles (albendazole) and probenzimidazoles (febantel) were used before 1993, ivermectin in 1993 and a drench containing levamisole and radoxanide in 1994. All drugs had been administered orally at a dosage calculated from the manufacturer's recommendations and the individual weight.

The small farms (Farms 2-8) were traditional smallholdings which were monitored monthly as part of a rural development project. The flock size on these farms ranged from 4 to 15 and the breeds consisted mainly of the local Sumatra Thin-tail and crosses with St Croix. Sheep were kept in a semi-intensive or intensive feeding system. They were allowed to graze on paddy fields, roadsides and in rubber plantations for a few hours a day (Farms 2-3) or fed in the barn with cut grass or leaves and waste products of the rice industry (Farms 4-8). All sheep on these farms, including young lambs were treated four times a year with febantel or albendazole. The drugs were administered orally; the dosage was calculated from the estimated weight.

Anthelmintic efficacy tests

On Farm 1 faecal egg count reduction tests (FECRT) were done in February-March (FECRT1) and May-June (FECRT2) following the guidelines of the World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) (Coles et al., 1992). Groups of 20 ewes of various genotypes, born in 1992 and 1993 were selected. They had not received any anthelmintic treatment in the 2 months prior to the study. All animals were weighed and faecal sampled on Day 0. The following anthelmintics were tested: albendazole at 3.8 mg

/kg (Valbazen, Smith Kline Beecham), febantel at 10.0 mg/kg (Rintal, Bayer) and ivermectin at 0.2 mg/kg (Ivomec, Merck, Sharp & Dohme) in FECRT1, and levamisole at 7.5 mg/kg (L-Tramisol, Janssen Pharmaceutica) in FECRT2. Albendazole, febantel and levamisole were administered orally by means of a calibrated syringe; for febantel and levamisole appropriate suspensions were prepared from the granulate prior to administration. Ivermectin was given subcutaneously. In each FECRT a non-treated control group of 15 or 20 ewes was included. A second faecal sample was taken from all animals including those of the control groups 14 days post-treatment (D14). Faecal strongyle egg counts were done using a modified McMaster technique with a sensitivity of 30 eggs per gram. Group composite faecal cultures were made from the pre- and post-treatment samples followed by larval collection and identification (Anon, 1986). Arithmetic mean post-treatment faecal egg counts of control and treated groups were used to calculate the reduction percentage. An efficacy of less than 95% and a 95% confidence level of less than 90% was taken as indicating the presence of anthelmintic resistant nematodes in the herds (Coles et al., 1992).

On the small farms (Farm 2-8) efficacy was estimated by performing faecal egg counts on groups of 4 to 9 sheep on days 0 and 14 after the routine three-monthly treatments with albendazole (Valbazen, Smith Kline) at 3.8 mg/kg. Efficacy was calculated using the formula:

$$\text{Efficacy \%} = \frac{\text{mean EPG prior to treatment} - \text{mean EPG post-treatment}}{\text{mean EPG prior to treatment}} \times 100$$

Group composite faecal cultures were made from the pre- and post-treatment samples followed by larval collection and identification (Anon, 1986).

Results

The results of the two FECRT on Farm 1 are shown in table 1. High efficacy ($\geq 95\%$) was found with all the anthelmintics tested. The 95% confidence interval was above 90% for albendazole, febantel and ivermectin. For levamisole (FECRT2) the lower 95% confidence level was only 84%.

The majority of the eggs shed by the sheep were from *H. contortus* and *T. colubriformis*. *Cooperia* spp. and *Oesophagostomum* spp. accounted for about 25% in the faecal cultures of the controls. In the post-treatment faecal cultures of the albendazole and ivermectin groups only *H. contortus* were found. In the post-treatment cultures of the

levamisole group larvae of 4 genera were recovered.

The efficacy of albendazole was 100% on all smallholder farms (Farms 2-8) tested (table 2). *H.*

contortus was the most important species found in the faecal cultures, followed by *Trichostrongylus* spp. No larvae were recovered in the post-treatment cultures.

TABLE 1. EFFICACY OF FOUR ANTHELMINTICS TESTED BY FAECAL EGG COUNT REDUCTION TEST (FECRT) IN SHEEP ON A LARGE BREEDING FARM (FARM 1) IN NORTH SUMATRA

Treatment	Dose	No. of animals per group	Mean EPG		Efficacy (%)	Confidence levels 95%		Generic composition of the cultures post-treatment* (%)			
			before treatment	after treatment		upper	lower	H	T	C	O
FECRT 1, February-March 1994											
Control		20	1,234	407				54	18	21	7
Albendazole	3.8 mg/kg	20	674	3	99	100	97	100	0	0	0
Febantel	10.0 mg/kg	20	1,463	2	100	100	97	no larvae in culture			
Ivermectin	0.2 mg/kg	20	1,710	6	99	100	92	100	0	0	0
FECRT 2, May-June 1994											
Control		15	452	221				52	26	10	12
Levamisole	7.5 mg/kg	20	786	12	95	98	84	44	43	7	6

* *H.*: *Haemonchus contortus*; *T.*: *Trichostrongylus* spp.; *C.*: *Cooperia* spp.; *O.*: *Oesophagostomum* spp.

TABLE 2. EFFICACY OF ALBENDAZOLE* IN SHEEP ON 7 TRADITIONAL FARMS (FARMS 2-8) IN NORTH SUMATRA

Farms	Mean EPG		Efficacy (%)	Generic composition of the cultures pre-treatment** (%)			
	before treatment (range)	after treatment		H	T	C	O
2	1,200 (630-6,090)	0	100	91	9	0	0
3	570 (120-5,100)	0	100	47	31	21	1
4	5,066 (60-20,190)	0	100	83	6	9	3
5	170 (150-210)	0	100	83	12	3	3
6	1,089 (120-2,640)	0	100	66	11	6	18
7	5,918 (60-20,310)	0	100	75	15	10	0
8	2,226 (210-5,220)	0	100	86	23	1	0

* Albendazole: Valbazen® Smith Kline Beecham, 3.8 mg/kg.

** *H.*: *Haemonchus contortus*; *T.*: *Trichostrongylus* spp.; *C.*: *Cooperia* spp.; *O.*: *Oesophagostomum* spp.

Discussion

The results of the present study demonstrated the high efficacy of (pro-) benzimidazoles, levamisole and ivermectin against strongyle infections on North-Sumatran sheep farms. The efficacy was apparently not affected by the regular anthelmintic treatments that were used to control nematode infections for several years. Although this study does not provide an overall view of the situation on anthelmintic efficacy in North-Sumatra, it is

interesting to compare results of the present study with the alarming situation in neighbouring peninsular Malaysia, where anthelmintic resistance has become widespread in small ruminants (Pandey and Sivaraj, 1994b). The problem in Malaysia has been found to be the result of the irresponsible use of anthelmintics and the movement of stock causing transfer of resistant nematodes from institutional to smallholder farms (Dorny et al., 1994; Sivaraj et al., 1994). In Sumatra, anthelmintics are not used as extensively as in Malaysia, primarily because they

are not affordable to the farmers. Also efforts are being made to use integrated control systems that do not rely entirely on anthelmintic treatments.

On Farm 1, management techniques such as rotational grazing, were adopted to reduce the frequency of anthelmintic treatments. Pasture rotation can effectively break the cycle of continuous infection between host and pasture. It was found that in humid tropical conditions infective stages develop within a few days from eggs, but their longevity is reduced due to exhaustion of stored energy (Banks et al., 1990; Carmichael, 1993). Although moderate numbers of larvae may persist for eight to ten weeks, the survival rate thereafter is negligible. These epidemiological observations were utilised to design a rotational grazing system with an ideal interval between grazing periods appearing to be around 10 to 12 weeks (Carmichael, 1993). It is clear that in plantations, several additional management factors apply such as regeneration of forages, which will depend on weather, light penetration, extent of grazing and composition of forage species, which have to be considered when designing rotational grazing systems (Ani et al., 1985). In commercial farms pasture rotation is often feasible, it is less practicable in traditional farms where unsupervised grazing by several flocks occurs along roadsides or rice field verges. In these cases, the challenge is to educate farmers on the benefits of rotation in which revisits of a few days to each area are extended to several weeks apart (Carmichael, 1993).

Pasture infectivity can also be reduced by decreasing stocking density. In smallholdings increasing the flock size will result in higher infectivity, especially when grazing space is limited and when the flock is not shepherded (P. Dorny, personal observation).

An alternative approach to reducing the frequency of anthelmintic treatments is to introduce or to select breeds which display a higher resistance towards the parasites (Pandey et al., 1994). Differences in susceptibility between breeds of sheep to nematode parasites are well established (Courtney, 1986). Relatively, high estimates of heritability of resistance in sheep were found, ranging from 0.3 to 0.5, values similar in magnitude to heritabilities of production characters such as fleece weight or body weight, for which selection has been demonstrably successful (Barger, 1989). Resistance to nematodes is not genetically correlated with production characters in the absence of infection, which means that selection for resistance should not interfere with existing selection programs for increased production (Albers et al., 1987; Windon and Dineen, 1984). However breeding for resistance is a relatively slow process. It was estimated

that progress in resistance achieved by a more or less realistic breeding scheme would be of the order of 1% per year (Albers and Gray, 1986).

Breeds that are known or were selected for a higher resistance to nematodes including, St Croix and Barbados Blackbelly, were recently introduced on Farm 1. Research on this farm is currently undertaken on the selection for resistance of crosses of these breeds with the local Sumatra Thin-tail breed. Rams of these selected crosses are distributed to smallholder farms in order to increase the productivity.

Only three broad-spectrum anthelmintic groups are available and it is not likely that new chemical groups will become available in the near future. Another implication is that if there is resistance to one drug of an anthelmintic group, side resistance to other drugs of the same group is found, even if those compounds have not yet been used on that property. To preserve the efficacy of anthelmintics, recommendations were proposed by different researchers (Coles and Roush, 1992; Coles et al., 1994; Dash et al., 1986). Apart from limiting the frequency of anthelmintic treatments and using the correct dose rates the use of anthelmintics of different groups in a 12-monthly rotation is generally recommended. This system was designed in temperate climatic conditions where only one generation of nematodes develops each year. Consequently only one generation has been subjected to the effects and the selection of the drugs used over the period of one year. As mentioned above, weather conditions in the humid tropics are optimal for maintaining a continuous cycle between host and parasite and as a result, several generations of worms will develop within the same year. This knowledge has led to the belief that anthelmintics should be rotated more rapidly in the humid tropics (Tajuddin and Chong, 1988). However this view is not supported by other authors as it is believed that "rapid rotation" might select rapidly for multiple resistance (Carmichael, 1993).

In conclusion, no indications of anthelmintic resistance were found on 8 sheep farms in the North-Sumatra province, Indonesia. The current control programme aimed to minimize the frequency of anthelmintic treatments should be continued. Regularly monitor the efficacy of the anthelmintics should be encouraged.

Acknowledgements

We are grateful to Mr. Leo P. Batubara and Dr. R.M. Gatenby for their help and support throughout this study. Mr. Jeplin Sihombing, Miss M. Hutaunik, Mr. Imanyanto and Mr. Mursyid are thanked for excellent technical

assistance. The work was supported by the Small Ruminant Collaborative Research Programme funded by the United States Agency for International Development and the STD3 Programme (TS3-CT92-0073) of European Union coordinated by the Institute of Tropical Medicine, Antwerp, Belgium.

Literature Cited

- Albers, G. A. A. and G. D. Gray. 1986. Breeding for worm resistance: a perspective. In: M. J. Howell (Editor) Parasitology-Quo Vadit? Proc. of the 6th Int. Congr. of Parasitology. Australian Academy of Science, Canberra pp. 559-566.
- Albers, G. A. A., G. D. Gray, L. R. Piper, J. S. F. Barker, L. F. LeJambre and I. A. Barger. 1987. The genetics of resistance and resilience to *Haemonchus contortus* infections in young Merino sheep. Int. J. Parasitol. 17:1355-1363.
- Ani, B. A., B. I. Tajuddin and D. T. Chong. 1985. Sheep rearing under rubber. Proc. of the 9th Ann. Conf. of the Malaysian Soc. of Anim. Prod. Serdang, Selangor, Malaysia, pp. 117-123.
- Anonymus. 1986. Manual of Veterinary Parasitological Laboratory Techniques. Ministry of Agriculture, Fisheries and Food, London, HMSO, UK, p. 152.
- Banks, D. J. D., R. Singh, I. A. Barger, B. Pratap and L. F. LeJambre. 1990. Development and survival of infective larvae of *Haemonchus contortus* and *Trichostrongylus colubriformis* on pasture in a tropical environment. Int. J. Parasitol. 20:155-160.
- Barger, I. A. 1989. Genetic resistance of hosts and its influence on epidemiology. Vet. Parasitol. 32:21-35.
- Bjorn, H. 1994. Workshop summary: Anthelmintic resistance. Vet. Parasitol. 54:321-325.
- Carmichael, I. H. 1993. Internal and external parasites as constraints to productivity of small ruminants in the humid tropics. In: M. Wodzicka-Tomaszewska, S. Gardiner, A. Djajanegara, I. M. Mastika and T. R. Winadarya (Editors) Small ruminant production in the humid tropics. Sebelas Maret University Press, Surakarta, Indonesia, pp. 284-335.
- Coles, G. C., C. Bauer, F. H. M. Borgsteede, S. Geerts, T. R. Klei, M. A. Taylor and P. J. Waller. 1992. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.). Methods for the detection of anthelmintic resistance in nematodes of veterinary importance. Vet. Parasitol. 44:35-44.
- Coles, G. C. and R. T. Roush. 1992. Slowing the spread of anthelmintic resistant nematodes of sheep and goats in the United Kingdom. Vet. Rec. 130:505-510.
- Coles, G. C., F. H. M. Borgsteede, S. Geerts. 1994. Recommendations for the control of anthelmintic resistant nematodes of farm animals in the EU. Vet. Rec. 134:205-206.
- Courtney, Ch. H. 1986. Host genetic factors in helminth control in sheep. In: Parasites: Epidemiology and Control. Veterinary Clinics of North-America. Food Animal Practice. Vol. 2, No. 2. University of Florida Agricultural Experimental Station Journal. Series NO 5750, pp. 433-438.
- Dash, K. M., R. L. Newman and E. Hall. 1986. Recommendations to minimise selection for anthelmintic resistance in nematode control programmes. In: N. Anderson and P. J. Waller (Editors) Resistance in Nematodes to Anthelmintic Drugs. C.S.I.R.O., Australia. Division of Animal Health. IV. Australian Wool Corporation. pp. 161-169.
- Daud-Ahmad, I. A., R. A. Sani and R. A. Halim. 1991. Gastrointestinal parasitism in goats. In S. Saithanoo and B. W. Norton (Editors): Goat production in the Asian Humid Tropics. Proc. of an Int. seminar held in Hat Yai, Thailand, 28-31 May 1991. Prince of Songkla University and the University of Queensland, pp. 201-205.
- Dorny, P., E. Claerebout, J. Vercruysee, A. Jalila and R. Sani. 1993. Benzimidazole resistance of *Haemonchus contortus* in goats in Malaysia, Vet. Rec. 133:423-424.
- Dorny, P., E. Claerebout, J. Vercruysee, R. Sani and A. Jalila. 1994. Anthelmintic resistance in goats in Peninsular Malaysia. Vet. Parasitol. 55:327-342.
- Dorny, P., C. Symoens, A. Jalila, J. Vercruysee and R. Sani 1995. Strongyle infections in sheep and goats under the traditional husbandry system in Peninsular Malaysia. Vet. Parasitol. 56:121-136.
- Handayani, S. W. and R. M. Gatenby. 1988. Effects of management system, legume feeding and anthelmintic treatment on the performance of lambs in North Sumatra. Trop. Anim. Hlth. Prod. 20:122-128.
- Kochapakdee, S., V. S. Pandey, W. Pralomkarn, S. Chondumrongkul, W. Ngampongsai and A. Lawpetchara 1995. Anthelmintic resistance in goats from Southern Thailand. Vet. Rec. in press.
- Kochapakdee, S., W. Pralomkarn, S. Chondumrongkul, S. Saithanoo and B. W. Norton 1991. Prevalence of internal parasites in Thai native female goats. In: S. Saithanoo and B. W. Norton (Editors): Goat production in the Asian Humid Tropics. Proc. of an Int. seminar held in Hat Yai, Thailand, 28-31 May 1991. Prince of Songkla University and the University

- of Queensland, pp. 206-212.
- Pandey, V. S. and S. Sivaraj. 1994a. Anthelmintic resistance in *Haemonchus contortus* from sheep in Malaysia. *Vet. Parasitol.* 53:67-74.
- Pandey, V. S. and S. Sivaraj. 1994b. Anthelmintic resistance: an emerging serious problem in small ruminants in Malaysia. In: Sustainable Animal Production and the Environment. Proc. of the 7th AAAP Anim. Sci. Congr., Bali, Indonesia, Vol II, Ikatan Sajana Ilmu-Ilmu Peternakan Indonesia, pp. 409-410.
- Pandey, V. S., A. Verhulst, R. M. Gatenby, S. Saithanoo, P. Barcelo and L. S. Monteiro. 1994. Genetic resistance to internal parasites in sheep and goats and its exploitation for increasing animal productivity in Southeast Asia: an example of international collaborative research. In: Subandriyo and R. M. Gatenby (Editors) Strategic development for small ruminant production in Asia and the Pacific. Proc. of a symposium held in conjunction with the 7th Asia-Australasian Assoc. of Anim. Prod. Soc. Congr., Denpasar, Bali, Indonesia, July 11-16, 1994, pp. 39-50.
- Sivaraj, S., P. Dorny, J. Vercruyssen and V. S. Pandey. 1994. Multiple and multigenic anthelmintic resistance on a sheep farm in Malaysia. *Vet. Parasitol.* 55:159-165.
- Sivaraj, S. and V. S. Pandey. 1994. Isolation of an ivermectin-resistant strain of *Haemonchus contortus* from sheep in Malaysia. *Vet. Rec.* 135:307-308.
- Tajuddin, I. and D. T. Chong. 1988. Rubber Research Institute of Malaysia. Research on sheep integration under rubber. Proc. of Symp. on Sheep Prod. in Malaysia, Centre for Tropical Animal Production and Disease Studies, Selangor, Malaysia, pp. 73-82.
- Wahab, A. Rahman. 1993. An assessment of thiabendazole-resistant nematodes in some smallholder goat farms of Malaysia using the egg hatch assay method. *Vet. Parasitol.* 51:159-161.
- Walkden-Brown, S. W. and D. J. D. Banks. 1986. Integrated small ruminant and cropping systems in Fiji with health as a major constraint. In: C. Devendra (Editor). Proc. of the Small Ruminant Production Systems in South and Southeast Asia. International Development Research Centre, Ottawa, pp. 289-310.
- Waller, P. J. 1994. The development of anthelmintic resistance in ruminant livestock. *Vet. Parasitol.* 56:233-243.
- Windon, R. G. and J. K. Dineen. 1984. Parasitological and immunological competence of lambs selected for high and low responsiveness to vaccination with irradiated *Trichostrongylus colubriformis* larvae. In: J. K. Dineen and P. W. Otteridge (Editors). Immunogenetic approaches to the control of endoparasites. C.S.I.R.O. Melbourne, pp. 13-28.