T.C.
ULUDAĞ ÜNİVERSİTESİ
VETERİNER FAK. DERGİSİ
Sayı: 1-2-3, Cilt: 5-6, Yıl: 6-7
(1986-1987)

THE EFFICACY OF 'VERMADAX' AND 'NILZAN' AGAINST NATURAL INFECTIONS OF DICROCOELIUM DENDRITICUM, FASCIOLA SPP. AND GASTRO – INTESTINAL NEMATODES

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SUMMARY

Efficacy of Vermadax (thiophanate + brotianide) and Nilzan (tetramisole + oxyclozanide) were studied in sheep, naturally infected with Dicrocoelium dendriticum. Fasciola hepatica, F. gigantica *and* gastro-intestinal nematodes *under the field conditions. Vermadax was administered orally at a dose of 0.25 ml/kg (50 mg/kg thiophanate + 5.6 mg/kg brotianide) body weight. The drug used was found highly effective against* D. dendriticum *(99.8 %),* gastro-intestinal nematodes *(99.3 %)* F. hepatica *(98.4 %),* F. gigantica *(64.8 %). On the other hand, Nilzan at a dosage of 1 tablet per 20 kg (15 mg/kg tetramisole + 15 mg/kg oxyclozanide) body weight, also given orally, was highly effective against* gastro-intestinal nematodes *(98.7 %) and* F. hepatica *(84.6 %). Nilzan was not effective on* D. dendriticum *and* F. gigantica.

Key Words: *Vermadax, Nilzan, Thiophanate, Brotianide, Tetramisole, Oxyclozanide, Dicrocoelium dendriticum, Fasciola, Gastro-intestinal nematodes, Treatment.*

ÖZET

Doğal Enfekte Koyunlarda Dicrocoelium Dendriticum, Fasciola spp. ve Mide-Barsak Nematod'larına Vermadax ve Nilzan'ın Etkisi

Bu araştırmada doğal enfekte koyunların Dicrocoelium dendriticum, Fasciola spp. *ve* mide-barsak nematodlarına *Vermadax ile Nilzan'ın etkisi incelenmiştir. Ağız yoluyla 0,25 ml/kg (50 mg/kg tiophanate + 5.6 mg/kg brotianide) dozda kullanılan Vermadax* D. dendriticum'a *% 99.8,* F. hepatica'ya *% 98.4,* F. gigantica'ya *% 64.8,* mide-barsak nematodlarına *% 99.3; 1 tablet/20 kg (15 mg/kg tetramisole + 15 mg/*

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kg oxyclozanide) dozda kullanılan Nilzan ise F. hepatica'ya *% 84.6* mide-barsak *nematodlarına % 98.7 etkili olmuş,* D. dendriticum *ve* F. gigantica'ya *etkisiz kalmıştır.*

INTRODUCTION

The incidence of helminthiasis in Turkey is generally found to be markedly high in the slaughter house examinations. These manifestations, showing seasonal variations, cause important clinical and economical problems in some districts. Özgencil[1] reported that 81 % of sheep and 65 % of cattle slaughtered in Ankara Meat Plant were found infected with *Fasciola hepatica* and/or *Dicrocoelium dendriticum*. In most cases, these two parasites were found to be present in the same animals (90 %). *Fasciola gigantica* was also detected in some cases. It was almost impossible to find an animal free of *gastro-intestinal nematodes*. These helminthic diseases are extremely important in farm animals since they cause highly significant economical losses.

Despite the increasing number of drugs marketed for the treatment of nematodiasis and fascioliasis, there is no existing remedy (used in the economical dosage) to cure dicrocoeliasis in most countries as well as in Turkey. The potential activity of many of those compounds including thiabendazole[2,3], albendazole[4,5,6], fenbendazole[7,8], mebendazole[3,9], cambendazole[10] derived from benzimidazole and praziquantel[11] and nitrophenylguanidine[12] against *D. dendriticum* were studied after the banning of Hetolin production, and the results revealed that these chemicals were active only when given at the economically unsuitable high dosages.

In recent years, Vermadax, composed of brotianide and thiophanate, was introducted to the market. Brotianide was reported to be active against *F. hepatica*[13,14,15,16], *F. gigantica*[17] and *D. dendriticum*[18], and thiophanate a known drug active against nematodes[19,20]. Thiophanate was also tried by Ambrosi and others[21] against *D. dendriticum* in naturally infected sheep and was found to be highly effective (99.9 %) at a dose of 200 mg/kg. Vermadax used in the treatment of *F. hepatica* for the first time, under natural conditions, was found to be effective at a rate of 96 % and 100 % at a dosage of 0.25 ml/kg[22].

MATERIALS AND METHODS

A sum of 45 Merino sheep, aged 2-7 years, selected from a flock reportedly contamined with *D. dendriticum, Fasciola spp.* and *gastro-intestinal nematodes* were used in this field trial. A week prior to the treatments, 75 sheep were chosen for fecal examinations by techniques of modified McMaster and modified Benedek. The number of helminth eggs per gram of feces (epg) were determined and 45 of these were selected because of the severely high epg value.

The animals were used for trials after dividing into 3 groups according to the severity of infection, age and their body weights. Group I, received 0.25 ml/kg of Vermadax solution (50 mg/kg thiophanate + 5.6 mg/kg brotianide) while the second group was treated with 1 tablet of Nilzan/20 kg of body weight (15 mg/kg tetramisole and 15 mg/kg oxyclozanide) orally for only once. The group III was kept as the untreated controls, under identical field and environmental conditions.

The duration of observation was 26 days and fecal samples were collected for epg determination on the days of 0, 7, 14 and 26 th day of trial, 5 out of 15 sheep from each group were slaughtered for postmortem evaluations. The pregnancy conditions, liver and carcass weights were obtained as the main parameters for the efficacy of the applied treatments. Liver, abomasum, small and large intestines were examined by naked eye and under stereomicroscope to fix the present alive parasites for identifications and counting.

RESULTS

a) FECAL EXAMINATIONS (Table I)

Dicrocoelium dendriticum: Vermadax treatment resulted in reduction of almost all if not all, in the number of epg. The epg number was averaging 267 at the start, and this was down to zero on the day 26. The corresponding epg numbers in Nilzan group were 409 and 107 respectively and this means a reduction of 73.8 percent.

Fasciola spp.: The average epg at the start was 207 which was also reduced to 0.5 giving a reduction of 99.8 percent for Vermadax and the corresponding epg was equal to 89.3 percent for Nilzan treated sheep.

Gastro-intestinal nematodes: The avarage epg at the beginning for Vermadax group was 663, that was down to zero giving a reduction equal to 100 percent. The corresponding numbers obtained from Nilzan treated group were 713 and 9.3 and the resulting reduction was 98.7 percent.

Table: I

The Average EPG at the Beginning and After the Treatment With Vermadax and Nilzan and the Corresponding Reduction

Treatment	Helminth spp.	EPG in Treatment Days		Reduction of Eggs
		0	26 th Days	
Vermadax		4006	0	
	mean	267	0	% 100
	D. dendriticum			
Nilzan		6104	1610	
	mean	409	107	% 73.8
Vermadax		3107	8	
	mean	207	0,5	% 99.8
	Fasciola spp.			
Nilzan		2093	224	
	mean	140	15	% 89.3
Vermadax		9950	0	
	mean	663	0	% 100
	Gastro-intestinal nematodes			
Nilzan		10700	140	
	mean	713	9.3	% 98.7

b) NECROPSY RESULTS (Tables II-IV)

Dicrocoelium dendriticum (Table II): The total number of alive parasites collected was 8647 in the untreated control animals, 21 in the Vermadax treated animals on the 26 th day, which compares with 8647 and 8416 in controls and Nilzan treated groups respectively after the treatment. And, this difference indicates a statistically insignificant ($P > 0.05$) efficacy for Nilzan.

Table: II

The Necropsy Findings of Alive *D. Dendriticum* in Groups Treated With Vermadax and Nilzan

Group	No of Alive D. Dendriticum	Efficacy
Vermadax	0, 1, 1, 2, 17 Total 21	99.8 %
Nilzan	481, 496, 1579, 1693, 4167 total 8416	2.7 % ($P > 0.05$)
Control	788, 845, 1642, 2448, 2924 total 8647	—

Table: III

The Antiparasitic Efficacy of Vermadax and Nilzan Against *Fasciola Spp.*

Treatment	No of Flukes at Necropsy				% Efficacy				Average %
	F. Hepatica		F. Gigantica		F. Hepatica		F. Gigantica		
	Mature	Immature	Mature	Immature	Mature	Immature	Mature	Immature	
Vermadax	0 2 0 1 0	0 0 0 1 0	0 0 0 0 0	0 0 0 6 0	98.7	95.0	100	50	96.2
Total	3	1	0	6	98.4		64.8		
Nilzan	2 5 6 9 2	5 2 2 4 1	0 0 1 1 0	5 5 2 4 5	89.4	30	60	—	76.8
Total	24	14	2	21	84.6		—		
Control	17 33 107 40 29	0 4 6 4 6	0 4 0 1 0	0 6 0 3 3	—	—	—	—	—
Total	226	20	5	12					

Fasciola spp. (Table III): The antiparasitic activity of Vermadax and Nilzan against the immature and adult forms of *F. hepatica* and *F. gigantica* is summarized in Table III. As it was seen, Vermadax was capable of killing the adults of *F. gigantica* totally (100 %) and the immature parasites (50,0 %), while the second drug, Nil-

zan, was lesser effective on adults of *F. gigantica* (60,0 %) and inactive for the immature forms. For *F. hepatica* the similar situation was observed. Vermadax killed 98.7 % of adults and 95.0 % of immature forms of *F. hepatica* while Nilzan was effective against the adults 89.4 % and 30.0 % against the young parasites. The average of antiparasitic activity of Vermadax and Nilzan for *Fasciola spp.* was calculated about 96.2 % and 76.8 % respectively.

Gastro-intestinal nematodes: Both drugs were found to be highly effective on several nematodes as the number of parasites in controls and in the treatment groups are seen in Table IV.

The average liver weights calculated for 5 sheep in each group were compared by the liver weight/body weight ratios and the results were 4.56 % Vermadax and 6.01 % for Nilzan that compare with the control values of 5.36 % which did not make any sence (inconclusive).

The pregnant ewes did not show any significant changes in their gestation period, body temperature and appetite due to these therapeutic trials.

Table: IV

The Efficacy of Vermadax and Nilzan Against the Gastrointestinal Nematodes

Nematodes Spp.	Vermadax	Nilzan	Control
	Number of Nematodes and % Efficacy	Number of Nematodes and % Efficacy	Number of Nematodes
Haemonchus contortus	5 (99.9)	0 (100)	3545
Trichostrongylus axei	22 (99.9)	40 (99.8)	23252
Ostertagia spp.	197 (95.1)	348 (91.3)	4021
Bunostomum trigonocephalum	5 (89.8)	3 (93.9)	49
Chabertia ovina	0 (100)	0 (100)	118
Oesophagostomum venulosum	1 (98.5)	0 (100)	67
Total	230 (99.3)	391 (98.7)	31187

DISCUSSION

The need for an effective antiparasitic drug which would kill all the present helminths in the animal body was great. Vermadax was introduced for this purpose as a potential anthelminthic wonder drug to kill most, if not all parasites. An ingredient of this drug, brotianide was reported as highly active against *Fasciola hepatica, Fasciola gigantica* and *Dicrocoelium dendriticum* in either naturally or experimentally infected animals[13,14,15,16,17,18]. Ambrosi and others[21] tried the other ingredient, thiophanate against *Dicrocoelium dendriticum* at a dosage of 200 mg/kg and observed a 99.9 % kill that was in accord with the previous findings[19,20], for nematodes.

These results were obtained in separate experiments that the efficacies of the ingredients were tested alone. After these, Middleberg and others[22] tested Vermadax as a composite drug against *F. hepatica* in naturally infected sheep at a dose of

2.5 ml/kg body weight, and obtained a 96-100 % efficacy in these animals. In our study, although the Vermadax used contained only 1/4 of the thiophanate used in experiment carried out by Ambrosi and others[21], it was still equally effective. Our results were also identical with the results reported by Middleberg and others[22].

The results of present study showed that Vermadax is a strong anthelmintic drug effective on *Gastro-intestinal nematodes, Fasciola spp.* and *D. dendriticum*, Nilzan is equally active on the *Gastro-intestinal nematodes*, lesser active against *Fasciola spp.* but inactive on *D. dendriticum.*

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