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Effectiveness of eprinomectin 0.5% pour-on against gastrointestinal nematodes in naturally infected cattle

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Abstract: Effectiveness of eprinomectin, which until now has not been assessed in Turkey, was tested against gastrointestinal nematodes of naturally infected cattle under field conditions in Adapazarı, Sakarya. Out of 25 cattle used in trial, 17 were treated with eprinomectin and 8 were kept as untreated controls. To determine gastrointestinal nematode fauna, a fecal culture was prepared from the mixed fecal samples of 25 trial cattle at 26-27 °C for 3 weeks. Eprinomectin 0.5% pour-on (Eprinomec 0.5% Dökme Çözelti®, TOPKİM) at the recommended dose of 1 mL/10 kg bw (0.5 mg active ingredient/kg bw) was applied along the backline of each animal (day 0). It was determined that the gastrointestinal nematode fauna of 25 trial cows comprised *Nematodirus* (17%), *Strongyloides* (9%), *Trichostrongylus* (24%), *Ostertagia* (20%), *Haemonchus* (12%), *Cooperia* (10%), *Oesophagostomum* (6%), and *Bunostomum* (2%) genera. A t-test for independent samples showed no significant difference ($P > 0.05$) between the log (EPG + 1) values of control and treatment groups on the treatment day (day 0), whereas the differences were significant ($P < 0.001$) on days 3, 10, and 17. Fecal egg count reduction percentage (effectiveness) was $> 99.5\%$ according to geometric means and $> 97.3\%$ according to arithmetic means. However, effectiveness against individual nematode species may differ somewhat from these percentages. No adverse reactions were observed in cattle treated with eprinomectin.

Key words: Cattle, gastrointestinal nematodes, eprinomectin, treatment

Eprinomectin % 0,5 dökme çözeltisi'nin doğal enfekte sığırlarda gastrointestinal nematodlara etkisi

Özet: Daha önce Türkiye'de etkinliği denenmemiş olan eprinomectinin Sakarya, Adapazarı'nda doğal şartlarda enfekte sığırlarda gastrointestinal nematodlara karşı etkinliği test edilmiştir. Denemeye alınan 25 sığırdan 17'sine (tedavi grubu) eprinomectin uygulanmış, 8 sığır ilaç uygulanmayarak kontrol grubu olarak bırakılmıştır. Sığırların gastro intestinal nematod faunasını belirlemek için çalışmaya alınan 25 sığırın dışkılarından alınan örnekler iyice karıştırılarak 26-27 °C'ta 3 hafta süre ile larva kültürü hazırlanmıştır. Eprinomectin % 0,5 dökme çözeltisi (Eprinomec % 0,5 Dökme Çözelti®, TOPKİM), önerilen doz olan 1 mL / 10 kg ca (0,5 mg aktif madde / kg ca) hesabıyla, her hayvana sırt çizgisi boyunca dökülerek uygulanmıştır. Çalışmaya alınan 25 sığırdan *Nematodirus* (% 17), *Trichostrongylus* (% 24), *Ostertagia* (% 20), *Haemonchus* (% 12), *Cooperia* (% 10), *Strongyloides* (% 9), *Oesophagostomum* (% 6) ve *Bunostomum* (% 2) cinslerinin oluşan bir gastrointestinal nematod faunası olduğu belirlenmiştir. Bağımsız örnekler için t-testinde, kontrol ve tedavi grupları log (EPG + 1) değerleri arasındaki fark, ilaç uygulama gününde (0'inci gün) önemsiz ($P > 0,05$); ilaç uygulamasını takip eden 3'üncü, 10'uncu ve 17'nci günlerde ise önemli ($P < 0,001$) bulunmuştur. Dışkıda yumurta sayısındaki azalmaya göre ilacın etkisi tedavi sonrası 3'üncü, 10'uncu ve 17'nci günlerde, geometrik ortalamaya göre % 99,5'in, aritmetik ortalamaya % 97,3'ün üzerinde bulunmuştur. Bununla birlikte bireysel nematod türlerine karşı ilacın etkisi bu oranlardan biraz farklı olabilir. Çalışma süresince ilacın hayvanlarda olumsuz bir etkisi gözlenmemiştir.

Anahtar sözcükler: Sığır, gastrointestinal nematod, eprinomectin, tedavi

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Introduction

The macrocyclic lactones have a very high (>98%) efficacy against all stages (including inhibited larvae) of the common cattle nematodes (1). Due to the fact that most of the macrocyclic lactones are excreted through milk, their use in dairy cattle has not been recommended with the exception of moxidectin and especially eprinomectin, which have below-threshold-limits concentrations in milk. Only 0.1% of the total dose of eprinomectin is eliminated in milk, resulting in no withholding period for milk worldwide (2).

Short or long coat length, coat being dry or wet prior to drug administration, or exposure to rain or sunshine post-administration have been reported to have no significant effects on efficacy of eprinomectin (3,4). Results obtained from some studies (3-7) on efficacy of topical eprinomectin administration are summarized in Table 1. Up-to-date records show no study regarding eprinomectin treatment in Turkey.

Materials and methods

Study design and animals: A field trial was conducted in a cattle farm located in the Adapazari district of Sakarya province in May and July, 2009. Adapazari is located in the northwest of Turkey and has semi humid/humid climatic conditions with warm summers and cool winters. Before beginning the trial (day -3), individual fecal samples were collected from the rectums of 55 grazing cattle (Holstein or Holstein crossbreed) without an anthelmintic treatment history in the 4 months prior to the trial. Based on fecal egg counts, 25 cows 2 to 6 years old were selected for the trial and the animals were allocated into 2 groups having near arithmetic and geometric means of eggs per gram feces (EPG) (17 animals for treatment and 8 for untreated control). Three days later (day 0), the treatment group was treated with eprinomectin. Rectal fecal sampling from each trial animal was repeated on days 0, 3, 10, and 17.

Table 1. Studies of eprinomectin efficacy on nematodes in induced and/or naturally infected cattle.

	Shoop et al. (5)		Gogolewski et al. (3)		Pitt et al. (4)		Williams et al. (6)		Yazwinski et al. (7)	
	Adult	Larva	Adult	Larva	Adult	Larva	Adult	Larva	Adult	Larva
<i>Haemonchus placei</i>	≥99%	≥99%	>99.5%	-	-	-	>99%	-	100%	-
<i>Haemonchus contortus</i>	-	-	-	-	>99%	>99%	-	-	-	-
<i>Ostertagia ostertagi</i>	≥99%	≥99%	>99.5%	>99.5%	>99%	>99%	-	-	99.9%	100%
<i>Ostertagia</i> spp.	-	-	-	-	-	-	>99%	>99%*	-	-
<i>Trichostrongylus axei</i>	≥99%	≥99%	>99.5%	-	>99%	>99%	>99%	-	100%	-
<i>T. colubriformis</i>	≥99%	≥99%	-	-	-	>99%	>99%	-	-	-
<i>Cooperia oncophora</i>	≥99%	≥99%	>99.5%	-	-	-	-	-	99.8%	-
<i>C. punctata</i>	≥99%	≥99%	-	-	-	-	-	-	99.6%	-
<i>C. surnabada</i>	-	-	-	-	-	-	-	-	98.9%	-
<i>C spatulata</i>	-	-	-	-	-	-	-	-	98.3%	-
<i>Cooperia</i> spp.	-	-	>99.5%	-	>99%	>99%	>99%	>99%	-	100%
<i>Nematodirus helvetianus</i>	≥99%	≥99%	>99.5%	>99.5%	>99%	>99%	-	-	99.7%	100%
<i>Oesophagostomum radiatum</i>	≥99%	≥99%	>99.5%	-	>99%	>99%	>99%	-	100%	100%
<i>Bunostomum phlebotomum</i>	-	-	-	-	-	-	>99%	-	-	-
<i>Trichuris</i> sp.	-	-	-	-	-	-	-	-	97.8%	84.3%
<i>Dictyocaulus viviparus</i>	≥99%	≥99%	>99.5%	-	>99%	>99%	>99%	-	100%	-

* Inhibited 4th stage larvae included

Drug dose and administration: A 0.5% pour-on formulation of eprinomectin (Eprinomec 0.5% Dökme Çözelti, TOPKİM İlaç AŞ) at the recommended dose of 1 mL/10 kg body weight (bw) (0.5 mg active ingredient/kg bw) was applied topically on the midline of the back of each animal. All animals were inspected for possible adverse effects for the first 24 h following treatment and also on the days (days 3, 10, and 17) fecal sampling was done.

Assessment of gastrointestinal nematode fauna: Small amounts (~ 5 g) from 25 fecal samples (day 0) were well mixed together to prepare fecal culture. Fecal culture was made according to the literature (8). The culture was incubated at 26-27 °C for 3 weeks. Larvae were recovered from the culture using the Baermann technique. The first 100 third stage larvae were identified from their morphological characteristics (8). An individual fecal culture for each animal was not made.

Infection detection and nematode egg counting: Fecal samples were individually examined for infection presence and for counting nematode eggs. The flotation technique was used to detect the presence of infection. EPGs were determined by a modified McMaster technique (8). In this technique, 4.5 g of feces was mixed with 40.5 cm³ of saturated saltwater. Number of eggs under both etched areas [2 × (1 × 1 × 0.15) cm³] of 2 chambers of the McMaster slide were counted and multiplied by 100/3 to calculate EPG. EPG of fecal samples that tested negative with the McMaster technique but positive with the flotation technique was accepted as half of 100/3, approximately 17.

Data analysis

To determine the significance of the difference between control and treatment groups, the t-test for independent samples was applied to the log-transformed EPGs (log (EPG + 1)).

The evaluation of drug effectiveness was based on fecal egg count reduction (FECR). FECR percentage was assessed using arithmetic and geometric means since Dobson et al. (9) emphasized the potential for a biased result when using geometric means in FECR tests. Effectiveness was calculated using the Henderson-Tilton formula (10) and was determined by the following equations:

$$\text{Geometric mean of EPGs} = \text{antilog} [(\Sigma \log(\text{EPG} + 1))/n] - 1$$

$$\text{Arithmetic mean of EPGs} = \Sigma \text{EPG}/n$$

$$\text{Effectiveness (FECR) (\%)} = 100 \times [1 - (\text{Ta}/\text{Ca}) \times (\text{Cb}/\text{Tb})]$$

Ta, Ca, Tb, and Cb represent arithmetic or geometric means of EPGs of the treatment (T) and control (C) groups, before (Cb, Tb) and after treatment (Ca, Ta).

Results

The larval differentiation showed that the gastrointestinal nematode fauna of the 25 trial cows comprised *Nematodirus* (17%), *Strongyloides* (9%), *Trichostrongylus* (24%), *Ostertagia* (20%), *Haemonchus* (12%), *Cooperia* (10%), *Oesophagostomum* (6%), and *Bunostomum* (2%) genera.

EPG values and FECR percentages (drug effectiveness) are presented in Table 2.

There was no significant difference ($P > 0.05$) between the EPGs of control and the treatment groups on the treatment day (day 0), whereas the differences were significant ($P < 0.001$) on days 3, 10, and 17. FECR percentages (effectiveness) according to geometric means were 99.59%, 99.68%, and 99.70% on days 3, 10, and 17, respectively. FECR percentages (effectiveness) according to arithmetic means were 97.65%, 97.91%, and 97.31% on days 3, 10, and 17, respectively (Table 2).

No adverse reactions and no abnormal clinical signs were observed in cattle following treatment.

Discussion

As it may be apparent from Table 1, topical formulation of eprinomectin has been reported to be highly effective against nematodes in cattle (3-7).

Efficacy of eprinomectin on adult and immature stages of nematodes of cattle has been found to be $\geq 99\%$ by Shoop et al. (5), $> 99\%$ by Pitt et al. (4) and Williams et al. (6), and $> 99.5\%$ by Gogolewski et al. (3).

Yazwinski et al. (7) have found eprinomectin to be 99.5% to 100% effective against a wide range of nematodes. As for adults of *Cooperia surnabada*, *C.*

Table 2. EPG values of treatment (T) and control (C) cattle and effectiveness of eprinomectin as assessed by FECR.

Group - Animals	Day -3	Treatment (Day 0)	Day 3	Day 10	Day 17
Treatment					
T-01	200	133	0	0	0
T-02	200	267	0	67	0
T-03	167	133	0	0	0
T-04	233	267	33	0	0
T-05	167	133	0	17*	0
T-06	433	533	0	0	0
T-07	667	800	0	0	0
T-08	333	267	0	0	0
T-09	333	267	17*	0	0
T-10	367	400	17*	0	33
T-11	567	533	0	0	0
T-12	267	267	0	0	0
T-13	933	933	0	0	0
T-14	533	533	0	17*	17*
T-15	367	400	0	0	133
T-16	933	1333	67	0	0
T-17	367	267	0	0	0
Geometric mean (GM)	360.32	353.25	1.2160	0.8008	0.9456
Arithmetic mean (AM)	415.71	439.18	7.8824	5.9412	10.765
Standard deviation	240.88	322.25	17.853	16.709	32.689
Control					
C-01	700	667	667	433	500
C-02	300	233	267	267	467
C-03	200	167	200	400	133
C-04	167	200	133	200	200
C-05	267	167	233	100	433
C-06	333	400	300	200	133
C-07	967	1167	600	467	1033
C-08	433	400	200	133	200
Geometric mean (GM)	356.69	336.05	281.90	241.44	304.73
Arithmetic mean (AM)	420.88	425.13	325.00	275.00	387.38
Standard deviation	276.60	344.55	197.54	141.20	301.80
P value **	>0.05	>0.05	<0.001	<0.001	<0.001
FECR % (geometric)***	-	-	99.59	99.68	99.70
FECR % (arithmetic)***	-	-	97.65	97.91	97.31

* Egg count in the samples MacMaster (-) but flotation (+) was accepted as 17

** t-test for independent samples (treated to control)

*** Fecal egg count reduction % (Drug effectiveness) = $100 \times [1 - (Ta/Ca) \times (Cb/Tb)]$

GMs or AMs of EPGs of control (C) and (T) treatment groups; after (a) and before (b) treatment

spatulata, and *Trichuris* spp., eprinomectin efficacy was 98.9%, 98.3%, and 97.8%, respectively. The authors also reported eprinomectin to be 84.3% effective on fourth-stage larvae of *Trichuris* spp.

Vercruyse et al. (11) state that the use of log-transformed parasite counts or egg counts for reflection of normal distribution to be more appropriate than non-transformed ones and they recommend geometric means for the calculation of percent of effectiveness instead of arithmetic means. However, Dobson et al. (9) report geometric means to often yield biased results and they recommend the use of arithmetic means to estimate efficacy and anthelmintic resistance detection.

Therefore, in the present study both geometric means and arithmetic means were used for calculation of effectiveness.

In our field trial, according the results of analyses from logarithm of (EPG + 1), there was no significant

difference ($P > 0.05$) between control and treatment groups on the treatment day (day 0), whereas the differences were significant ($P < 0.001$) on days 3, 10, and 17. Effectiveness of eprinomectin (FECR percentage) against the gastrointestinal nematode fauna of cattle, which comprised *Nematodirus* (17%), *Strongyloides* (9%), *Trichostrongylus* (24%), *Ostertagia* (20%), *Haemonchus* (12%), *Cooperia* (10%), *Oesophagostomum* (6%), and *Bunostomum* (2%) genera, was 99.59% on day 3, 99.68% on day 10, and 99.70% on day 17 according to geometric means. Meanwhile, eprinomectin effectiveness (FECR percentage) according to arithmetic means was 97.65% on day 3, 97.91% on day 10, and 97.31% on day 17. However, effectiveness against individual nematode species may differ somewhat from effectiveness against total gastrointestinal nematode fauna in cattle mentioned above.

Eprinomectin has been found safe for use in cattle (4-7) and in our trial also we did not observe any adverse effects on treated animals.

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