Protective Efficacy of Doramectin Against Experimental Infestation with *Hyalomma anatolicum* in Rabbits

Khadeega M. Osman* and T. Hassan
Faculty of Veterinary Medicine,
University of Khartoum, Shambat, Sudan

ABSTRACT

The objective of this study was to determine the protective efficacy of doramectin against experimental infestation with *Hyalomma anatolicum* in rabbits. The drug was subcutaneously injected in rabbits at a dose rate of 1 mg/kg body weight, 2 days and 4 days before infestation. The results showed that there was highly significant decrease in weight of engorged female ticks (0.0616±0.0371g) compared with the control (0.3646±0.1424 g), in the weight of egg batch produced, decreased hatchability percentage by 19.83% on day 4 post–injection. The two groups showed significant prolongation of feeding and pre-oviposition periods and decreased oviposition periods. In the two groups, the estimated reproductive factor was significantly reduced, and inhibition of oviposition was 15.45% on day 2 post-injection and 90.79% on day 4 post-injection. It is concluded that doramectin gives protection against tick infestation as well as treatment in animals exposed to ticks.

Key words: Doramectin; efficacy; tick infestation
*Corresponding author: E-mail: khgandato@yahoo.com

INTRODUCTION

Ticks are distributed worldwide and have significantly impact on human and animal health (Gosh *et al*., 2007). They are economically the most important pests of cattle and other domestic species in tropical and subtropical countries and considered as vectors of a number of pathogenic microorganisms including *Babesia*, *Theileria*, rickettsiae, viruses, bacteria and spirochaetes (Jongejan and Uilenberg, 2004). The only food for the ticks is blood. They are voracious blood suckers; loss of blood for their rapid development impoverishes the hosts. Although, economic losses due to ticks are mainly due to the diseases which they transmit (Garcia, 2003), financial losses associated with nagging irritation and depreciation of the value of skins and hides (up to 20-30%) are also significant (Biswas, 2003). *H. anatolicum* has a mixed three-host and two-host pattern of life cycle. The three-host life cycle may convert to a partial two-host type when the ticks feed on rabbits. (Osama, 2012). Doramectin is an avermectin B1 produced from *Streptomyces avermitilis* is a potent endectocide (Saeki *et al*., 1997; Toutain, *et al*., 1997)

widely used in veterinary medicine. It affects gamma amino butyric acid (GABA)-gated chloride channels (Harder, 2002). Gamma amino butyric acid is an inhibitory transmitter in enteric interneurons (Krantis, 2000, Tsai, 2005). This study was designed to evaluate the protective efficacy of doramectin against tick infestation represented by *H. anatolicum* in veterinary field in Sudan.

MATERIALS AND METHODS

Experimental animals

Ten healthy rabbits were divided into 3 groups, each rabbit was infested with 20 (10 males and 10 females) adult *H. anatolicum* ticks. Group 1 was infested with ticks non treated control, group 2 was injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before applying ticks, group 3 was injected with doramectin subcutaneously at dosage rate of 1 mg/kg 4 days before applying ticks. The drug used was Doramectin 1% (Dectomax, Pfizer NY, USA) injectable solution.

Parameters

Feeding periods of ticks were recorded in days. Dropped engorged females from each animal were separately weighed, incubated at 27°C and relative humidity 75% eggs laying. Preoviposition and oviposition periods were recorded in days. The egg batch for each female was weighed in grams. The eggs were incubated at 27°C and relative humidity 75% for hatching and percentage of hatchability was calculated. Estimated reproduction was determined as follows

$$ER = \frac{\text{weight of eggs laid (g)}}{\text{Number of females}} \times \text{estimated hatch (\%)} \times 20\,000 \text{ (\# eggs per g)}$$

RESULTS

Effect of doramectin on the feeding periods, pre-oviposition and oviposition periods of *H. anatolicum*

The feeding period was significantly prolonged ($p \leq 0.05$) in both groups 2and 4 compared with group 1(Table 1). The pre-oviposition period of *H. anatolicum* was significantly prolonged ($p \leq 0.05$) in both groups 2and 4 compared with group 1 (Table 2). There was highly significant ($p \leq 0.05$) reduction in oviposition period in both groups 2 and 4 compared with group 1(Table 3).

Effect of doramectin on weights of engorged females, weights of egg batches and percentage hatchability of *H. anatolicum*

Engorged females from group 3 injected with doramectin 4 days before ticks application showed highly significant decrease ($p \leq 0.05$) in engorgement weights compared with the control group, while engorged females from group 2 injected with doramectin 2 days before ticks application had no significant decrease in engorgement weights (Table 4). Weights of egg batches laid by females of group 3 showed a highly significant decrease ($p \leq 0.05$) in compared with group 1, while weights of egg batches laid by females of group 2 showed no significant decrease (Table 5). There was significant decrease ($p \leq 0.05$) and highly significant decrease in hatchability of eggs in groups 2 and 3 respectively compared with group 1 (Table 6).

Effect of doramectin on estimated reproduction

Estimated reproduction significantly reduced in group 2 and highly significantly reduced in group 4 compared with group 1(Table 7).

Effect of doramectin on inhibition of oviposition

All female ticks in the control group succeeded to lay eggs while in group 2 there was 15.45% inhibition of oviposition and 90.79% inhibition of oviposition in group 3 (Table 8).

DISCUSSION

Avermectins are highly potent drugs and show activity against a wide range of parasites including internal and external parasites (Brander *et al*., 1993). Doramectin as a member of avermectins having these qualities was used in this study and its protective efficacy against *H. anatolicum* infestation was evaluated. Results showed that the drug proved to be highly efficacious as it prevented some ticks from gaining access to the animals and sucking blood. Those which succeeded to feed showed significantly prolonged feeding and pre-oviposition periods and oviposition periods significantly reduced. There were significant decreases in the weights of engorged female ticks among the group injected with doramectin 4 days before infestation indicating that the drug prevented ticks from sucking blood essential for laying eggs and this coincides with the report by FAO (2004) that an ideal acaricide would have sufficient residual effect on female ticks to prevent egg laying. Deficient feeding also significantly reduced oviposition period. Similar results were recorded by Muniz *et al.* (1995) and Gonazales *et al.* (1993) using doramectin against *Boophilus microplus* infestation on cattle. The estimated reproduction for treated groups was significantly reduced. The efficacy of the acaricide was determined by comparing the estimated reproduction (ER) of each group of

treated ticks with that of the control ticks (FAO, 2004). Variations between the two treated groups which received treatment with doramectin 2 and 4 days before tick infestation may be linked with the pharmacokinetics of the drug which showed slow absorption rates after subcutaneous injection as the peak plasma concentrations was 5 days post injection (Wicks *et al.*, 1993; Toutain *et al.*, 1997). It is concluded that doramectin is highly efficacious against tick infestations and can be used prophylactically to reduce pasture contamination with tick population.

Table 1. Effect of doramectin on weight of engorged females of *H. anatolicum*

Groups	Weight of engorged females (g)
Group 1	0.3646±0.14
Group 2	0.1768±0.18
Group 3	0.0616±0.04**

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
**significant ($P \leq 0.01$)

Table 2. Effect of doramectin on weight of eggs of *H. anatolicum*

Groups	Weight of eggs (g)
Group 1	**0.1915±0.09**
Group 2	0.0923±0.12
Group 3	0.0139**±0.02****

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
**significant ($P \leq 0.01$)

Table 3. Effect of doramectin on hatchability % eggs of *H. anatolicum*

Groups	Hatchability %
Group 1	**92.48±3.51**
Group 2	78.67±11.6*
Group 3	19.83**±34.35****

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
*significant ($P\leq 0.05$), **significant ($P\leq 0.01$)

Table 4. Effect of doramectin on feeding period of females *H. anatolicum*

Groups	Feeding period (days)
Group 1	7.7±0.5
Group 2	12±1.14*
Group 3	13±1.73*

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
*significant (P≤ 0.05)

Table 5. Effect of doramectin on pre-oviposition period of females *H. anatolicum*

Groups	Pre-oviposition period (days)
Group 1	5.5±0. 71
Group 2	9.3±4.16*
Group 3	7±0.00

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
*significant (P≤ 0.05)

Table 6. Effect of doramectin on ovposition period of female *H. anatolicum*

Groups	Oviposition period (days)
Group 1	**23.5±0.58**
Group 2	15.67±4.04
Group 3	14**±0.00**

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection

Table 7. Effect of doramectin on Estimated reproduction (ER) of *H. anatolicum*

Groups	ER
Group 1	**971471.2013**
Group 2	821407.3529*
Group 3	89492.53247**

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
*significant (P≤ 0.05), **significant (P≤ 0.01)

Table 8. Effect of doramectin on % inhibition of oviposition of *H. anatolicum*

Groups	% inhibition of oviposition
Group 1	0.00
Group 2	15.45*
Group 3	90.79***

Group 1= untrearted control
Group 2 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 2 days before infection
Group 3 = Injected with doramectin subcutaneously at dosage rate of 1mg/kg 4 days before infection
*significant (P≤ 0.05), ***significant (P≤ 0.001)

REFERENCES

Biswas, S. (2003). Role of veterinarians in the care and management during harvest of skin in livestock species. In Proc. National seminar on lather industry in today′s perspective. Kolkata, India, pp 62-64.

Brander, G. C., Pugh, D. M., Bywater, R. J. and Jenkins, W. L. (1993). *Veterinary Applied Pharmacology and Therapeutics*, 5th edition. Bailliere Tindall, London. pp. 534.

FAO, "Acaricide resistance: diagnosis, management and prevention," in Guidelines Resistance Management and Integrated Parasite Control in Ruminants, pp. 56 . Animal Production and Health Division, Agriculture Department, Food and Agriculture Organization of the United Nations, Rome, Italy, 2004.

Garcia, Z. (2003). Integrated control of *Boophilus microplus* in cattle. In: Proc. 11th Int. Congr. Int. Society for Animal Hygiene, Mexico city, Mexico.

Gonzales, J. C., Muniz, R. A., Farias, A., Goncalves, L. C. and Rew, R. S.(1993). Therapeutic and persistent efficacy of doramectin against *Boophilus microplus* in cattle. *Vet. Parasitol.* **49**(**1**): 107-109.

Gosh, S., Azhahianambi, P. and Yadav, M. P. (2007). Upcoming and future strategies of tick control: a review. *J. Vect. Borne Dis.* **44**: 79-89.

Harder, A. (2002). Chemotherapeutic approaches to nematodes: current knowledge and outlook. *Parasitol. Res*. **88**: 272-277.

Jongejan, F. and G. Uilenberg. (2004). The global importance of ticks. *Parasitology*, **129**: 1-12.

Krantis, A. (2000). GABA in the mammalian enteric nervous system. *News Physiol. Sci*. **15:** 284-290.

Muniz, R. A., Hernandez, F. Lombardero, O., Leite, R. C., Moreno, J., Errecalde, J. and Goncalves, L.C. (1995). Efficacy of injectable doramectin against natural *Boophilus microplus* infestations in cattle. *Am. J. Vet. Res.* **56(4)** 460-463.

Osama, H. (2012). Note on the life cycle of *Hyalomma anatolicum anatolicum* (Acari: Ixodidae) on rabbits and goats. *J. Agric. Vet. Sci* **5(10)**: 53-57).

Saeki, H., Fujii, T. Fukumoto, S-I., Kagota, K., Taneichi, A. Takeda, S. Toutain, P. L., Upson, D. W., Terhune, T. N. and Mckenzie, M. E. (1997): Comparative pharmacokinetics of doramectin and ivermectin in cattle. *Vet. Parasitol*. **72**: 3-8.

Tsai, L. H. (2005). Function of GABAergic and glutamatergic neurons in the stomach. *J. Biomed. Sci.* **12**: 255-266.

Tsukaguchi, M. (1997). Efficacy of doramectin against intestinal nematodes and sarcoptic mange mites in naturally infected sheep. *J. Vet. Med. Sci.* **59:** 129 - 132.

Wicks, S.R., Kaye, B., Weatherley, A.J., Lewis, D. and Davison, E.(1993). Effect of formulation on the pharmacokinetic and efficacy of doramectin. *Vet. Parasitol*. **49(1)**: 17-26.