TÜBİTAK

Turkish Journal of Veterinary and Animal Sciences

http://journals.tubitak.gov.tr/veterinary/

Research Article

Turk J Vet Anim Sci
(2018) 42: 29-33
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doi:10.3906/vet-1707-42

# Comparative clinical and parasitological efficacy of moxidectin pour-on, ivermectin, and piperazine citrate on *Toxocara vitulorum* infection in buffalo calves (*Bubalus bubalis*): a randomized clinical trial

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**Received:** 14.07.2017 • **Accepted/Published Online:** 06.01.2018 • **Final Version:** 16.02.2018

**Abstract:** *Toxocara vitulorum* is an important intestinal nematode that causes great economic losses in farm animals worldwide. However, there is a paucity in the development of effective and safe anthelmintic drugs against this parasite in buffalo calves. Therefore, this study aimed to evaluate the antitoxocariasis efficacy of moxidectin, ivermectin, and piperazine citrate in buffalo calves. To achieve this purpose, 130 buffalo calves were randomly selected from Kafr El-Sheikh governorate, Egypt, and were examined for the presence of *Toxocara vitulorum*. Thirty calves were identified to be infected. Diseased calves were allocated randomly into 3 groups (10 each). The first group received moxidectin pour-on, the second group received ivermectin, and the third received piperazine citrate. Clinical, hematological, and parasitological responses of treated animals were assessed at 7, 14, 28, and 56 days after treatment. The fastest clinical recovery and complete elimination of parasite eggs from feces were exhibited in calves treated with moxidectin. Significant inhibition of eosinophil counts was observed in all treated calves at 1 week following treatment. From the obtained data, we conclude that moxidectin is an alternative effective and safe drug for treatment of buffalo calves infected with *Toxocara vitulorum* when administrated in the pour-on route under field conditions.

**Key words:** *Toxocara vitulorum*, buffalo calves, moxidectin pour-on, Egypt

## 1. Introduction

*Toxocara vitulorum*, a large gastrointestinal nematode, affects ruminants and causes clinical problems in calves worldwide (1,2). It commonly infects buffalo calves, especially in tropical and subtropical countries (3). *T. vitulorum* can also cause clinical problems in adult cattle (4). Young calves acquire the infection mainly through the colostrum of their infected dams during the first days after birth (1). The larvae penetrate the wall of the calves' small intestines 2–8 h later and go straight to the liver via the portal vein, while a few enter the mesenteric lymph nodes. Next, the infection spreads to other organs of the body, including the lungs, muscles, brain, kidneys, and peripheral lymph nodes (5). Generally, infection with *T. vitulorum* is frequently manifested by diarrhea, poor performance, and poor growth rate (6), but high morbidity and mortality in buffalo calves, particularly in calves aged 15 to 50 days, were recorded (5). In other cases, intestinal obstruction due to heavy infestation may manifest the disease (7).

In Egypt, infestation with *T. vitulorum* in buffalo calves is a common clinical problem causing economic losses (8). Unfortunately, there is paucity in anthelmintic development for use in treatment in this widespread disease in buffalo calves. Therefore, this study was planned to compare the anthelmintic effects of moxidectin pour-on, ivermectin, and piperazine citrate in buffalo calves naturally infected with *T. vitulorum*. The clinical efficacy of moxidectin and ivermectin was evaluated in a previous study (9) in calves naturally infected with *T. vitulorum*, but that study included bovine calves and the moxidectin was administrated subcutaneously. The route of drug administration affects its efficacy (10); therefore, moxidectin was used in this study in pour-on form. To the best of the authors' knowledge, this is the first study to apply such a comparative evaluation in buffalo calves naturally infected with *T. vitulorum.*

## 2. Materials and methods

### 2.1. Animals

A total of 130 buffalo calves from smallholder farms in Kafr El-Sheikh governorate, Egypt, were examined for the presence of *T. vitulorum.* The calves' ages ranged from 2 weeks to 2 months. The animals were showing diarrhea (n

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= 34) or constipation (n = 21), or else they were apparently healthy (n = 75). All institutional and national guidelines for the care and use of animals were followed according to the Egyptian Medical Research Ethics Committee (No. 14–126).

**2.2. Clinical examination**

Complete case history and physical examination for each animal were obtained according to the standard methods (11). Body condition, fecal consistency, presence of abdominal pain, respiratory rate, heart rate, rectal temperature, appetite, and coat condition were scored and the sum of all of them was recorded for each animal before treatment and at 7, 14, 28 and 56 days after treatment (12).

**2.3. Parasitological examination**

Fecal samples were collected directly from the rectum of each calf and were examined for the presence of *T. vitulorum* using standard techniques (13). The fecal egg count was examined before treatment to confirm the presence of the infection and after treatment to evaluate the drug's efficacy for the elimination of the parasite and consequently to select the potential anthelmintic candidate for *T. vitulorum* infection.

**2.4. Hematological examination**

Blood samples were collected from each animal via jugular vein puncture and complete blood count was performed using an electronic cell counter (MS9; Rhône Mérieux, France). Total blood count was performed together with clinical and parasitological examinations.

**2.5. Treatment**

Of 55 buffalo calves clinically infected by *T. vitulorum*, 30 calves were identified as having positive fecal egg counts and were allocated randomly into three groups (10 each). Calves in the first group were treated with moxidectin pour-on (Cydectin Pour-On, Fort Dodge Animal Health, Japan) at a dose rate of 0.5 mg $kg^{-1}$. Ivermectin (Merck Sharp, USA) was administrated subcutaneously to the calves of the second group at a dose rate of 0.2 mg $kg^{-1}$. Calves in the third group received an oral dose (300 mg $kg^{-1}$) of piperazine citrate (El-Nasr Company, Egypt). A single dose of each drug under investigation was used in this study. Clinical, hematological, and parasitological responses were determined in each treated group before treatment as well as on days 7, 14, 28, and 56 following the treatments to evaluate the efficiency of each used regimen.

**2.6. Data analysis**

Analysis of data was done using a commercial statistical software program (JMP for Windows Version 5.1, SAS Institute, Cary, NC, USA). First the Kruskal–Wallis nonparametric ANOVA test was used to examine the homogeneity of groups of calves, the fecal egg counts, and the clinical index scores on the first day of admission. Then the main effect of intervention and time was determined using repeated measures MANOVA on the basis of hematological parameters and fecal egg count data. The Wilks lambda test was selected for assessment of within-group differences and evidence of time × drug interaction. In the case that a statistically significant difference between treated groups was exhibited by the Wilks lambda test, one-way ANOVA with post hoc Tukey–Kramer HSD multiple comparison tests were used to identify which group was statistically significant different from the other groups. Differences between means at $P < 0.05$ were considered significant. At different time points, the effect of treatments on clinical sum scores was evaluated statistically by using the Kruskal–Wallis with post hoc Dunn multiple comparison tests. At $P < 0.05$, the result was considered significant.

## 3. Results

The severity of clinical signs varied according to the age of calf and the degree of infestation without any alteration in body temperature in calves. Diarrhea was observed in 20 (67%) infected calves. On the other hand, 9 (30%) calves exhibited constipation with dark discoloration of feces and slight tympany. Pica was shown in 19 (63%) calves. One week after treatment by anthelmintic drugs, these clinical signs start to disappear and the clinical sum scores differed significantly in the moxidectin-treated group in comparison with other treatment groups (Table 1). Two weeks later, complete clinical recovery was observed in calves treated with moxidectin, indicating the clinical efficacy of moxidectin by pour-on route in treatment of buffalo calves suffering from *T. vitulorum*.

On the hematological level, eosinophils were the sole parameter that showed significant variation in *T. vitulorum*-infected calves. One week after treatment, a significant reduction of eosinophil counts was observed, especially in moxidectin- and piperazine citrate-treated calves. Eight weeks after treatment by moxidectin and piperazine citrate, eosinophil counts had returned to the normal level (Table 2). The infection had completely disappeared from the feces of calves treated with 0.5 mg $kg^{-1}$ moxidectin pour-on 1 week after treatment (Table 3). Taken together, the clinical efficacy with significant reductions in eosinophil counts and disappearance of helminthic eggs in animal feces in moxidectin-treated calves highlights the superiority of this medication in the treatment of buffalo calves naturally infected with *T. vitulorum*.

## 4. Discussion

In tropical countries, toxocariasis is one of the most serious parasitic diseases causing high mortality and morbidity in buffalo calves (14). The adult buffalo is the source of infection while suckling calves play a potential

**Table 1.** Clinical index scores (median) in buffalo calves naturally infected with *T. vitulorum* and treated with moxidectin (0.5 mg $kg^{-1}$), ivermectin (200 μg $kg^{-1}$), or piperazine citrate (300 mg $kg^{-1}$).

| Drug | Days after treatment | | | | |
|---|---|---|---|---|---|
| | 0 | 7 | 14 | 28 | 56 |
| Moxidectin (n = 10) | 10 | 7 [a] | 1 [a] | 0 [a] | 0 |
| Ivermectin (n = 10) | 11 | 10 [b] | 6 [b] | 3 [b] | 1 |
| Piperazine citrate (n = 10) | 11 | 9 [b] | 5 [b] | 1 [a] | 0 |

[a,b]: In the same column, medians with different superscripted letters are significantly different at $P < 0.05$.

**Table 2.** Eosinophil counts (cells/μL, mean ± SD) in buffalo calves infected with *T. vitulorum* and treated with moxidectin (0.5 mg $kg^{-1}$), ivermectin (0.2 mg $kg^{-1}$), or piperazine citrate (300 mg $kg^{-1}$).

| Drug | Before treatment | Days after treatment | | | |
|---|---|---|---|---|---|
| | | 7 | 14 | 28 | 56 |
| Moxidectin (n = 10) | 2524 ± 65 | 1232 ± 25 [a] | 910 ± 48 [a] | 750 ± 55 [a] | 710 ± 64 [a] |
| Ivermectin (n = 10) | 2498 ± 78 | 1859 ± 58 [b] | 1398 ± 49 [b] | 1214 ± 57 [b] | 1129 ± 36 [b] |
| Piperazine citrate (n = 10) | 2436 ± 93 | 1388 ± 37 [a] | 864 ± 27 [a] | 612 ± 65 [a] | 620 ± 24 [a] |

[a,b]: In the same column, means with different superscripted letters are significantly different at $P < 0.05$.
MANOVA fit, $P < 0.01$. Wilks lambda test for treatment × time interaction, $P < 0.05$

**Table 3.** Fecal egg counts in buffalo calves infected with *T. vitulorum* and treated with moxidectin (0.5 mg $kg^{-1}$), ivermectin (0.2 mg $kg^{-1}$), or piperazine citrate (300 mg $kg^{-1}$).

| Drug | Before treatment | Days after treatment | | | |
|---|---|---|---|---|---|
| | | 7 | 14 | 28 | 56 |
| Moxidectin (n = 10) | 10.000 ± 1500 | 0.0 [a] | 0.0 [a] | 0.0 [a] | 0.0 [a] |
| Ivermectin (n = 10) | 11.000 ± 2000 | 1500 ± 110 [b] | 1500 ± 90 [a] | 1200 ± 110 [b] | 600 ± 55 [b] |
| Piperazine citrate (n = 10) | 11.000 ± 1600 | 2000 ± 90 [c] | 1400 ± 70 [a] | 1000 ± 105 [b] | 150 ± 30 [c] |

[a,b,c]: In the same column, means with different superscripted letters are significantly different at $P < 0.05$.
MANOVA fit, $P < 0.01$. Wilks lambda test for treatment × time interaction, $P < 0.05$.

role for maintenance of the infection. The larvae do not develop into adults in the adult animal but remain as third-stage larvae; when infected dams become pregnant, the larvae migrate from the liver to the mammary glands and suckling calves receive the infection via milk (9). Three to four weeks later, the larvae develop into adults and then begin shedding thousands of eggs in the feces of infected calves (15). Therefore, treatment of infected young calves is critical in controlling toxocariasis. In this regard, piperazine, pyrantel, febantel, oxfendazole, levamisole (16), ivermectin (17), fenbendazole (18), and eprinomectin (15) have exhibited efficacy against *T. vitulorum*. However, side effects including diarrhea and restlessness with parasite resistance were observed in some animals treated with piperazine citrate and other traditionally used antitoxocariasis agents (9). Therefore, searching for more efficacious and safe antitoxocariasis candidates is an urgent issue. This is the first study to

compare the antitoxocariasis efficacy of moxidectin pour-on with other traditional antitoxocariasis drugs in buffalo calves. Moxidectin is a potent, broad-spectrum endectocide known for its efficacy against a wide range of nematodes (19). Fortunately, no side effects were reported from the usage of moxidectin by pour-on method in buffalo (20).

Calves under investigation were showing diarrhea, constipation, and pica at variable rates. In contrast, a previous study stated that diarrhea was recorded in 100% of calves with toxocariasis (20). This discrepancy might be attributed to the presence of a massive number of parasites in calves' intestinal tracts, causing constipation. Eosinophilia detected in diseased calves was in accordance with findings of a previous report (21).

Interestingly, the clinical index scores differed significantly among treatment groups, suggesting rapid response in calves treated with moxidectin pour-on. In the present study, the inferior efficacy of ivermectin compared with moxidectin and piperazine citrate may be attributed to the development of resistance to such drugs due to misuse.

On the parasitological level, the present study revealed the supremacy of moxidectin pour-on in the treatment of buffalo calves naturally infected with *T. vitulorum*. In a similar comparison study in bovine calves, moxidectin and ivermectin were administered subcutaneously and exhibited equal efficacy in the treatment of *T. vitulorum* (15). The differences in animal species and routes of anthelmintic drug administration might explain such inconsistency.

At the end of the study, although there was no significant difference in the recovery rates in calves, moxidectin pour-on showed rapid recovery when compared with other treatments. Moreover, no drugs showed any adverse effects, although ivermectin and piperazine have been found to cause side effects in other studies (22). In lactating buffalo, rapid and high excretion of moxidectin in the milk should be considered (23). Fortunately, infection with *T. vitulorum* is more common in calves; consequently, no precaution need be considered in lactating buffalo.

The limitations of the present study should be mentioned. First, the clinical signs are not typical for all treatment groups, as infected calves may be constipated or diarrheic. We overcame this problem by random allocation of treatment groups. Therefore, each group had all forms of clinical signs. The second limitation is that the dose of the drugs was not the same. However, the dose instructions of the manufacturers were followed.

In summary, moxidectin can be used as a conventional anthelmintic for the treatment of buffalo calves naturally infected with *T. vitulorum* by the pour-on method simultaneously with the application of appropriate management procedures. Further studies are warranted to analyze the synergistic or antagonistic effects of these drugs when used in combination with each other and to determine the best effective composition ratio for the growth inhibition of *T. vitulorum* in clinical practice.

**Acknowledgments**

The authors would like to thank the staff members of the Fort Dodge Animal Health Pharmaceutical Company, Japan, for providing their product (moxidectin). The authors would also like to thank the owners and staff of the studied farms in Egypt.

## References

1. Avcıoğlu H, Balkaya İ. Prevalence of *Toxocara vitulorum* in calves in Erzurum, Turkey. Kafkas Univ Vet Fak 2011; 17: 345-347.
2. Venjakob PL, Thiele G, Clausen PH, Nijhof AM. *Toxocara vitulorum* infection in German beef cattle. Parasitol Res 2017; 116: 1085-1088.
3. Raza M, Murtaza S, Ayaz M, Akhtar S, Arshad H, Basit A, Bachaya HA, Ali M, Khan MI. *Toxocara vitulorum* infestation and associated risk factors in cattle and buffalo at Multan district, Pakistan. Science International (Lahore) 2013; 25: 291-294.
4. Samimi AS, Rezaei M, Radfar MH, Nikvarz A, Khedri J. *Toxocara vitulorum* in an adult Holstein cow from arid area: a case report. Sci Parasitol 2016; 17: 53-56.
5. Starke WA, Machado RZ, Bechara GH, Zocoller MC. Skin hypersensitivity tests in buffaloes parasitized with *Toxocara vitulorum*. Vet Parasitol 1996; 63: 283-290.
6. Ahmed R, Wani Z, Allaie I, Bushra M, Hussain H. *Toxocara vitulorum* in a suckling calf: a case study. J Parasit Dis 2016; 40: 1330-1331.
7. Van der Steen L, Pardon B, Sarre C, Valgaeren B, Van Hende D, Vlaminck L, Deprez P. Intestinal obstruction by *Toxocara vitulorum* in a calf. Vlaams Diergeneeskundig Tijdschrift 2014; 83: 299-305.
8. Sultan K, Omar M, Desouky AY, El-Seify MA. Molecular and phylogenetic study on *Toxocara vitulorum* from cattle in the mid-Delta of Egypt. J Parasit Dis 2015; 39: 584-587.
9. Avcioglu H, Balkaya I. Efficacy of eprinomectin against *Toxocara vitulorum* in calves. Trop Anim Health Prod 2011; 43: 283-286.
10. Salama AA, AbouLaila M, Terkawi MA, Mousa A, El-Sify A, Allaam M, Zaghawa A, Yokoyama N, Igarashi I. Inhibitory effect of allicin on the growth of *Babesia* and *Theileria equi* parasites. Parasitol Res 2014; 113: 275-283.

11. Radostits O, Gay CC, Hinchcliff K, Constable P, Jacobs D, Ikede B. Veterinary Medicine: A Textbook of the Diseases of Cattle, Sheep, Pigs, Goats and Horses. St Louis, MO, USA: Elsevier; 2007.

12. Ihler CF. A field survey on anthelmintic resistance in equine small strongyles in Norway. Acta Vet Scand 1995; 36: 135-143.

13. Kelly WR. Veterinary Clinical Diagnosis. St Louis, MO, USA: Elsevier Science Health Science Division; 1984.

14. Srivastava A, Sharma D. Studies on the occurrence, clinical features and pathomorphological aspects of ascariasis in buffalo calves. Veterinary Research Journal 1981; 4: 160-162.

15. Roberts JA. The egg production of *Toxocara vitulorum* in Asian buffalo (*Bubalus bubalis*). Vet Parasitol 1990; 37: 113-120.

16. Roberts JA. *Toxocara vitulorum*: treatment based on the duration of the infectivity of buffalo cows (*Bubalus bubalis*) for their calves. J Vet Pharmacol Ther 1989; 12: 5-13.

17. Mahieu M, Naves M. Incidence of *Toxocara vitulorum* in creole calves of Guadeloupe. Trop Anim Health Prod 2008; 40: 243-248.

18. Davila G, Irsik M, Greiner EC. *Toxocara vitulorum* in beef calves in North Central Florida. Vet Parasitol 2010; 168: 261-263.

19. Cobb R, Boeckh A. Moxidectin: a review of chemistry, pharmacokinetics and use in horses. Parasit Vectors 2009; 25: S5.

20. El-Khodery SA, Ishii M, Osman SA, Al-Gaabary MH. Comparative therapeutic effect of moxidectin, doramectin and ivermectin on psoroptes mites infestation in buffalo (*Bubalus bubalis*). Trop Anim Health Prod 2009; 41: 1505-1511.

21. Islam K, Shil N, Islam M, Das S. Incidence of ascariasis in calves reared under rural condition. Bangladesh J Vet Med 2012; 3: 21-23.

22. Rajkhowa S, Bujarbaruah K, Rajkhowa C. Haemato-biochemical changes in ascarosis of Mithun calves. Indian Vet J 2004; 81: 571-572.

23. Muller KR, Dwyer C. Suspected levamisole intoxication in calves. N Z Vet J 2016; 64: 257-260.