Dose confirmation study of a 10 g liter^{-1} non-aqueous injectable formulation of moxidectin against naturally acquired infestations of cattle lice on cattle in New York

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Abstract: This study demonstrated that a moxidectin 10 g liter^{-1} non-aqueous injectable formulation, injected subcutaneously in cattle at a dose of either 0.2 or 0.3 mg moxidectin kg^{-1} body weight was safe and highly effective in the almost complete elimination (>99% efficacy) for 56 days of both the nymphal and adult stages of naturally acquired infestations of the three species of sucking lice commonly found on cattle, *Haematopinus eurysternus* (Nitzsch), *Linognathus vituli* (L), and *Solenopotes capillatus* (Enderlein). The level of efficacy was never greater than 90% with either dose against *Bovicola bovis* (L). No adverse effects were noted on cattle from either of the moxidectin doses used.

Keywords: cattle biting louse; *Bovicola bovis*; shortnosed cattle louse; *Haematopinus eurysternus*; longnosed cattle louse; *Linognathus vituli*; little blue cattle louse; *Solenopotes capillatus*; moxidectin

1 INTRODUCTION

Cattle in New York are often infested with more than one species of cattle louse. In a previous survey that documented the prevalence of cattle lice in New York, it was reported that all herds examined were infested with lice.[1] Animals infested with cattle lice are often hard to manage and show signs of anemia and reduced productivity.[2] Cattle weight gains have been shown to be affected by heavy louse infestations.[3]

Moxidectin, [6*R*,23*E*, 25*S*(*E*)]-5-*O*-demethyl-28-deoxy-25-(1,3-dimethyl-1-butenyl)-6,28-epoxy-23-(methoxyimino)milbemycin B, recently registered as a pour-on formulation in the United States, provides control of both external and internal parasites of cattle, including cattle lice, mites, cattle grubs, lungworms, and gastro-intestinal roundworms. The objective of this study was to confirm the effectiveness of moxidectin in a 10 g liter^{-1} non-aqueous injectable formulation following subcutaneous administration to cattle at a dose of either 0.2 or 0.3 mg moxidectin kg^{-1} body weight (bw) against cattle lice.

2 MATERIALS AND METHODS

2.1 Experimental materials used

Moxidectin is a second-generation endectocide manufactured by Fort Dodge Animal Health, chemically classified as a milbemycin in the macrocyclic lactone family. The active ingredient used in this study was administered in a 10 g liter^{-1} non-aqueous injectable formulation, (Cydectin™, ex Fort Dodge Animal Health)

2.2 Test animals

A total of 42 Hereford cross-breed calves of both sexes were purchased from local livestock markets in New York State. Body weights on the day prior to treatment (Day −1) ranged from 126.7 to 261.5 kg.

Shortly after purchase the 42 animals were double ear-tagged and maintained together as a single group. Following treatment, the animals were maintained by treatment group in three separate pens in a modified three-sided barn with unrestricted access to the outdoors. Pens were designed with double solid fences to prevent contact with animals from different groups. Animal rations consisted of haylage and corn silage. Free-choice water was provided *ad libitum*. There were no suspected contaminants in either the feed or water.

2.3 Experimental design

A randomized complete block design consisting of 10 blocks with three animals each was used. Details of the three groups are presented in Table 1.

2.4 Selection and allocation of animals

All cattle were naturally infested with some or all of four cattle louse species. A pre-study assessment was performed on Day −6 in order to evaluate the overall

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Table 1. Identification and details of treatment groups

Treatment group	Test article	Moxidectin dose (mg AI kg^{-1} bw)	Number of animals
1	Blank vehicle	0.0	10
2	Moxidectin non-aqueous injectable	0.2	10
3	Moxidectin non-aqueous injectable	0.3	10

louse infestation of the group and to eliminate any animals with low counts. Nine animals were eliminated for low lice infestations, and one animal eliminated because of poor disposition. Lice counts were made on the remaining 32 animals on Day −1 (14 January 1998). Four species of lice were observed, the cattle biting louse, *Bovicola bovis* (L), the shortnosed cattle louse, *Haematopinus eurysternus* (Nitzsch), the longnosed cattle louse, *Linognathus vituli* (L), and the little blue cattle louse, *Solenopotes capillatus* (Enderlein). The 30 animals with the highest *S capillatus* counts were ranked in decreasing louse infestation order and the animals arranged in 10 blocks of three animals each. Within each block, animals were assigned to either Group 1, 2 or 3 by draw-from-the-hat.

2.5 Animal health and treatment

Animals were first examined for abnormalities at the potential injection site prior to treatment and further observed for adverse reactions to treatment at 2–4 h post-treatment on Day 0. Additionally, the injection site for each animal was examined for abnormalities on Days 7 and 14. Daily health observations were made on the grouped animals.

On Day −1 cattle were moved onto the scale, weighed, and doses calculated for each animal based on its body weight. Treatment occurred on Day 0 (15 January 1998) and application was made subcutaneously on the left side of the neck just in front of the shoulder.

2.6 Procedures and data recorded

Animals were individually restrained in a squeeze chute, and their lice counted from selected predilection sites (specific locations on cattle that lice frequent) with the aid of high-intensity halogen lamps. Lice were counted and identified by species and life stage (adults or nymphs) in eight examination sites by individuals blinded to treatment. The location and dimensions of these sites were as follows: topline (5×15 cm), withers (5×15 cm), around right eye (10×15 cm), right cheek (5×10 cm), muzzle (5×25 cm), around left eye (10×15 cm), left cheek (5×10 cm), and dewlap (5×15 cm). These sites include the predilection sites of the four species of lice.[4] Speciation was consistent with published keys.[5] The total number and stage of each species of lice were recorded on Days −1, 7, 14, 21, 28, 35, 42, 49, and 56.

2.7 Calculations and statistical analysis

Data analyzed included lice counts from Day −1 and post-treatment Days 7, 14, 21, 28, 35, 42, 49, and 56. Statistical analyses on lice counts were performed separately for each species and total counts combining adults and nymphs. If fewer than six of the 10 animals in the control group were infested with a particular species of louse, the infestation was judged as insufficient for analysis. These lice counts were transformed by a $Y = \log_{10}(\text{count} + 1)$ transformation prior to statistical analysis. The transformed lice counts were analyzed using a two-way Analysis of Variance (ANOVA) with block and treatment effects in the model. The treatment effect in the ANOVA was tested against the residual error at the 5% level of significance. The Least Square Means (Lsmean) for all groups were obtained and the treated groups were compared to the control group by the one-sided Dunnett's *t*-test at the 5% level of significance. Percentage efficacy based on either arithmetic or geometric means was calculated for analyzed post-treatment lice counts, as follows:

$$\% \text{ Efficacy} = \frac{[\text{Mean Count Control} - \text{Mean Count Treated}]}{\text{Mean Count Control}} * 100$$

where the geometric mean was calculated as $\text{Gmean} = 10^{\text{LCOUNT}} - 1$.

3 RESULTS AND DISCUSSION

3.1 Lice counts

Data analysis was conducted using both geometric and arithmetic means. Similar results were obtained with both analyses, therefore, only geometric means are presented. Mean lice counts and percent efficacy for the four louse species are presented in Tables 2 and 3. The number of animals positive for lice in each group are documented in Table 4. Cattle in this trial were considered to be moderately parasitized, based on the lice counts observed in the blank vehicle-treated controls (Tables 2 and 3). The 10 g liter^{-1} non-aqueous injectable formulation of moxidectin was >99% effective against all three species of sucking lice, the shortnosed cattle louse *(H eurysternus)*, the longnosed cattle louse *(L vituli)*, and the little blue cattle louse *(S capillatus)* at both 0.2 and 0.3 mg moxidectin kg^{-1} bw (Tables 2 and 3) from Days 7 through 56 post-treatment. The cattle biting louse, *B bovis*, seemed to be slightly affected by the drug on Day 14 at both doses, and on Day 7 at the higher dose.

		Geometric mean[a]			Percentage efficacy[b]	
		Moxidectin (mg kg^{-1} bw)			Moxidectin (mg kg^{-1} bw)	
Species of louse	Day	0	0.2	0.3	0.2	0.3
Bovicola bovis	−1	22.0	19.2	29.6		
	7	33.3	38.7	12.2*	–	63.21
	14	35.8	27.7	33.0	22.60	7.59
	21	19.3	31.5	30.9	–	–
	28	16.9	21.7	29.8	–	–
	35	13.5	40.1	31.2	–	–
	42	13.4	71.5	32.5	–	–
	49	16.0	49.6	17.5	–	–
	56	13.4	45.4	25.6	–	–
Haematopinus eurysternus	−1	4.5	3.8	1.4		
	7	3.4	0.0*	0.0*	100	100
	14	3.6	0.0*	0.0*	100	100
	21	19.7	0.0*	0.1*	100	99.24
	28	17.7	0.0*	0.1*	100	99.60
	35	8.8	0.0*	0.0*	100	100
	42	6.1	0.0*	0.0*	100	100
	49	5.3	0.0*	0.0*	100	100
	56	4.7	0.0*	0.0*	100	100

Table 2. Geometric means and percentage efficacy of total (nymphs and adults) *Bovicola bovis* and *Haematopinus eurysternus* counts for vehicle-treated controls and moxidectin non-aqueous injectable-treated animals

[a] *Treatment group means significantly different from controls: alpha = 0.05.
[b] (−) indicates the% efficacy was < 0.

		Geometric mean[a]			Percentage efficacy	
		Moxidectin (mg kg^{-1} bw)			Moxidectin (mg kg^{-1} bw)	
Species of louse	Day	0	0.2	0.3	0.2	0.3
Linognathus vituli	−1	43.7	43.5	26.6		
	7	27.7	0.0*	0.0*	100	100
	14	28.5	0.0*	0.0*	100	100
	21	17.8	0.0*	0.0*	100	100
	28	12.9	0.0*	0.0*	100	100
	35	18.5	0.0*	0.0*	100	100
	42	8.2	0.0*	0.0*	100	100
	49	8.7	0.0*	0.0*	100	100
	56	7.7	0.0*	0.0*	100	100
Solenopotes capillatus	−1	72.4	78.4	71.2		
	7	74.5	0.0*	0.0*	100	100
	14	66.4	0.0*	0.0*	100	100
	21	86.5	0.0*	0.2*	100	99.73
	28	68.4	0.0*	0.2*	100	99.69
	35	69.0	0.0*	0.2*	100	99.64
	42	61.8	0.0*	0.2*	100	99.68
	49	52.9	0.0*	0.2*	100	99.67
	56	50.5	0.0*	0.1*	100	99.77

Table 3. Geometric means and percentage efficacy of total (nymphs and adults) *Linognathus vituli* and *Solenopotes capillatus* counts for vehicle-treated controls and moxidectin non-aqueous injectable-treated animals

[a] *Treatment group means significantly different from controls: alpha = 0.05.

However, at neither of these counting times did the efficacy reach >90%, and there was no efficacy for this species after Day 21.

3.2 Animal health

At the pre-treatment injection-site observation, only one animal had a noticeable nodule at the injection site, and this nodule was not observed post-treatment. Two animals were observed rubbing the left side and one animal had a bloody nose from jumping the fence. None of the pretreatment observations was present in these two post-treatment observations and all animals were noted as being normal at the injection site. No adverse effects of the moxidectin 10 g liter^{-1} non-

Table 4. Number of animals positive for lice following treatment with moxidectin non-aqueous injectable at two dose levels

		No of positive animals in group/total no of animals in group		
		Moxidectin dose (mg kg^{-1} bw)		
Species of louse	*Day*	*0*	*0.2*	*0.3*
Bovicola bovis	7	10/10	10/10	9/10
	14	10/10	10/10	10/10
	21	10/10	10/10	10/10
	28	10/10	10/10	10/10
	35	10/10	10/10	10/10
	42	10/10	10/10	10/10
	49	10/10	10/10	10/10
	56	10/10	10/10	10/10
Haematopinus eurysternus	7	7/10	0/10	0/10
	14	6/10	0/10	0/10
	21	9/10	0/10	1/10
	28	10/10	0/10	1/10
	35	9/10	0/10	0/10
	42	8/10	0/10	0/10
	49	6/10	0/10	0/10
	56	6/10	0/10	0/10
Linognathus vituli	7	10/10	0/10	0/10
	14	10/10	0/10	0/10
	21	10/10	0/10	0/10
	28	10/10	0/10	0/10
	35	10/10	0/10	0/10
	42	10/10	0/10	0/10
	49	10/10	0/10	0/10
	56	9/10	0/10	0/10
Solenopotes capillatus	7	10/10	0/10	0/10
	14	10/10	0/10	0/10
	21	10/10	0/10	1/10
	28	10/10	0/10	1/10
	35	10/10	0/10	1/10
	42	10/10	0/10	1/10
	49	10/10	0/10	1/10
	56	10/10	0/10	1/10

aqueous injectable formulation at a dose of either 0.2 or 0.3 mg moxidectin kg^{-1} bw or of the injectable vehicle were noted in this trial.

4 CONCLUSION

This study demonstrated that the moxidectin 10 g liter^{-1} nonaqueous injectable formulation, injected subcutaneously in cattle at a dose of either 0.2 or 0.3 mg moxidectin kg^{-1} bw was safe and highly effective in the almost complete elimination (>99% efficacy) for 56 days of both the nymphal and adult stages of naturally acquired infestations of the three species of sucking lice commonly found on cattle, *H eurysternus*, *L vituli*, and *S capillatus*. The level of efficacy was never greater than 90% with either dose of moxidectin non-aqueous injectable formulation against *B bovis*.

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