



Original Research

The Efficacy of Meloxicam Oral Suspension for Controlling Pain and Inflammation After Castration in Horses



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ABSTRACT

The objective of the study was to evaluate the efficacy of a meloxicam oral suspension (MOS) for pain and inflammation control after castration in horses. The study consisted of 88 healthy, unbroken, 2-year-old mixed breed horses (primarily Quarter horse and draft type). Group 1 animals ($n = 44$) received MOS at the dose of 0.6 mg per kg body weight administered orally at the time of castration then daily for two consecutive days. Group 2 animals ($n = 44$) received 0.9% saline at the dose of 1 mL per 25-kg body weight administered orally at the time of castration then daily for two consecutive days. Animals were castrated on day 0 and observed for clinical signs of pain and inflammation for four (4) consecutive days. Pain behavior scores and visual analog scores were significantly greater in control animals over meloxicam-treated animals at all observation periods ($P < .05$). The Stiffness Score at the time of leaving the chute was significantly different in control animals over meloxicam-treated animals at all observation periods ($P < .05$). The meloxicam-treated animals had significantly greater movement indices 24 to 96 hours after castration ($P < .05$). Meloxicam-treated animals had significantly lower swelling than control animals at all observation periods (day 1, day 2, and day 3; $P < .05$). It is concluded that daily administration of MOS at a dose of 0.6 mg/kg for 3 days significantly reduces postsurgical pain and inflammation in horses for at least 4 days after castration.

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1. Introduction

Castration is the most common surgical procedure performed on horses [1–4]. Although it is considered a routine elective procedure, castration is a major, invasive surgery with the potential for considerable postsurgical complications and postoperative pain. The Canadian Veterinary

Medical Association and American Veterinary Medical Association recommend the use of perioperative analgesics for castration of all horses, mules, and donkeys [5,6].

Currently, veterinarians use nonsteroidal anti-inflammatory agents (NSAIDs) and narcotics for postsurgical control of pain [5–9]; however, there are few published studies evaluating the efficacy of anti-inflammatory and analgesic agents after castration in horses [10–13]. Meloxicam has been evaluated as a method to control pain after castration in horses, but there was an insufficient number of animals (three in each

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treatment group) to demonstrate significant differences [11]. Because of the wide variation in behavior of individual animals, larger sample sizes are needed to show significant differences between treatment groups when evaluating the effects of pain medications on postsurgical pain. Although several large studies in food animals demonstrate the effects of NSAIDs in managing postoperative pain after castration, to our knowledge, these studies have not yet been performed in horses for a postoperative period of longer than 24 hours [10–13].

Recently, a meloxicam oral suspension (MOS) (15 mg/mL meloxicam) has been developed for postsurgical pain and inflammation in cattle and horses (Alberta Veterinary Laboratories, Calgary, Alberta, Canada). Currently, MOS is registered in Canada for the control of pain and inflammation in cattle undergoing surgical or band castration. This article describes the pharmacokinetic and efficacy studies of MOS for controlling pain and inflammation after surgical castration in horses at daily dosage of 0.6 mg/kg.

2. Materials and Methods

2.1. Pharmacokinetic Study

2.1.1. Study Design

The pharmacokinetic study was not a blinded study. All horses received meloxicam at a dose of 0.6 mg per kg body weight orally once daily for five treatments (times 0, 14, 48, 72, and 96 hours). The meloxicam was administered into the mouth via a syringe with a long plastic extension to ensure that all the medication was swallowed. The study was conducted according to good clinical practice (VICH GL GL9 [GCP]—GOOD CLINICAL PRACTISE [June 2000]). The study was reviewed and approved by an Institutional Ethical Care and Use Committee.

2.1.2. Animals

In the pharmacokinetic study, horses were healthy Quarter horses (six geldings and six nonpregnant mares) between 8 and 20 years of age. The mean weight was 542 ± 85.1 kg (range, 220–702 kg). Horses were identified with a numbered neck collar.

2.1.3. Blood Sample Collection

Blood samples (approximately 10 mL) were collected in labeled, heparinized tubes (Green Top) from the jugular vein of each animal at the following times: –1 hr (pre-medication), 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 24, 26, 48, 50, 72, 74, 96, and 98 hours. Plasma was separated by centrifugation (2000g) in a temperature-controlled centrifuge (approximately 5°C) for 20 minutes. After separation, plasma was withdrawn and aliquoted into pre-labeled plastic vials (minimum of three). Samples were placed in frozen storage (approximately –20°C) to wait processing for analysis.

2.1.4. Plasma Meloxicam Analysis

Samples were subjected to *in vitro* analysis for quantification of meloxicam by a validated procedure using a high-performance liquid chromatography system (HPLC) according to a previously reported validated procedure

[14]. An Agilent 1200 HPLC (Mississauga, Ontario) equipped with a quaternary pump, an auto sampler, UV detector, and Chem Station software was used for all analysis. Peroxicam was used as an internal standard.

The analytical methods were fully documented and validated *a priori* to demonstrate (where applicable) acceptable linearity over the entire concentration range (without extrapolation), precision (reproducibility), accuracy, specificity, sensitivity (limit of quantitation), recovery, and stability of the analyte in the target matrix under anticipated storage conditions and intervals of the study. Preparation and storage of in-process analytical samples accommodated the requirements of the method. Standards and controls were prepared for and analyzed in each run to assure that the complete analytical method, sample preparation, extraction, clean-up, and instrumental analysis perform according to acceptable criteria, as indicated by precision and accuracy determinations.

Pharmacokinetic analysis was performed using validated software (PK Solutions, Montrose, CO).

2.2. Castration Efficacy Study

2.2.1. Study Design

This was a randomized, controlled, blinded study. The number of animals in each treatment group was based on power calculations for each variable evaluated. Eighty-eight young (2 years), healthy horses were randomly assigned to two treatment groups. Group 1 horses ($n = 44$) received MOS at the dose of 0.6 mg per kg body weight (1 mL per 25-kg body weight) administered orally at the time of castration then once daily for two (2) consecutive days. Group 2 horses ($n = 44$) received 0.9% saline at the dose of 1 mL per 25-kg body weight administered at the time of castration then once daily for two (2) consecutive days. Individuals scoring animals, caring for the animals, and performing health assessments and body weights were blinded to the treatment groups. The statistician was unblinded at the end of the study. Animals were castrated on day 0 and observed for clinical signs of pain and inflammation for four (4) consecutive days. The study was performed over three consecutive weeks with 28, 30, and 30 horses examined each week, respectively. Horses were randomly assigned to treatment groups, each week of the study so that an equal number of animals in each group were represented each week.

The study was conducted according to good clinical practice (VICH GL GL9 [GCP]—GOOD CLINICAL PRACTISE [June 2000]). The study was reviewed and approved by an Institutional Ethical Care and Use Committee.

2.2.2. Animals

All horses were unbroken, healthy, 2 years of age, and of mixed breeds (primarily Quarter horse and draft type). Horses were identified with a numbered neck collar and number sprayed on the hip. The MOS-treated animals weighed 484.9 ± 115.8 kg (mean and standard deviation) with a minimum and maximum weight of 316 kg and 852 kg, respectively. The saline-treated animals weighed 445.2 ± 77.2 kg (mean and standard deviation) with a

minimum and maximum body weight of 296 kg and 705 kg, respectively.

2.2.3. Feed, Water, and Housing

All horses were placed on a barley silage ration (58.4% dry matter) before and during the study. The analysis of feed on a dry matter basis was 15.1% crude protein (47% soluble protein and 70% degradable protein), 5.4% lignin, 24.7% acid detergent fiber, 34% neutral detergent fiber, 3.5% water soluble carbohydrates, 2.6% simple sugars, 24.6% starch, 39% nonfibrous carbohydrates, 39.9% fat, 5.2% ash, and 7.32% total digestible nitrogen. The animals were group housed in a triangular shaped pen (30 meters × 40 meters × 40 meters) with 25 meters of bunk space and two automatic waterers. They had free access to water and feed throughout the study. They were provided with straw bedding and a 20% porosity fence for wind and weather protection. Horses from both treatment groups were kept in the same pen.

2.2.4. Castration Procedure

As horses were unbroke, they were restrained in a chute with a hydraulic tilt table. Surgical pain control was achieved using a combination of sedation and local anesthesia. Horses were sedated with 0.5 mg/kg xylazine HCl (Xylazine, 100 mg/mL, Rompun, Bayer HealthCare, Mississauga, Ontario, Canada) IV. Approximately, 20 to 30 mL of lidocaine hydrochloride with epinephrine (2% lidocaine, Zoetis Canada, Kirkland, Quebec) was then infiltrated in and around each spermatic cord. Another 10 mL was infiltrated subcutaneously at the base of the scrotum on each side of the median raphe. A total of 50-mL lidocaine was used in each horse. The surgical site was cleaned and disinfected with povidone iodine surgical scrub (Betadine, Wyeth, Guelph Ontario) followed by an isopropyl alcohol (99% Isopropyl Alcohol, Alberta Veterinary Laboratories, Calgary, Alberta) rinse. Horses were castrated using an open castration technique. Briefly, a 15-cm skin incision was made over each testicle at the base of the scrotum using a scalpel. The incision was extended through subcutaneous tissues and the vaginal tunic to expose the testes and spermatic cord. The testicle, epididymis, and spermatic cord were isolated, and an emasculator was placed over each spermatic cord and clamped for a minimum of 2 minutes to achieve hemostasis. Skin incisions were stretched and left open to heal by second intention.

2.2.5. General Health Observations

Animals were observed for general health daily throughout the study. Animals were continually monitored for the first 6 hours postcastration for adverse events such as bleeding and colic.

2.2.6. Behavior Score

A Composite Pain Scale (CPS) was used to evaluate behavioral signs of pain in horses on day 0 (late afternoon, at least 2 hours after castration), day 1 (early morning), day 2 (early morning), and day 3 (early morning). This numerical rating scale is made up of nine categories of behavior related to pain after castration in

Table 1

Behavioral score for daily evaluation of animals after castration.

Behavior	Observation	Score
Attitude	Bright and alert (responsive to surroundings)	0
	Quiet	1
	Restless and agitated	2
	Depressed and unresponsive	3
Flank watching	Does not look at flank	0
	Looks intermittently at flank (1–3 times in 5 min)	1
	Repeatedly looks at flank or kicks at abdomen (3–4 times in 5 min)	2
	Lies down, rolling, or continual kicking at abdomen (>5 times 5 min)	3
Head carriage	Head (poll) positioned normally above withers	0
	Head (poll) held level with withers	1
	Head (poll) lowered below withers	2
Weight shifting	Normal weight distribution on all four limbs	0
	Intermittently shifting weight on hind limbs	1
	Continually shifting weight on hind limbs	2
Activity	At feeder and eating normally	0
	Standing or lying quietly with other horses	1
	Standing alone away from others	2
	Recumbent and uncomfortable	3
Overall	Comfortable	0
	Mildly painful	1
	Moderately painful	2
	In severe pain	3
Maximum score		16

horses with a maximum possible score of 23 points (one category was not included in the total composite score as it was only assessed on days 0 and 3; see Table 1). Categories included evaluation of attitude, flank watching, head carriage, weight shifting, activity, movement, swelling, response to palpation, and overall pain. The scale is based on other scales developed for pain assessment in horses and dogs [15–17] but modified to reflect specific behaviors seen in horses after castration [11]. Horses were observed in their home pen and while being moved through the chute system (during their daily treatment). Three observers, blinded to treatment groups, scored all horses to minimize interobserver variance. Observers were experienced in normal horse behaviors and were trained on the use of the scoring system before initiating the trial. Observation began at least 2 to 6 hours after castration or treatment from the edge of the pen where the observer would not interfere with the horses' normal behavior. Horses were not observed during times when they were lying down and/or asleep or during feeding time. Each observation period was approximately 2 hours in duration, and each horse was provided a score after 4 minutes of continual observation. There was no precastration observation.

2.2.7. Visual Analog Scores

A visual analog score (VAS) was performed by three blinded observers on days 0, 1, 2, and 3. VAS is a subjective measure of pain where an experienced observer places a mark on a 100-mm line where one end represents no pain and the opposite end severe pain. The distance from the beginning of the line (no pain) to the observer's mark is measured in millimeters. Observers

based their pain score on their observation of the horses during the time the CPS was performed and each observer scored all horses.

2.2.8. Stiffness Score and Stride Length Measurement

Stride length was measured at days 0 (before castration), 1, 2, and 3 after being castrated. Video images were obtained as the horse moved past a portion of an alley located at the end of the squeeze chute. Video was analyzed by an observer blinded to treatment. Only horses which passed the video at a trot were used in the analysis. To obtain stride length in the horses, measures were taken sequentially as the video was advanced slowly frame by frame so that an accurate measure between one hind hoof leaving the ground and the next hind hoof hitting the ground could be obtained. Stride length was recorded as the distance measured from the toe of one hoof to the toe of the opposite hoof after calculating the distance between two reference points in the photograph. The reference points were the fence posts of the alley which had a standard measured distance.

A subjective measure of hind limb stiffness was recorded on days 0, 1, 2, and 3 while the horses were being moved through the chute system. Stiffness was assigned as 0 = normal (moving normally and freely), 1 = mild stiffness (slightly stiff in hind legs but still moving freely), 2 = moderate stiffness (obvious hind limb stiffness), 3 = severe stiffness (reluctant to move), and 4 = very severe stiffness (unwilling to move).

2.2.9. Accelerometers (Movement Evaluation)

ICE TAG (IceRobotics Ltd, Edinburgh EH30 9 TF, Scotland, UK) accelerometers were used to continuously monitor the movement of animals after castration (day 0 to day 3). Accelerometers were placed on the left hind limb above the fetlock while the horse was restrained on the tilt table at the time of castration. It was removed on day 3 while the wound sites and swelling were evaluated on the tilt table. The information was downloaded on the computer. The motion index is a measurement developed by IceRobotics that provides a broad measurement of the animal's activity level. The calculation is performed per second. For any time period, the index is summed to provide total activity for the period. Although the movement index was evaluated continuously, information was recorded each minute of the day. The Movement Index data were only analyzed when all the horses were in their home pen (not during treatment, castration, or movement evaluation).

2.2.10. Inflammation and Temperature Measurement (Day 3)

Sheath swelling was measured using callipers on day 3. Digital callipers were placed horizontally across the prepuce at the widest aspect, and the width was measured.

Incision site temperature was also measured using a surface thermometer (Mastercraft Digital Temperature Reader, Canadian Tire, Canada). The surface skin temperature was recorded in the interincisional area.

2.2.11. Sheath Swelling Score

Scrotal swelling of each horse was scored on days 0, 1, 2, and 3. Scoring was performed chute side during the daily

treatments by an individual blinded to the treatment groups. A simple descriptive scale was used: 0 = no swelling, 1 = slight swelling, 2 = moderate swelling, and 3 = severe swelling as a category in the CPS.

2.3. Statistical Analysis

The mean peak (2 hours) and trough (24 hours) plasma meloxicam concentrations on each day were compared with day 0 means using a *t* test. Movement index, stride length, sheath thickness, and skin temperatures were compared using a *t* test. Mean CPS pain scores, VAS, stiffness and stride lengths, ICE TAG motion index, sheath swelling and inflammation measures, and scrotal swelling score were analyzed using Mann–Whitney test (GraphPad, La Jolla, CA). The differences between the meloxicam treated and the control group were considered significant when $P < .05$.

3. Results

3.1. Pharmacokinetics/Pharmacodynamics

The pharmacokinetics data are summarized in Table 2. The mean plasma meloxicam concentration versus time plot is provided in Fig. 1. Peak (2 hours posttreatment) and trough (just before treatments on days 1, 2, 3, and 4) plasma meloxicam concentrations were also measured (Fig. 1). There were no differences among the days 0, 1, 2, 3, and 4 peak (2 hours) and trough (24 hours) plasma meloxicam concentrations ($P > .05$). Administration of MOS daily over 5 days was not associated with accumulation of the plasma meloxicam.

3.2. Castration Study

The results of the scores and measurements are summarized in Table 3.

3.2.1. Behavior Score

The median Behavior Score was significantly greater in control animals over meloxicam-treated animals at all observation periods (day 0: meloxicam = 3.0 vs. control = 4.0,

Table 2

Pharmacokinetic parameters after administration of meloxicam oral suspension to horses.

Variable	Unit	Mean	Standard Deviation
C_{\max}	µg/mL	1.70	0.32
T_{\max}	Hr	2.08	0.47
AUC_t	(µg-hr/mL)	14.08	1.66
AUC_{∞}	(µg-hr/mL)	17.68	2.09
T1/2	Hr	12.98	3.81
MRT	Hr	17.68	2.09
$CL_{(obs\ area)}$	mL/hr	34.3	4.16

Abbreviations: AUC_t , area under blood plasma concentration of meloxicam versus time curve at time *t*; AUC_{∞} , area under blood plasma concentration of meloxicam versus time curve extrapolated to infinity; C_{\max} , maximal observed blood plasma meloxicam concentration; $CL_{(obs\ area)}$, systemic clearance based on observed data points; MRT, mean residence time or time for 63.2% of administered meloxicam dose to be eliminated; T_{\max} , time at maximum observed plasma meloxicam concentration; T1/2, time for concentration of plasma meloxicam to diminish by one half.

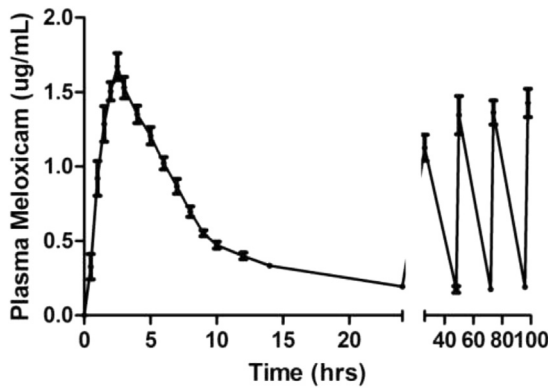


Fig. 1. Plasma meloxicam concentration versus time plots. (Data represent mean \pm standard error of all 12 horses.)

$P = .0005$; day 1: meloxicam = 2.0 vs. control = 4.0, $P < .0001$; day 2: meloxicam = 2.0 vs. control = 3.0, $P = .0048$; day 3: meloxicam = 2.0 vs. control = 3.0, $P = .0051$).

3.2.2. Visual Analog Scores

The Visual Analog Score was significantly greater in control animals over meloxicam-treated animals at all observation periods (day 0: meloxicam = 18.0 vs. control = 28.5, $P = .0023$; day 1: meloxicam = 10.0 vs. control = 25.5, $P < .0001$; day 2: meloxicam = 8.5 vs. control = 17.0, $P = .0006$; day 3: meloxicam = 9.0 vs. control = 15.0, $P = .0040$).

3.2.3. Stiffness Score and Stride Length Measurement

Most horses had normal movements at all observation periods. For this reason, the mean movement scores were

very low. In spite of this, the movement score at the time of leaving the chute was significantly greater in control animals over meloxicam-treated animals at all observation periods. On day 1 after castration, stride length was significantly longer in the meloxicam-treated horses ($n = 25$) than in controls ($n = 24$) (meloxicam = 179.6 cm vs. control = 156.7 cm, $P < .006$). There was no significant difference between groups or difference from day 0 measurements at any other time period.

3.2.4. ICE TAG Accelerometers (Movement Evaluation)

During period 1 (6:00 PM [day 0]–7:00 AM [day 1]), there was no difference between the control and meloxicam-treated animals (treated = 7,765 vs. control = 6,479, $P = .096$), but for period 2 (10:00 AM [day 1]–7:00 AM [day 2]) and period 3 (10:00 AM [day 2]–7:00 AM [day 3]), the meloxicam-treated animals had significantly greater movement indices (treated = 16,150 vs. control = 11,760, $P = .0052$ and treated = 18,900 vs. control = 13,240, $P = .0255$), respectively.

3.2.5. Inflammation and Temperature Measurement (Day 3)

Meloxicam-treated animals had significantly less sheath swelling than control animals (treated = 59.56 mm, control = 87.00 mm, $P < .0001$). There was no difference in skin surface temperature between control and meloxicam-treated animals.

3.2.6. Sheath Swelling Score

It was believed that a more accurate Sheath Swelling Score was achieved when the animals were on the tilt table (day 3). The Sheath Swelling Score at the time of the treatments (day 1 and day 2) and while on the tilt table

Table 3

Behavior and observation result summaries for castrated horses treated with meloxicam and the control group.

Measurement	Time Period	Meloxicam	Control	P Value
Mann-Whitney Test		Median	Median	
Behavioral score	Day 0	3.0	4.0	.0005
	Day 1	2.0	4.0	<.0001
	Day 2	2.0	3.0	.0048
	Day 3	2.0	3.0	.0051
Visual Analog Score	Day 0	18.0	28.5	.0023
	Day 1	10.0	25.5	<.0001
	Day 2	8.5	17.0	.0006
	Day 3	9.0	15.0	.0040
Stiffness Score	Day 1	0.0	0.0	<.0001
	Day 2	0.0	0.0	<.0001
	Day 3	0.0	0.0	.017
Sheath Swelling Score	Day 1	0.0	1.0	<.0001
	Day 2	0.5	2.0	<.0001
	Day 3	1.0	2.0	.0008
<i>t</i> Test		Mean \pm SE	Mean \pm SE	
Movement Index (ICE Tag)	Period 1 ^a	7,765 \pm 581	6,479 \pm 497	.096
	Period 2 ^a	16,150 \pm 928	11,760 \pm 753	.0052
	Period 3 ^a	18,900 \pm 1,573	13,240 \pm 1,632	.0255
Stride length change (cm)	Day 1	4.02 \pm 4.53	-3.47 \pm 4.36	.243
	Day 2	-2.58 \pm 5.76	-2.84 \pm 3.99	.969
	Day 3	-1.40 \pm 4.35	-3.99 \pm 3.14	.629
Sheath thickness (mm)	Day 3	59.56 \pm 4.98	87.00 \pm 4.97	.0002
Skin temperature ($^{\circ}$ C)	Day 3	33.73 \pm 0.24	34.02 \pm 0.36	.5157

Abbreviation: SE, standard error.

^a Period 1 indicates 6:00 PM (day 0) to 7:00 AM (day 1); period 2 indicates 10:00 AM (day 1) to 7:00 AM (day 2); and period 3 indicates 10:00 AM (day 2) to 7:00 AM (day 3).

(day 3) was significantly greater in control animals (day 1: treatment = 0.0, control = 1.0, $P < .0001$; day 2: treatment = 0.5, control = 2.0, $P < .0001$; day 3: treatment = 1.0, control = 2.0, $P < .0008$) over meloxicam-treated animals at all observation periods (day 1, day 2, and day 3).

4. Discussion

Meloxicam oral suspension was developed for cattle, sheep, goats, and horses to control pain and inflammation after castration and other surgical procedures. The product is easy to deliver by direct oral dosing or can be top dressed on feed. As meloxicam is tasteless, it can be administered in the feed, eliminating the need to restrain the horse (unpublished results).

The pharmacokinetic and pharmacodynamics behavior of commercial and noncommercial oral, IV, and intramuscular injection meloxicam products have been reported [14,18–21]. The pharmacokinetic parameters of MOS are similar to those reported for other oral meloxicam medication to horses. The EC50 for meloxicam using an established carpus lameness model is reported to be 0.16 $\mu\text{g}/\text{mL}$ [18] and 0.20 $\mu\text{g}/\text{mL}$ [19]. Meloxicam oral suspension at a dosage of 0.6 mg/kg provided plasma concentrations that exceeded the EC50 within 1 hour of administration and were maintained for over 24 hours. In addition, the mean residence time or time for 63.2% of administered meloxicam dose to be eliminated was approximately 17 hours, which makes daily dosing of meloxicam appropriate. Multiple dosing of meloxicam for 5 days did not change plasma peak and trough concentrations of meloxicam, which supports long-term efficacy and safety. This has been observed with other meloxicam preparations [14,20,21].

There has been considerable research in pain mitigation during castration in food animal species [22–24]. Larger studies in horses have been lacking [10,12,13]. To our knowledge, this is the first clinical trial evaluating postoperative pain management in a large number of horses for up to 4 days after surgery. This study supports the findings in other species that postoperative pain lasts for at least several days after castration. Horses continued to show signs of pain and surgical site swelling on day 3 after castration, which would suggest that pain medication should be continued at least until this time period.

It has been shown that behavioral parameters can be valuable in assessment of pain, but there is limited information for horses. The measurement of predefined postures and movements has been shown to be useful in comparing animals receiving analgesics and placebos [25–27]. Pain scales and time budget of behavior have been shown to be useful in evaluation of orthopedic pain using a synovitis model [28]. In this study, behavioral analysis was performed using a composite evaluation system modified from the published literature [11,16,17]. It was important that there was more than one evaluator, they were experienced in horse behavior, they were blinded to the treatment groups, and they were validated as an appropriate observer [17]. As the horses in this study were unhandled animals, the Composite Pain Score used was developed to be able to evaluate the horses from a distance and focused on easily recognizable behaviors. The combination of

behavioral scores is controversial but was conducted as there is considerable variation in behavioral expressions among horses. Horse grimace scales have also been shown to effectively assess pain behaviors; however, facial expressions would have been difficult to evaluate in this study [29]. The behavioral scores and the visual analog scores were highly significantly different between the meloxicam treated and placebo horses for all four observational periods, which would support the benefits of NSAID treatment in the first few days after castration.

The Stiffness Score was obtained after the horses were released from the restraining chute where they received their treatments. As these were unbroken horses that have had minimal handling, the Stiffness Score would be considered to be less useful as they were easily excited and could hide movement alterations. This is confirmed as most horses had a normal movement score. In spite of this, there was a significant difference in the mean scores between groups. Stride length has been used as a measure of postoperative pain in other species [22,23]. Some of the challenges in this study were the high variability of stride length between horses, the number of horses who cantered past the video camera, and the dynamic nature of movement in horses, where both hind legs do not contact the ground at the same time at the trot.

Leg accelerometers have been used extensively in continually monitoring behaviors in dairy cattle [30,31]. Validation studies conducted before initiating the study using the ICE Tag monitoring system showed that only the Movement Index could be used with horses. The Movement Index is generated based on the general walking movement of the animal. This Index can be valuable in documenting postcastration complications such as swelling, where animals have reduced movement [30,31]. Meloxicam-treated animals had significantly increased Movement Index compared with placebo animals for observation periods 2 and 3 which indicates that the meloxicam-treated horses are more active within the paddock.

The prepuce sheath swelling was scored in the chute on days 1 and 2, but on day 3, it was scored on the tilt table. It was very clear that swelling could be best evaluated on the tilt table where a thorough examination could be performed. The severity of sheath swelling became more severe from day 1 through day 3 for both treatment groups; however, there was a very significant reduction in swelling in the meloxicam-treated animals compared with controls. This difference was confirmed with the caliper measurements of the sheath thickness. The sheath thickness was significantly reduced in the meloxicam-treated animals which demonstrates the anti-inflammatory effects of meloxicam in horses. As some treated animals still had swollen sheaths on day 3, it was believed that additional daily meloxicam treatments would have been beneficial in these cases.

The intracincisional skin surface temperature was not different between the treatment groups. This was not surprising as variance among measurements was high and subject to environmental influences.

As meloxicam is tasteless, it can be administered in the feed, eliminating the need to restrain the horse (unpublished results).

5. Conclusions

Daily administration of MOS at a dose of 0.6 mg/kg for 3 days significantly reduces postsurgical pain and inflammation in horses for at least 4 days after castration. Meloxicam oral suspension may provide the veterinary practitioner with a simple, safe, and effective method to control pain and inflammation after castration in horses. Provision of pain control and reduction of inflammation should decrease the recovery period after castration. It is expected that MOS could also be used for control of pain and inflammation for other surgical procedures, but further research needs to be conducted to demonstrate these benefits.

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References

- [1] Kilcoyne I, Watson JL, Kass PH, Spier SJ. Incidence, management, and outcome of complications of castration in equids: 324 cases (1998–2008). *J Am Vet Med Assoc* 2013;242:820–5.
- [2] Moll DH, Pelzer KD, Pleasant RS, Modranski PD. A survey of equine castration complications. *J Equine Vet Sci* 1995;15:522–6.
- [3] Searle D, Dart AJ, Dart CM, Hodgson DR. Equine castration: review of anatomy, approaches, techniques and complications in normal, cryptorchid and monorchid horses. *Aust Vet J* 1999;77:428–33.
- [4] Mason BJ, Newton JR, Payne RJ, Pilsworth RC. Costs and complications of equine castration: a UK practice based study comparing standing nonsutured and recumbent sutured techniques. *Equine Vet J* 2005;37:468–72.
- [5] Castration of horses, donkeys, and mules—position statement. *Can Vet Med Assoc*. 2014. <http://www.canadianveterinarians.net/documents/castration-of-horses-donkeys-and-mules>. Accessed April 21, 2015.
- [6] Pain in Animals. *Am Vet Med Assoc*. <https://www.avma.org/KB/Policies/Pages/Pain-in-Animals.aspx>. Accessed April 21, 2014.
- [7] Muir WW. Pain therapy in horses. *Equine Vet J* 2005;37:98–100.
- [8] Green P. Castration of horses and analgesia. *Vet Rec* 2001;149:159–60.
- [9] Price J, Eager RA, Welsh EM, Waran NK. Current practice relating to equine castration in the UK. *Res Vet Sci* 2005;78:277–80.
- [10] Love EJ, Taylor PM, Clark C, Whay HR, Murrell J. Analgesic effect of butorphanol in ponies following castration. *Equine Vet J* 2009;41:552–6.
- [11] Schaafsma MK. Assessment of pain in horses after surgical castration composition of a pain scale. Utrecht University; 2009 [PhD Thesis], Utrecht.
- [12] Love EJ, Taylor PM, Whay HR, Murrell J. Postcastration analgesia in ponies using buprenorphine hydrochloride. *Vet Rec* 2013;172:635.
- [13] Sanz MG, Sellon DC, Cary JA, Hines NT, Farnsworth KD. Analgesic effects of butorphanol tartrate and phenylbutazone administered alone and in combination in young horses undergoing routine castration. *J Am Vet Med Assoc* 2009;235:1194–203.
- [14] Toutain PL, Reymond N, Laroute V, Garcia P, Popot MA, Bonnaire Y, et al. Pharmacokinetics of meloxicam in plasma and urine of horses. *Am J Vet Res* 2004;65:1542–7.
- [15] Van Loon JPA. Analgesia in the horse; various approaches for assessment and treatment of pain and nociception in equines. Utrecht University; 2012 [PhD Thesis], Utrecht.
- [16] Murrell JC, Psatha EP, Scott EM, Reid J, Hellebrekers LJ. Application of a modified form of the Glasgow pain scale in a veterinary teaching centre in the Netherlands. *Vet Rec* 2008;162:403–8.
- [17] Dalla Costa E, Rabolini A, Scelsa A, Canali E, Minerio M. A study on inter-observer reliability of castration pain assessment in horses. In: Krüge K, editor. *Proc 2nd IESM Int Equine Sci Meet 2012*. Xenophon Verlag; 2012, p. 52.
- [18] Lees P, Sedgwick AD, Higgins AJ, Pugh KE, Busch U. Pharmacodynamics and pharmacokinetics of meloxicam in the horse. *Br Vet J* 1991;147:97–108.
- [19] Toutain PL, Cester CC. Pharmacokinetic-pharmacodynamic relationships and dose response to meloxicam in horses with induced arthritis in the right carpal joint. *Am J Vet Res* 2004b;65:1533–41.
- [20] Noble G, Edwards S, Lievaert J, Pippia J, Boston R, Raidal SL. Pharmacokinetics and safety of single and multiple oral doses of meloxicam in adult horses. *J Vet Intern Med* 2012;26:1192–2001.
- [21] Vander Werf KA, Davis EG, Kukanich B. Pharmacokinetics and adverse effects of oral meloxicam tablets in healthy adult horses. *J Vet Pharmacol Ther* 2013;36:376–81.
- [22] Currah JM, Hendrick SH, Stookey JM. The behavioural assessment of alleviation of pain associated with castration in beef calves treated with flunixin meglumine and caudal lidocaine epidural anesthesia with epinephrine. *Can Vet J* 2009;50:375–82.
- [23] Coetzee JF. Assessment and management of pain associated with castration in cattle. *Vet Clin North Am Food Anim Pract* 2013;29:75–101.
- [24] Kluyvers-Poodt M, Zonderland J, Verbrakk J, Lambooi E, Hellebrekers LJ. Pain behaviour after castration of piglets; effect of pain relief with lidocaine and/or meloxicam. *Anim* 2013;7:1158–62.
- [25] Price J, Marques JM, Welsh EM, Waran NK. Pilot epidemiological study of attitudes towards pain in horses. *Vet Rec* 2002;151:570–5.
- [26] Pritchett LC, Ulibarri C, Roberts MC, Schneider RK, Sellon DC. Identification of potential physiological and behavioural indicators of postoperative pain in horses after exploratory coeliotomy for colic. *Appl Anim Behav Sci* 2003;80:31–43.
- [27] Raekallio M, Taylor PM, Bennett RC. Preliminary investigations of pain and analgesia assessment in horses administered phenylbutazone or placebo after arthroscopic surgery. *Vet Surg* 1997;26:150–5.
- [28] Bussières G, Jaques C, Lainay O, Beauchamp G, Leblond A, Cadore JL, et al. Development of a composite orthopaedic pain scale in horses. *Res Vet Sci* 2008;85:294–306.
- [29] Dalla Costa E, Minerio M, Lebelt D, Stucke D, Canali E, Leach MC. Development of the Horse Grimace Scale (HGS) as a pain assessment tool in horses undergoing routine castration. *PLoS One* 2014; 19:e92281.
- [30] Bewley JW, Boyce RE, Roberts DJ, Coffey MP, Schutz MM. Comparison of two methods of assessing dairy cow body condition score. *J Dairy Res* 2008;77:95–8.
- [31] Mølgaard L, Damgaard BM, Bjerre-Harpoth V, Herskin MS. Effects of percutaneous needle liver biopsy on dairy cow behaviour. *Res Vet Sci* 2012;93:1248–54.