Comparison of firocoxib and meloxicam for pain mitigation in goats undergoing surgical castration

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OBJECTIVE
This study sought to determine whether firocoxib (FIRO) or meloxicam (MEL) was effective at providing analgesia after surgical castration in goats.

ANIMALS
18 intact male crossbred goats (6 to 8 months old) were enrolled with a mean weight of 32.6 (± 2.9) kg.

METHODS
Surgical castration was done under injectable anesthesia by a licensed veterinarian. Twelve bucks were surgically castrated and given either FIRO (n = 6) or MEL (n = 6). Six bucks served as controls (CNTLs) and were not castrated. Outcome measurements included visual analogue scale, infrared thermography, plasma cortisol, plasma substance P, and kinetic gait analysis. All outcome measurements were obtained at –24, 4, 8, 24, 48, and 72 hours.

RESULTS
All 3 treatments were significantly different from each other at the 24- and 48-hour time points, with MEL animals having lower visual analogue scale scores when compared to FIRO animals; CNTL animals exhibited the lowest plasma cortisol levels (3.19 ng/mL; 95% CI, –1.21 to 7.59 ng/mL) followed by FIRO (7.45 ng/mL; 95% CI, 3.10 to 11.80 ng/mL) and MEL (10.24 ng/mL; 95% CI, 5.87 to 14.60 ng/mL). FIRO had an average mean decrease in gait velocity change (–54.17 cm/s; 95% CI, –92.99 to –15.35 cm/s), while MEL had an increase in gait velocity when compared to baseline values (14.54 cm/s; 95% CI, –24.27 to 53.36 cm/s). Control animals had an average mean of –3.06 cm/s (95% CI, –41.88 to 35.75 cm/s).

CLINICAL RELEVANCE
Results from this study showed that there were some analgesic effects from administering MEL when compared to bucks that received a placebo treatment (CNTL).

Keywords: castration, firocoxib, goat, meloxicam, pain

Surgical castration is a frequent practice in livestock management. Castration is commonly performed on intact male food animals to reduce aggression, prevent indiscriminate breeding, and improve carcass quality.1 Castration has been cited as a source of pain and stress in cattle,2 but a specific pain scale to evaluate and demonstrate postoperative pain in goats had not been developed until recent years. Analgesia is used to provide pain relief and reduce stress in livestock animals undergoing castration. There are currently no approved analgesic drugs for surgical castration in goats in the US. Veterinarians must extrapolate analgesic data from other livestock species to treat pain in goats. Sheep and cattle are commonly used as references, but specific pain protocols are needed to accurately assess and treat pain responses in goats.

For male goats intended to be kept as pets, castration is recommended closer to sexual maturity (6 to 8 months old) to allow for increased urethral diameter to reduce incidence of blockage in the male urethra.3 Blockages in the male urinary tract, often referred to as obstructive urolithiasis, is a condition that is complex and multifactorial.3 Obstructive urolithiasis of male ruminants is difficult to manage, causing significant economic losses and compromising animal welfare.4,5 Surgery is the most common treatment for obstructive urolithiasis,6 which insinuates welfare concerns for the animal and economic burdens for owners.
Although urolithiasis is a multifactorial condition that is mainly due to diet components, maximizing urethral diameter in small ruminants intended as pets is encouraged to help prevent this condition. Therefore, it is important to prevent blockages from occurring in pet goats by castrating at an older age when compared to production animals.

Firocoxib (FIRO) is an NSAID that is a fast-acting cyclooxygenase-2 selective inhibitor.\textsuperscript{7} Cyclooxygenase plays a significant role in the production of prostaglandins, which are produced by mammalian tissues and facilitate intercellular communication of various processes.\textsuperscript{8,9} FIRO has been shown to be useful in inhibiting pain responses in horses and in dogs. The pharmacokinetics of FIRO in goats has been previously described in older adult female goats using a paste formulation with a bioavailability of 71%.\textsuperscript{10} Orally administered FIRO at 0.5 mg/kg is rapidly absorbed, with a $t_{\text{max}}$ of 0.77 hours and an oral bioavailability of 77%. FIRO also has a long terminal half-life of 27 hours.

Meloxicam (MEL) is an oxicam-class NSAID that is a preferential inhibitor of cyclooxygenase-2.\textsuperscript{11} It is used commonly in livestock production due to its longer half-life (10.7 hours) and high oral bioavailability (96%).\textsuperscript{12,13} MEL has been shown previously to help mitigate pain responses in livestock animals, such as cattle and sheep, along with small animal species, including dogs and cats, following oral dosing.

The objective of this study was to investigate the analgesic effects of FIRO and MEL administered orally before surgical castration in goats using associated pain biomarkers previously described in cattle.\textsuperscript{2} We hypothesized that either FIRO or MEL, when administered before surgical castration, would provide some analgesia benefits by lowering visual analogue scale (VAS) scores, decreasing infrared ocular temperatures, lowering cortisol values and substance P (Sub P), and increasing stride length and gait velocity.

**Methods**

This study was approved by the Institutional Animal Care and Use Committee at Kansas State University (protocol No. 4627).

**Animals and study design**

Eighteen intact male crossbred goats (6 to 8 months old) were enrolled with a mean weight ($\pm$ SD) of 32.6 $\pm$ 2.9 kg. All individuals on trial had 2 descended testicles, as determined by a licensed veterinarian. Goats were kept in group housing (pens) and were fed exclusively a diet of brome hay ad libitum. Goats had free access to water and minerals for supplementation. The study was conducted over a 2-week period, with 1 week dedicated to acclimation and 1 week focused on castration, data collection, and poststudy monitoring. Each individual enrolled in the study (goat) was both the experimental and observational unit. Following the 1-week acclimation period, a random number generator (random.org) was used to assign each of the goats to 1 of the 3 treatments:

- **FIRO-castration ($n = 6$)**—Surgical castration was performed. FIRO (Equioxx Tablets; Boehringer Ingelheim Animal Health) was administered at 1 mg/kg through oral tablet administration (gelatin bolus administered with balling gun [Torpac]) at induction (0 hours) and then after at 0.5 mg/kg orally at 24 and 48 hours after castration.

- **MEL-castration ($n = 6$)**—Surgical castration was performed. MEL (Zydus Pharmaceuticals Inc) was administered at 2 mg/kg through oral administration (gelatin bolus administered with balling gun) at induction (0 hours) and then after at 1 mg/kg orally at 24 and 48 hours after castration.

- **Control ($n = 6$)**—Surgical castration was not performed. A placebo treatment was administered to individuals orally (whey protein powder in gelatin bolus administered with balling gun) at induction (0 hours) and then after at 1 mg/kg orally at 24 and 48 hours after sedation.

**Castration procedure**

Twelve goats were castrated for the study. All goats, including control (CNTL) goats, were fasted for 24 hours prior to the procedure. All goats were sedated with xylazine hydrochloride (0.04 mg/kg, IV; Akron Inc) and ketamine (2.0 mg/kg, IV; Putney Inc). Goats that were castrated were taken to a surgical suite. The castration site was clipped and steriley prepped for surgery. Both spermatic cords were blocked with lidocaine injection (1 mL/cord; 2 mL total; 2%; MWI Animal Health) prior to surgical castration when animals were under general anesthesia. Two licensed veterinarians performed and assisted during all castration procedures. Animals were monitored for respiratory rate and heart rate under anesthesia and after surgery until they regained full consciousness. Following the castration procedure, or after 10 minutes of time for the CNTL goats, each goat was administered an anesthetic reversal agent, atipamezole, at 0.05 mg/kg IM (Zoetis Inc).

**Outcome variables**

All outcomes were measured for each goat at -24, 4, 8, 24, 48, and 72 hours. Outcomes of interest included VAS, infrared thermography (IRT), blood plasma cortisol and Sub P, and kinetic gait analysis (KGA; Figure 1).

**Visual analogue scale**

A VAS score was adapted from Martin et al\textsuperscript{14} to quantify pain in goats based on visual parameters correlated to pain. VAS consisted of a 100-mm line with “NO PAIN” anchoring the left side and “SEVERE PAIN” to the right. The following parameters were used to assess pain: depression, tail swishing or flicking, full body stance, head carriage, spinal alignment, and movement. No pain was characterized by being alert and quick to show interest, no tail swishing, a normal stance, head carriage above spine level, a straight spine, moving freely around the pen, and ears forward. Severe pain was characterized by being dull and showing no interest, more than 3 tail swishes/...
Blood samples were collected via jugular venipuncture from each goat (6 mL of whole blood) at −24, 4, 8, 24, 48, and 72 hours. Blood was collected in a 3-mL heparinized vacutainer (Greiner Bio-One North America Inc) and placed on ice until plasma cortisol and Sub P levels could be processed. Time from collection to processing was 2 hours or shorter for all samples. Sub P concentrations were determined through RIA via methods described by Kleinhenz et al. A standard curve (range, 20 to 1,280 pg/mL) was created by diluting synthetic secreted protein (SP; Phoenix Pharmaceuticals) with RIA buffer (50 mM sodium phosphate dibasic heptahydrate, 13 mM disodium EDTA, 150 mM sodium chloride, 1 mM benzamidine hydrochloride, 0.1% gelatin, 0.02% sodium azide; pH 7.4). For analysis, 100 µL of sample, standard, or QC was aliquoted into plain 12 × 75-mm conical bottom tubes followed by 100 µL of rabbit anti-SP primary antibody (1:20,000; Phoenix Pharmaceuticals). Iodine-125-SP tracer (custom iodination by PerkinElmer) was diluted with RIA buffer to 20,000 counts/min. After, 100 µL was added to the sample, standard, and QC tubes. Samples were covered and stored at 4 °C for 48 hours. At the end of the 48-hour incubation, samples were placed on ice, and 100 µL of normal rabbit plasma (1:80) and goat anti-rabbit secondary antibody (1:40; Jackson ImmunoResearch) were added to each tube. Samples were then incubated at room temperature for 10 minutes and placed back on ice, and 100 µL of blank bovine plasma was added to the standards and QCs. All tubes then had 1 mL of 12% polypropylene glycol in 0.85% sodium chloride added. Samples were centrifuged at 3,000 X g for 30 minutes at 4 °C, and the supernatant was aspirated. Tubes were counted on a γ counter (Wizard2; PerkinElmer). Raw data values were uploaded onto MyAssays Desktop, version 7.0.211.1238 (MyAssays Ltd), for concentration determination. Standard curves were plotted as a 4-parameter logistic curve. Samples with a coefficient of variation (CV) > 18% were reanalyzed. The intra-assay and interassay CV were determined to be 26.30% and 10.42%, respectively.

Plasma cortisol

Blood samples were collected from each goat (6 mL of whole blood) at −24, 4, 8, 24, 48, and 72 hours. Blood was collected in a 3-mL heparinized vacutainer (Greiner Bio-One North America Inc) and placed on ice until plasma cortisol and Sub P levels could be processed. Plasma cortisol concentrations from each sample were analyzed in duplicate with a radioimmunoassay (RIA) system using methods adapted from Kleinhenz et al. Plasma cortisol concentrations were determined with a commercially available RIA kit (MP Biomedicals) following manufacturer specifications with minor modifications as previously described (Martin et al.). The standard curve was created and extended to include 1 and 3 ng/mL by diluting the 10- and 30-ng/mL manufacturer-supplied standards, 1:10 respectively. The standard curve ranged from 1 to 300 ng/mL. Two unique CNTLs (25 and 150 ng/mL) were performed at the beginning and end of each sample set to determine interassay variability. Plain 12 X 75-mm polypropylene tubes served as blank tubes to calculate nonspecific binding. From each sample, 50 µL, including standards and quality control (QC), was utilized for analysis. Samples were incubated at room temperature for 30 minutes before addition of radioactive iodine (1-125) per manufacturer instructions. Tubes were counted on a γ counter (Wizard2; PerkinElmer). Raw data values were uploaded onto MyAssays Desktop, version 7.0.211.1238 (MyAssays Ltd), for concentration determination. Standard curves were plotted as a 4-parameter logistic curve. Samples with a coefficient of variation (CV) > 18% were reanalyzed. The intra-assay and interassay CV were determined to be 6.6% and 7.96%, respectively.
Kinetic gait analysis

A commercially available floor mat–based pressure/force measurement system (Walkway; Tekscan Inc) was utilized to record and analyze the gait of each goat. Measurements for KGA were collected at –24, 4, 8, 24, 48, and 72 hours, respectively. Goats were freely walked across the mat in a chute-like fashion at each time point. Video synchronization was used to ensure consistent gait among individuals for each time point. Data from pressure force measurements were analyzed with Walkway, version 7.7 (Tekscan Inc). Data collected, including contact pressure, contact area, impulse, and stance phase duration of each foot, were assessed via the methods described in Kleinhenz et al.2 Study definitions for outcomes are presented in Table 1.

Statistical analysis

Plasma cortisol and Sub P data were log transformed to normalized data prior to statistical analysis. The outcome responses of IRT, KGA, and plasma cortisol were analyzed via linear mixed models with individual goat as the experimental unit in JMP, version 15.1 (SAS Institute Inc). Goats nested in a treatment group were designated as a random effect, with treatment, time, treatment-by-time interaction, and replicate designated as fixed effects. F tests were utilized for testing the significance of main effects and interactions. Pairwise comparisons with significant overall differences were performed using the Tukey test for honestly significant difference. Statistical significance was determined a priori at \( P \leq .05 \). Data were presented as least squares means.

Results

VAS scoring

The VAS outcomes did not differ by treatment \((P = 1.00)\) but did differ by time point \((P < .0001)\) or treatment-by-time-point interaction \((P < .0001; \text{Figure 2})\). VAS scores for animals in the CNTL group stayed consistent throughout the study around the 0-mm mark. VAS scores for animals in the FIRO and MEL groups were similar at the 4-hour time point. All 3 treatments were significantly different from each other at the 24- and 48-hour time points, with MEL animals having lower VAS scores when compared to FIRO animals.

Infrared thermography

The IRT maximum temperatures did not differ by treatment \((P = .08)\) or treatment-over-time interaction \((P = .41)\) but did differ by time point \((P \leq .0001)\). These data are summarized in Table 2. Highest temperatures were seen at the 48-hour time point for FIRO \((39.45 °C; 95\% \text{ CI}, 38.99 to 39.90 °C; \text{least squares mean followed by 95\% CI})\), the 72-hour time point for MEL \((38.92 °C; 95\% \text{ CI}, 38.48 to 39.37 °C), and the 72-hour time point for CNTL \((39.35 °C; 95\% \text{ CI}, 38.90 to 39.80 °C). The lowest temperatures were seen for FIRO at the –24-hour time point \((37.95 °C; 95\% \text{ CI}, 37.49 to 38.40 °C), MEL at the –24-hour

Table 1—Definitions of kinetic gait analysis biomechanical markers.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Definition (unit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stance time</td>
<td>The time that passes in a gait cycle of 1 extremity (s)</td>
</tr>
<tr>
<td>Stride length</td>
<td>The distance between 2 successive placements of the same extremity (cm)</td>
</tr>
<tr>
<td>Force</td>
<td>The maximum force measured for a single step from a single extremity (kg)</td>
</tr>
<tr>
<td>Impulse</td>
<td>The maximum force applied per unit of time measured (kg X s)</td>
</tr>
<tr>
<td>Contact area</td>
<td>The peak pressure measured from a singular footfall (kg/cm²)</td>
</tr>
<tr>
<td>Gait distance</td>
<td>The distance along the line of progression, from posterior of the first left or right front stance to posterior of the last left or right front stance (cm)</td>
</tr>
<tr>
<td>Gait velocity</td>
<td>The gait distance is divided by gait time (cm/s)</td>
</tr>
</tbody>
</table>

Figure 2—Visual analogue scores (A) and cortisol concentrations (B) over time for goats that underwent surgical castration and were administered FIRO (triangles; \(n = 6\)) or MEL (squares; \(n = 6\)) and goats kept intact (not castrated) serving as controls and administered a placebo treatment (ie, CNTL goats; \(n = 6\)).
time point (37.99 °C; 95% CI, 37.55 to 38.43 °C), and CNTL at the 24-hour time point (38.37 °C; 95% CI, 37.91 to 38.82 °C).

**Plasma cortisol**

Plasma cortisol differed by treatment ($P = .0128$), by time point ($P < .001$), and by a treatment-over-time interaction ($P = .003$; Table 2; Figure 2). CNTL animals exhibited the lowest plasma cortisol levels (3.19 ng/mL; 95% CI, –1.21 to 7.59 ng/mL), followed by FIRO (7.45 ng/mL; 95% CI, 3.10 to 11.80 ng/mL) and MEL (10.24 ng/mL; 95% CI, 5.87 to 14.60 ng/mL). FIRO plasma cortisol levels were lowest at 72 hours (4.13 ng/mL; 95% CI, –1.27 to 9.54 ng/mL) and highest at 4 hours (16.31 ng/mL; 95% CI, 10.90 to 21.72 ng/mL). MEL plasma cortisol levels were lowest at 8 hours (4.63 ng/mL; 95% CI, –1.07 to 10.32 ng/mL) and highest at 4 hours (18.56 ng/mL; 95% CI, 13.15 to 23.97 ng/mL). CNTL plasma cortisol levels were lowest at 4 hours (1.32 ng/mL; 95% CI, –4.39 to 7.04 ng/mL) and highest at –24 hours (10.42 ng/mL; 95% CI, 5.00 to 15.82 ng/mL).

**Plasma Sub P**

Plasma Sub P did not differ by treatment ($P = .62$), by time point ($P = .054$), or by a treatment-by-time-point interaction ($P = .47$; Table 2). The overall mean plasma Sub P by treatment was reported to be FIRO (503.45 pg/mL; 95% CI, 372.84 to 634.05 pg/mL), MEL (586.05 pg/mL; 95% CI, 455.45 to 716.66 pg/mL), and CNTL (572.77 pg/mL; 95% CI, 442.17 to 703.37 pg/mL), respectively.

**Kinetic gait analysis**

Kinetic gait analysis outcomes are shown in Table 3 with select outcomes shown in Figure 3.

- **Stance time (s)**—Front limb stance time did not differ by treatment ($P = .28$), by treatment-by-time-point interaction ($P = .99$), or by time point ($P = .47$).
- The rear limb stance time did not differ by treatment ($P = .06$), by time point ($P = .95$), or by treatment-by-time-point interaction ($P = .28$).
- **Stride length (cm)**—Front limb stride length differed by treatment ($P = .01$) but did not differ by a treatment-by-time-point interaction ($P = .59$) or by

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**Table 2**—Overall mean (95% CI) infrared thermography temperature (°C) of the left medial canthus (eye), cortisol (ng/mL), and substance P (pg/mL) in goats that underwent surgical castration and were administered firocoxib (FIRO; n = 6) or meloxicam (MEL; n = 6) and goats kept intact (not castrated) serving as controls and administered a placebo treatment (CNTL; n = 6).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FIRO</th>
<th>MEL</th>
<th>CNTL</th>
<th>Treatment</th>
<th>Time</th>
<th>Treatment X time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrared thermography (°C)</td>
<td>37.95 (37.49 to 38.40)</td>
<td>37.99 (37.55 to 38.43)</td>
<td>38.60 (38.15 to 39.05)</td>
<td>.08</td>
<td>&lt; .0001</td>
<td>.41</td>
</tr>
<tr>
<td>Cortisol (ng/mL)</td>
<td>7.45 (3.10 to 11.80)</td>
<td>10.24 (5.87 to 14.60)</td>
<td>3.19 (-1.21 to 7.59)</td>
<td>.0128</td>
<td>&lt; .0001</td>
<td>.003</td>
</tr>
<tr>
<td>Substance P (pg/mL)</td>
<td>503.45 (372.84 to 634.05)</td>
<td>586.05 (455.45 to 716.6)</td>
<td>572.77 (442.17 to 703.37)</td>
<td>.05</td>
<td>.25</td>
<td>.62</td>
</tr>
</tbody>
</table>

**Table 3**—Overall mean (95% CI) outcome measures from kinetic gait analysis in goats that underwent surgical castration and were administered FIRO (n = 6) or MEL (n = 6) and CNTL goats (n = 6).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FIRO</th>
<th>MEL</th>
<th>CNTL</th>
<th>Treatment</th>
<th>Time</th>
<th>Treatment X time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Front foot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stance time (s)</td>
<td>0.001 (-0.07 to 0.07)</td>
<td>-0.05 (-0.12 to 0.02)</td>
<td>0.03 (-0.04 to 0.10)</td>
<td>.28</td>
<td>.99</td>
<td>.47</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>-19.76 (-30.90 to -8.61)</td>
<td>5.61 (-5.52 to 16.77)</td>
<td>-8.11 (-12.96 to 9.32)</td>
<td>.01</td>
<td>.59</td>
<td>.12</td>
</tr>
<tr>
<td>Force (kg)</td>
<td>-1.98 (-3.56 to -0.40)</td>
<td>0.89 (-0.68 to 2.47)</td>
<td>-0.95 (-2.20)</td>
<td>.02</td>
<td>.80</td>
<td>.11</td>
</tr>
<tr>
<td>Impulse (kg X s)</td>
<td>0.13 (-0.37 to 0.64)</td>
<td>-0.47 (-0.98 to 0.03)</td>
<td>0.21 (-0.29 to 0.72)</td>
<td>.11</td>
<td>.97</td>
<td>.37</td>
</tr>
<tr>
<td>Contact pressure (kg/cm²)</td>
<td>-20.52 (-39.86 to -1.45)</td>
<td>-0.98 (-20.32 to 18.35)</td>
<td>12.40 (-6.93 to 31.74)</td>
<td>.06</td>
<td>.72</td>
<td>.42</td>
</tr>
<tr>
<td>Rear foot</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stance time (s)</td>
<td>0.011 (-0.04 to 0.08)</td>
<td>-0.07 (-0.13 to 0.004)</td>
<td>0.03 (-0.03 to 0.09)</td>
<td>.06</td>
<td>.95</td>
<td>.28</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>-18.24 (-30.31 to -6.17)</td>
<td>3.76 (-8.30 to 15.83)</td>
<td>-11.90 (-20.23)</td>
<td>.03</td>
<td>.62</td>
<td>.14</td>
</tr>
<tr>
<td>Force (kg)</td>
<td>-1.13 (-2.04 to -0.23)</td>
<td>0.26 (-0.64 to 1.16)</td>
<td>-0.23 (-0.15)</td>
<td>.02</td>
<td>.23</td>
<td>.46</td>
</tr>
<tr>
<td>Impulse (kg X s)</td>
<td>-0.06 (-0.39 to 0.27)</td>
<td>-0.54 (-0.08 to -0.20)</td>
<td>0.12 (-0.15 to 0.25)</td>
<td>.01</td>
<td>.92</td>
<td>.18</td>
</tr>
<tr>
<td>Contact pressure (kg/cm²)</td>
<td>-17.51 (-35.61 to 0.58)</td>
<td>1.16 (-16.93 to 19.26)</td>
<td>7.92 (-8.38 to 27.82)</td>
<td>.10</td>
<td>.35</td>
<td>.58</td>
</tr>
<tr>
<td>Gait distance change (cm)</td>
<td>2.91 (-11.65 to 17.48)</td>
<td>-7.40 (-21.96 to 7.16)</td>
<td>-8.88 (-23.45 to 5.68)</td>
<td>.43</td>
<td>.78</td>
<td>.81</td>
</tr>
<tr>
<td>Gait velocity v change (cm/s)</td>
<td>-54.17 (-92.99 to -15.35)</td>
<td>14.54 (-24.27 to 53.36)</td>
<td>-3.06 (-41.88 to 35.75)</td>
<td>.045</td>
<td>.82</td>
<td>.56</td>
</tr>
</tbody>
</table>

LS = Least squares.

LS means (95% CI)
time point ($P = .12$). FIRO had a shorter overall stride length when compared to baseline measurements ($-19.76$ cm; 95% CI, $-30.90$ to $-8.61$ cm). MEL had the longest overall stride length when compared to baseline measurements ($5.62$ cm; 95% CI, $-5.52$ to $16.77$ cm). CNTL stride length was slightly shorter when compared to baseline measurements ($1.81$ cm; 95% CI, $-12.96$ to $9.32$ cm).

Rear limb stride length differed by treatment ($P = .03$) but did not differ by treatment-by-time-point interaction ($P = .14$) or by time point ($P = .62$). FIRO had a shorter overall stride length when compared to baseline measurements ($-18.24$ cm; 95% CI, $-30.31$ to $-6.17$ cm). MEL had the longest overall stride length when compared to baseline measurements ($5.62$ cm; 95% CI, $-5.52$ to $16.77$ cm). CNTL stride length was slightly longer when compared to baseline measurements ($0.16$ cm; 95% CI, $-11.90$ to $12.23$ cm).

**Force (kg)**—The front limb force did differ by treatment ($P = .02$) but did not differ by time point ($P = .80$) or by a treatment-by-time-point interaction ($P = .91$). FIRO had a lower overall force when compared to baseline measurements ($-1.98$ kg; 95% CI, $-3.56$ to $-0.40$ kg). MEL and CNTL had a slightly stronger force when compared to baseline measurements ($0.89$ kg [95% CI, $-0.68$ to $2.47$ kg] and $0.62$ kg [95% CI, $-0.95$ to $2.20$ kg], respectively).

The rear limb force differed by treatment ($P = .02$) but did not differ by time point ($P = .23$) or by a treatment-by-time-point interaction ($P = .46$). FIRO had a lower overall force when compared to baseline measurements ($-1.13$ kg; 95% CI, $-2.04$ to $-0.23$ kg). MEL and CNTL had a slightly stronger force when compared to baseline measurements ($0.26$ kg [95% CI, $-0.64$ to $1.16$ kg] and $0.66$ kg [95% CI, $-0.23$ to $1.57$ kg], respectively).

**Impulse (kg X s)**—Front foot impulse did not differ by treatment ($P = .11$), by time point ($P = .97$), or by treatment-by-time-point interaction ($P = .37$). Rear foot impulse differed by treatment ($P = .01$) but did not differ by time point ($P = .92$) or by a treatment-by-time-point interaction ($P = .18$). FIRO had a slightly lower impulse measurement when compared to baseline measurements ($-0.06$ kg X s; 95% CI, $-0.39$ to $0.27$ kg X s). MEL had the lowest overall impulse measurement when compared to baseline measurements ($-0.54$ kg X s; 95% CI, $-0.88$ to $-0.20$ kg X s). CNTL stride length was a slightly higher impulse measurement when compared to baseline measurements ($0.21$ kg X s; 95% CI, $-0.12$ to $0.55$ kg X s).

**Contact pressure (kg/cm$^2$)**—Front foot contact pressure did not differ by treatment ($P = .06$), by time point ($P = .72$), or by a treatment-by-time-point interaction ($P = .42$). Rear foot contact pressure did not differ by treatment ($P = .10$), by time point ($P = .35$), or by a treatment-by-time-point interaction ($P = .58$).

**Gait distance (cm)**—Gait distance change from baseline values ($-24h$) did not differ by treatment ($P = .43$), by time point ($P = .78$), or by a treatment-by-time-point interaction ($P = .81$).

**Gait velocity change from baseline (cm/s)**—Gait velocity change from baseline values ($-24$ hours) differed by treatment ($P = .045$) but did not differ by time point ($P = .8243$) or by a treatment-by-time-effect ($P = .5646$). FIRO had an average mean decrease in gait velocity change ($-54.17$ cm/s; 95% CI, $-92.99$ to $-15.35$ cm/s), while MEL had an increase in gait velocity when compared to baseline values ($14.54$ cm/s).
cm/s; 95% CI, -24.27 to 53.36 cm/s). CNTL animals had an average mean of -3.06 cm/s (95% CI, -41.88 to 35.75 cm/s).

Discussion

The primary objective of this study was to determine whether FIRO or MEL were effective at providing analgesia in goats after surgical castration. The MEL dosing regimen was the current treatment plan utilized by clinicians at Kansas State’s Veterinary Health Center for goats of this age. Data from this study suggest that both FIRO and MEL can provide some analgesic effect when administered to goats orally prior to surgical castration.

The differences in IRT over time are likely due to environmental influences. The animals were group housed with access to outdoor runs. A weather event (thunderstorm) occurred on the first day, keeping the ambient temperature cooler than subsequent study days. When this paper was written, no record of Sub P levels in goats was reported in the literature. FIRO had lower Sub P values at all time points included in this study after castration when compared to MEL and CNTL values. These data indicate that Sub P may not be a reliable biomarker for castration pain in goats.

MEL-treated individuals displayed lower VAS scores when compared to FIRO-treated individuals, indicating they appeared to the observer to be in less pain. MEL had similar or positive gait changes when compared to CNTL animals. The average for stride length increased slightly from baselines in both front and hind limb force in the MEL group. MEL and CNTL individuals had a slightly stronger force when compared to baseline measurements in both front and hind limb force. MEL had the lowest overall impulse measurement when compared to baseline measurements. MEL-treated goats also had an increase in gait velocity when compared to baseline measurements. CNTL animals had a slight decrease in gait velocity, comparatively, suggesting that individuals in the MEL group were experiencing less pain compared to FIRO, as their pressure mat outcomes more closely resembled those of the CNTL group.

This is the first report to compare MEL and FIRO in goats following surgical castration. A study by Brusin et al. compared MEL to flunixin in goats for postcastration analgesia. That study found flunixin to be superior to MEL for pain sensitivity based on von Frey filament tests. Following ring castration and tail-docking in sheep, MEL-treated sheep had lower average daily gains compared to FIRO sheep, with the first 2 weeks following the procedures being the most pronounced. A paper comparing FIRO and MEL following castration in horses found no differences between the 2 drugs on stiffness and preputial swelling.

Strengths of the study reported here include utilizing the novel pain measurement outcomes KGA and plasma Sub P. These 2 outcomes have not been utilized in goat pain management research previously. Additionally, KGA was used as the pivotal outcome for the pain label approval of transdermal flunixin. MEL was effective at reducing visually assessed pain behaviors and positively affecting gait measurements. Visual pain behaviors were scored by VAS. Pain behaviors result in an increase in VAS score (higher score = more pain behaviors shown). Animals given MEL seemed more comfortable after surgical castration based on behavior parameters of VAS scoring when compared to FIRO. The average scores of MEL were more comparable to CNTL averages when looking at VAS scores. When pressure mat values were looked at, MEL had values that most closely resembled individuals of the CNTL group, suggesting that MEL provided sufficient analgesia after surgical castration.

FIRO and MEL used for pain control following castration are considered extralabel drug uses in the US. Prescribing veterinarians in the US are encouraged to contact the Food Animal Residue Avoidance Database for assistance in determining a meat withdrawal interval. Veterinarians outside the US are encouraged to contact regulatory officials for assistance in determining when FIRO or MEL concentrations are below maximum residue limits for their country.

Limitations of this study included the small sample size, not using a castrated CNTL group for comparison purposes (a group that was castrated and did not receive postoperative analgesia), and the unknown pharmacokinetics of FIRO and MEL dosing regimens used in this group of goats. Sample size for the current study was determined from data regarding cortisol in goats and cattle following surgical castration, and a sample size of 6 animals/treatment group was determined. An increase in sample size would give more statistical power in the statistical analysis. A castrated CNTL group was not used, as castration is a common husbandry practice proven to be painful to livestock animals of varying species, including goats. With animal welfare considerations in mind, a castrated CNTL group was not implemented. Additional work is needed to provide prescribing veterinarians meat withdrawal intervals for goats treated with MEL or FIRO.

Based on data collected from this study, there is evidence to suggest that MEL can provide some analgesia after surgical castration in goats. This is indicated by changes in VAS and KGA. These data show that administration of MEL perioperatively in goats provided varying degrees of pain relief. FIRO lowered plasma cortisol at later time points, but treated goats had higher VAS scores and persistent changes in gait following castration. Further research is needed to better understand the most effective analgesic drug for goats following painful husbandry procedures such as castration.

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Disclosures

The authors have nothing to disclose. No AI-assisted technologies were used in the generation of this manuscript.
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