ABSTRACT

The objective was to evaluate the analgesic efficacy of pre- and postoperative administration of meloxicam on the postsurgical convalescence period of lame dairy cows undergoing resection of the coffin joint. In a blinded, placebo-controlled, explorative clinical trial, 19 lame German Holstein-Friesian cows weighing 536 ± 98 kg (mean ± SD) and aged 5.7 ± 2.8 yr were included. All cows suffered from unilateral lameness due to septic arthritis of the coffin joint. Lame cows were randomly allocated to either the meloxicam group (n = 9) or the control group (n = 10) and received an intravenous injection of meloxicam (0.5 mg/kg of BW) or an equal volume of saline immediately before surgery (d 0) and once daily from d 1 to 4. All cows received a retrograde intravenous local anesthesia (20 mL of procaine 2%) before the surgical intervention. Heart rate, respiratory rate, body temperature, plasma concentrations of cortisol, as well as production parameters (milk yield and feed intake) were evaluated from d 0 to 7. The gait of the animals was assessed daily by lameness scores and by monitoring the cows’ activity by means of pedometers attached to both hind legs. Possible adverse effects on abomasal mucosal integrity were monitored by fecal occult blood tests and blood cell counts from d 0 to 7 and on d 14. Under meloxicam treatment plasma cortisol levels, lameness scores, and body temperature were significantly reduced compared with controls. While being treated with meloxicam, the time cows were standing per day was significantly longer compared with controls. In the healthy limb significantly more steps were registered in meloxicam-treated cows than in controls. Feed intake and milk yield were not significantly affected by meloxicam. No group differences were found in number of positive tests for fecal occult blood or blood cell counts. In conclusion, repeated meloxicam application demonstrated effective analgesia in the postsurgical period after resection of septically infected coffin joints in dairy cows without indications of evoking adverse effects on abomasal integrity.

Key words: coffin joint resection, meloxicam, pain, analgesic efficacy

INTRODUCTION

Claw disorders, which are responsible for 90% of lameness in cattle (van Amstel and Shearer, 2006), are highly prevalent in large dairy herds (Clarkson et al., 1996; Whay et al., 1998). Current studies in dairy herds found mean prevalences of 39.1% (Main et al., 2010) and 36.8% (range 0 to 79.2%; Barker et al., 2010). In addition to economic losses due to treatment expenses and decrease in productivity (Amory et al., 2008), the associated tissue trauma is perceived as painful by the affected animal (Whay et al., 1998).

Pain is initiated because of tissue damage and inflammatory response associated with claw lesions (Rushen et al., 2007). Depending on severity of the lesions and the period these lesions are left inadequately treated, pain may even sensitize the peripheral and central nociceptive system and result in hyperalgesia (Whay et al., 1998, 2005). Furthermore, the lack of adequate and prompt surgical treatment of typical claw disorders (e.g., sole ulcer, abscess, white line disease, and interdigital necrosis) infection may spread to neighboring structures, manifesting in septic arthritis of the coffin joint (Starke et al., 2007). In these cases, extensive surgical intervention is indicated (Heppelmann et al., 2009a). Because every surgical intervention inevitably results in pain, radical surgery on the bovine digit demands the implementation of an adequate perioperative pain management.

Retrograde intravenous application of local anesthetic proved to successfully diminish pain caused by surgical manipulation for a period of approximately 2
The explorative study was performed as blinded, randomized, and placebo-controlled clinical trial. Septic arthritis of the coffin joint was diagnosed the day before surgery by means of clinical examination, radiography, arthrocentesis (Starke et al., 2007), and sonography (Heppelmann et al., 2008b). All examinations were performed in lateral recumbency on a surgical tipping table without prior application of sedatives. After diagnosis of septic arthritis, cows were fitted with an indwelling jugular vein catheter (WVI jugular catheter, Walter; Veterinär-Instrumente e.K., Baruth/Mark, Germany) after surgical preparation of the skin and local anesthesia (5 mL of 2% procaine-hydrochloride s.c., Procasel 2%; Selectavet GmbH, Weyarn-Holzolling, Germany). The jugular vein catheter was sutured to the skin and additionally covered with a bandage to avoid contamination and mechanical irritation. For maintaining patency, catheters were flushed with heparinized 0.9% saline solution (Braun GmbH, Melsungen; 10,000 IU of heparin/L, heparin-calcium, Ratiopharm GmbH, Ulm, Germany) after insertion and each blood sampling. Catheters were removed on d 7.

Cows were randomly allocated to either the meloxicam group (MEL; n = 9) or placebo (control, CON) group (n = 10), receiving meloxicam (0.5 mg/kg of BW i.v.; Metacam; Boehringer Ingelheim GmbH, Ingelheim, Germany) or an equal volume of sterile isotonic saline solution (0.9% sodium chloride solution i.v., NaCl 0.9% ad us. vet. B. Braun, B. Braun Vet Care GmbH, Tuttingen, Germany), respectively. Initial administration took place in the stable before surgery on d 0 and was then repeated once daily at 0800 h for another 4 consecutive d postoperatively. Fifteen minutes after drug application cows were moved to the surgical room and turned into lateral recumbency for surgical intervention. All cows, regardless of their allocated group, received a retrograde intravenous local anesthetic (20 mL of 2% procaine-hydrochloride) combined with 3,000,000 U of sodium penicillin G dissolved (Dietz et al., 1980) in 10 mL of sterile sodium chloride solution (300,000 U/mL; Aulicin; Albrecht GmbH & Co. KG, Aulendorf, Germany) after surgical preparation of the skin and lo- cation of the surgical site. The jugular vein catheter was sutured to the skin and additionally covered with a bandage to avoid contamination and mechanical irritation. For maintaining patency, catheters were flushed with heparinized 0.9% saline solution (Braun GmbH, Melsungen; 10,000 IU of heparin/L, heparin-calcium, Ratiopharm GmbH, Ulm, Germany) after insertion and each blood sampling. Catheters were removed on d 7.

The explorative study was performed as blinded, randomized, and placebo-controlled clinical trial. Septic arthritis of the coffin joint was diagnosed the day before surgery by means of clinical examination, radiography, arthrocentesis (Starke et al., 2007), and sonography (Heppelmann et al., 2008b). All examinations were performed in lateral recumbency on a surgical tipping table without prior application of sedatives. After diagnosis of septic arthritis, cows were fitted with an indwelling jugular vein catheter (WVI jugular catheter, Walter; Veterinär-Instrumente e.K., Baruth/Mark, Germany) after surgical preparation of the skin and local anesthesia (5 mL of 2% procaine-hydrochloride s.c., Procasel 2%; Selectavet GmbH, Weyarn-Holzolling, Germany). The jugular vein catheter was sutured to the skin and additionally covered with a bandage to avoid contamination and mechanical irritation. For maintaining patency, catheters were flushed with heparinized 0.9% saline solution (Braun GmbH, Melsungen; 10,000 IU of heparin/L, heparin-calcium, Ratiopharm GmbH, Ulm, Germany) after insertion and each blood sampling. Catheters were removed on d 7.

Cows were randomly allocated to either the meloxicam group (MEL; n = 9) or placebo (control, CON) group (n = 10), receiving meloxicam (0.5 mg/kg of BW i.v.; Metacam; Boehringer Ingelheim GmbH, Ingelheim, Germany) or an equal volume of sterile isotonic saline solution (0.9% sodium chloride solution i.v., NaCl 0.9% ad us. vet. B. Braun, B. Braun Vet Care GmbH, Tuttingen, Germany), respectively. Initial administration took place in the stable before surgery on d 0 and was then repeated once daily at 0800 h for another 4 consecutive d postoperatively. Fifteen minutes after drug application cows were moved to the surgical room and turned into lateral recumbency for surgical intervention. All cows, regardless of their allocated group, received a retrograde intravenous local anesthetic (20 mL of 2% procaine-hydrochloride) combined with 3,000,000 U of sodium penicillin G dissolved (Dietz et al., 1980) in 10 mL of sterile sodium chloride solution (300,000 U/mL; Aulicin; Albrecht GmbH & Co. KG, Aulendorf, Germany) using the technique of Antalovsky (1965). Thereafter, surgical resection of the affected coffin joint was performed (Nuss and Weaver, 1991; Starke et al., 2007). Briefly, the horn was removed to expose the corium of the heel and the plantar third of the sole. The distal end of the deep flexor tendon, the heel cushion, and the distal sesamoid bone were removed. The branch of the deep flexor tendon to the second phalanx was protected during this procedure. An air-powered surgical drill (630 kPa; 21,000 rpm; Bosch AG, Gerlingen-Schillerhöhe, Germany) with a 6-mm diameter bit was used to remove the tuberculum flexorium, and a 1-cm canal was drilled diagonally through the distal interphalangeal joint from plantar to proximodorsal in directing to a point 1 cm below.
the coronary band. Water was used for cooling during the drilling procedure. Benzyl penicillin (Tardomyce; Bayer AG, Leverkusen, Germany) was instilled into the opened flexor tendon sheath and the wound cavity. A wooden block (Demotec 95; Demotec Siegfried Demel, Nidderau, Germany) was attached to the opposite claw. All cows received systemic antibiotic treatment (10 mg/kg of ampicillin trihydrate s.c.; Ampisus 20 S; Alvetra GmbH, Neumünster, Germany) twice daily for 5 d.

**Data Collection**

**Clinical Parameters.** Heart rate (HR), respiratory rate (RR), and rectal body temperature were measured daily at 0700 h and feed intake and milk yield were assessed daily for 7 consecutive days after the intervention. The HR was determined by counting the heart beats in 1 min by auscultation, RR by counting thoracic excursions for a period of 1 min, and rectal temperature by a digital thermometer. Daily milk yield (kg/d) was recorded as the sum of the morning (at 0630 h) and evening (at 1500 h) milking. Rations were fed twice daily at 0700 h and 1900 h. Orts were removed immediately before feeding. Dry matter intake was registered as the amount of feed offered minus the recorded orts on a DM basis.

**Gait Score.** Gait assessment was carried out while the cow was rising, while it was standing, and while walking over a distance of 20 m in a straight line on a concrete floor led by a handler. Two experienced observers, masked to the treatment group assignment, assessed scores for each cow each day using a numeric rating scale with 5 major scores and intermediate levels (Table 1). The average of both scores was taken for statistical analysis.

**Activity.** Pedometers (Ice Tag System, versions 2.004 and 2.009; IceRobotics Ltd., Edinburgh, UK) were strapped to the metatarsus of the lame and sound limb. According to the manufacturers’ information, pedometers contain a 3-axis accelerometer that takes 16 readings per second and measures acceleration relative to gravity. A change in acceleration thus determines whether or not the animal is making a stepping action. Recordings were performed while cows were in their individual pens continuously from d 0 to 7. The time animals were standing per day (h/d), the daily bouts of standing (n/d), the duration of standing bouts (h), and the number of registered steps in the affected and in the

**Table 1.** Definition of gait assessment according to 5 major lameness scores (I to V) and intermediate levels for the affected hind limb used in the present study, assessed during rising, standing after rising (observation for 10 min), and halter-guided walking over a distance of 20 m on a concrete floor (modified according to Dirksen et al., 1990; Sprecher et al., 1997; Flower and Weary, 2006)

<table>
<thead>
<tr>
<th>Clinical lameness</th>
<th>Lameness score</th>
<th>Allocated score</th>
<th>Description of lameness</th>
</tr>
</thead>
</table>
| Not lame (normal gait) | 0 | 0 | Rising: quick and easy  
Standing: weight bearing equally on all 4 legs  
Walking: fluid and smooth movement, symmetrical gait, imprint of fore limb into imprint of hind limb, straight back, steady head carriage |
| Mildly lame | + | 1 | Rising: quick and easy  
Standing: weight bearing of affected limb occasionally slightly reduced  
Walking: almost fluid and smooth movement, imprint of hind limb into or slightly behind imprint of fore limb, almost straight back |
| Moderately lame | + | 4 | Rising: weight bearing of affected limb reduced for a short period immediately after rising |
| Lame | + | 7 | Rising: weight bearing of affected limb clearly reduced for a short period |
| Severe | + | 10 | Rising: weight bearing of affected limb clearly reduced during rising and repeatedly lifted after rising |
| Highly severe | V | 13 | Rising: struggling to rise without putting weight bearing on affected limb  
Standing: almost no weight bearing on affected limb  
Walking: almost no weight bearing on affected limb, vigorous encouragement needed for movement |

Concerning lameness score, a “+” signifies the tendency of the main score toward the lower score and a “−” towards the higher score.
sound limb per hour while animals were standing were registered. A ratio was calculated between registered steps in the lame and the sound limb (step ratio = steps lame limb/stepssound limb).

**Sample Collection and Analysis.** Venous blood samples were collected into heparinized and EDTA-covered tubes from the jugular vein catheter each morning at 0700 h for 7 d. Another blood sample was taken on d 14 via direct venipuncture. Heparinized blood samples were immediately centrifuged (at 1,500 × g for 10 min at 4°C) and plasma was stored at −20°C until analysis of cortisol (d 0 to 7; chemiluminescent enzyme immunoassay; Siemens Healthcare Diagnostics GmbH, Eschborn, Germany). Leucocytes, erythrocytes, platelets, packed cell volume, and hemoglobin concentrations were measured immediately after collection from EDTA tubes using a flow cytometer (d 0 to 7 and d 14; Celtac α, MEK 61086; Nihon Kohden Europe GmbH, Rosbach vor der Höhe, Germany). Fecal samples were collected after measurement of body temperature on d 0 to 7 and on d 14 postsurgery and were macroscopically examined and tested for occult blood using a guaiac fecal test (hemo FEC test; Roche Diagnostics GmbH, Munich, Germany) according to the manufacturers’ instructions.

**Statistical Analysis**

Statistical analyses were performed with SAS (version 9.2; SAS Institute Inc., Cary, NC). All parameters were tested for deviation from normal distribution within groups by means of the Shapiro-Wilk-Test (PROC UNIVARIATE). To estimate the effects of group, time and their interaction, a 2-way ANOVA for repeated measurements on 1 factor (SAS PROC GLM) was used if the data were normally distributed. For not normally distributed parameters (variables plasma cortisol, standing time, standing bouts, duration of standing bouts, steps of affected limb, steps of sound limb, and step ratio) and lameness score these analyses of variance were done by ranks.

The decision if a statistically significant treatment effect can be assumed is based on the outcome of the global F-tests from the ANOVA. Differences of means between groups were tested with the 2-sample t-test (normally distributed variables) or Wilcoxon 2-sample test (not normally distributed variables) on every experimental day. Differences between measurements at different experimental days and the baseline within groups were tested using the t-test for paired observations for normally distributed variables; otherwise, the matched-pairs signed rank test was used. This procedure followed suggestions for the evaluation of medicinal products in clinical trials made by the European Medicines Agency, Committee for Proprietary Medicinal Products (2002). Frequencies of positive fecal occult blood tests were designated to be tested for group differences by the Fisher exact test.

Although data of not normally distributed variables and lameness scores are presented as medians with 25 and 75% percentiles, other data are presented as means ± standard deviation. The level of statistical significance was set at P < 0.05 and a statistical trend was assumed at the level of P < 0.1. Results of multiple comparisons of group means at different experimental days are only presented when the global F-test for group was less than P < 0.1.

**RESULTS**

**Plasma Cortisol and Clinical Parameters**

Average plasma concentrations of cortisol were significantly lower in MEL cows compared with CON cows (group effect: P = 0.006; Table 2). No time and group × time effects were found for plasma cortisol.

No group effect (P = 0.11) but a significant time effect (P = 0.004) and interaction effect of group × time (P = 0.021) were found for HR. Whereas HR decreased significantly in cows after MEL treatment during the study period, HR remained almost unchanged in CON cows. No significant main effects were found for RR.

Although body temperature was, on average, significantly lower in MEL cows (group effect: P = 0.025) compared with CON cows, differences between groups and changes within groups over time were small. Time and group × time interaction revealed no significant effects on mean body temperature.

**Lameness Score, Feed Intake, Milk Yield, and Activity**

Statistical analysis revealed a significant group effect on lameness scores (P = 0.024). Scores were lower under MEL treatment compared with those for CON cows. The significant time effect (P < 0.001) for lameness scores reflects the mainly reduced lameness scores from d 1 to 5 compared with d 0 in MEL cows.

For DMI, only a significant time effect (P < 0.001) was revealed. Mean DMI for CON cows was 12.3 ± 2.7 kg/d and 13.2 ± 1.4 kg/d for MEL cows on d 0 (P = 0.91) and increased until d 7 to 13.9 ± 2.8 kg/d and 13.7 ± 3.4 kg/d, respectively (P = 0.86; main effects: group: P = 0.86, group × time: P = 0.88). The mean milk yield of CON cows and MEL cows was not significantly different on d 0 (14.5 ± 6.2 kg/d vs. 16.2 ± 5.5 kg/d, respectively; P = 0.51) and did not change noticeably over time (d 7: 15.5 ± 5.6 kg/d vs. 17.4 ±
Table 2. Plasma concentration of cortisol, heart rate, respiratory rate, body temperature, and lameness score of dairy cows on the day of surgical resection of the septic infected coffin joint (d 0) and over 7 d after surgery.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Main effect2 (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>G</td>
</tr>
<tr>
<td>Plasma cortisol (ng/mL)</td>
<td>Control 3</td>
<td>6.5</td>
<td>9.5</td>
<td>11.3</td>
<td>11.9</td>
<td>10.1</td>
<td>8.4</td>
<td>7.8</td>
<td>10.7</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>(4.7–12.8)</td>
<td>(5.7–14.9)</td>
<td>(6.6–13.1)</td>
<td>(4.6–15.2)</td>
<td>(7.1–11.7)</td>
<td>(3.9–12.4)</td>
<td>(5.4–10.8)</td>
<td>(7.5–14.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meloxicam 3</td>
<td>6.1</td>
<td>6.0</td>
<td>3.2</td>
<td>4.5</td>
<td>5.6</td>
<td>3.2</td>
<td>4.8</td>
<td>5.6</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>(5.0–9.1)</td>
<td>(4.4–8.7)</td>
<td>(2.7–5.6)</td>
<td>(2.2–6.4)</td>
<td>(1.5–9.1)</td>
<td>(1.5–4.8)</td>
<td>(3.9–8.6)</td>
<td>(4.2–6.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group difference4</td>
<td>1.0</td>
<td>0.28</td>
<td>0.032</td>
<td>0.21</td>
<td>0.048</td>
<td>0.027</td>
<td>0.38</td>
<td>0.015</td>
<td>0.01</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>Control 5</td>
<td>73 ± 6</td>
<td>80 ± 10</td>
<td>79 ± 8</td>
<td>78 ± 13</td>
<td>77 ± 13</td>
<td>73 ± 9</td>
<td>75 ± 10</td>
<td>75 ± 11</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>Meloxicam 5</td>
<td>77 ± 11</td>
<td>73 ± 6</td>
<td>71 ± 10</td>
<td>68 ± 8</td>
<td>67 ± 6</td>
<td>66 ± 8</td>
<td>67 ± 7</td>
<td>69 ± 7</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>(beats/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>Control 5</td>
<td>38 ± 15</td>
<td>38 ± 11</td>
<td>37 ± 10</td>
<td>42 ± 17</td>
<td>41 ± 14</td>
<td>41 ± 16</td>
<td>40 ± 12</td>
<td>37 ± 12</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>Meloxicam 5</td>
<td>40 ± 15</td>
<td>36 ± 10</td>
<td>34 ± 12</td>
<td>33 ± 9</td>
<td>30 ± 7</td>
<td>35 ± 9</td>
<td>36 ± 9</td>
<td>33 ± 8</td>
<td>0.025</td>
</tr>
<tr>
<td></td>
<td>(breaths/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>Control 5</td>
<td>39.0 ± 0.3</td>
<td>38.9 ± 0.7</td>
<td>39.0 ± 0.3</td>
<td>39.0 ± 0.3</td>
<td>39.0 ± 0.3</td>
<td>39.0 ± 0.3</td>
<td>38.9 ± 0.2</td>
<td>38.9 ± 0.2</td>
<td>0.024 &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Meloxicam 5</td>
<td>38.9 ± 0.2</td>
<td>38.8 ± 0.1</td>
<td>38.7 ± 0.1</td>
<td>38.6 ± 0.1</td>
<td>38.6 ± 0.2</td>
<td>38.7 ± 0.2</td>
<td>38.8 ± 0.2</td>
<td>38.9 ± 0.2</td>
<td>0.024 &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(°C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group difference4</td>
<td>0.51</td>
<td>0.63</td>
<td>0.008</td>
<td>0.006</td>
<td>0.015</td>
<td>0.082</td>
<td>0.19</td>
<td>0.76</td>
<td>0.004</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>Control 5</td>
<td>10.5</td>
<td>10.0</td>
<td>10.0</td>
<td>9.5</td>
<td>9.5</td>
<td>9.0</td>
<td>8.5</td>
<td>8.0</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td>Meloxicam 3</td>
<td>10.0</td>
<td>8.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>7.0</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td>(°C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group difference4</td>
<td>0.28</td>
<td>0.068</td>
<td>0.031</td>
<td>0.030</td>
<td>0.053</td>
<td>0.080</td>
<td>0.22</td>
<td>0.094</td>
<td>0.004</td>
</tr>
</tbody>
</table>

1 All cows received for surgery regional intravenous anesthesia with 20 mL of procaine and either meloxicam (0.5 mg/kg of BW; i.v.; n = 10) or sodium chloride (control; n = 9) in an equal volume 30 min before the intervention and on d 1 to 4. Bold values differ significantly (P < 0.05) from the baseline (d 0).
2 Analysis of variance: T = time effect; G = group effect; G × T = group × time effect.
3 Medians (with 25th and 75th percentiles in parentheses).
4 P-value of group differences in corresponding means at specific time points.
5 Means ± SD.
6 Score range: 0 to 13; score 0: not lame; score 2: mildly lame; score 5: moderately lame; score 8: lame; score 11: severely lame; score 13: no weight bearing while standing and walking.
5.7 kg/d, respectively; main effects: group: \( P = 0.35 \),
time: \( P = 0.12 \), group \( \times \) time: \( P = 0.80 \).

The average time cows spent standing per day was
significantly longer in MEL cows than in CON cows
(group effect: \( P < 0.001 \), group \( \times \) time effect:
\( P = 0.013 \); Table 3). Although the number of standing bouts
was not significantly different between groups (group
effect: \( P = 0.99 \)) the number of bouts decreased over
time in both groups (time effect: \( P = 0.028 \)). Statistical
analysis of the duration of standing bouts revealed
a trend for group (\( P = 0.058 \)) and time effects
(\( P = 0.067 \); Table 3). Whereas under MEL treatment,
the duration of standing bouts increased, the duration in
CON cows remained almost unchanged.

The steps per hour taken by the affected limb (Table
3) were, on average, not significantly different between
groups (group effect: \( P = 0.84 \)) and revealed no ef-
fect for interaction of group \( \times \) time, but altogether
decreased over time (time effect: \( P < 0.001 \)). Steps per
hour registered in the sound limb (Table 3) were, on
average, significantly higher in MEL cows than in CON
cows (group effect: \( P = 0.018 \)). The time (\( P = 0.003 \))
and group \( \times \) time effects (\( P = 0.043 \)) were significant.
Whereas the number of steps in the sound limb of MEL
cows remained almost unchanged over time, in CON
cows, the number of steps was significantly reduced in
the days after surgery.

The ratio in steps between the affected and the sound
limb was significantly higher in CON cows compared
with MEL cows (group effect: \( P = 0.018 \)). Although the
average step ratio increased in the days after surgery
compared with baseline in CON cows, ratios in MEL
cows remained almost unchanged during the study pe-
riod (time effect: \( P = 0.031 \), group \( \times \) time effect:
\( P = 0.005 \); Table 3).

Blood Cell Count and Fecal Occult Blood

No statistically significant differences were observed
between the groups regarding blood counts of erythro-
cytes, leucocytes, and platelets as well as blood hemo-
globin concentration and packed cell volume in the first
week postoperatively as well as on d 14 (Table 4). The
result of the hemo FEC test was consistently negative
in all MEL as well as all CON cows.

DISCUSSION

The evaluation of results of plasma cortisol concen-
trations, HR, activity, and gait scores of this study in-
dicate an analgesic effect of the NSAID meloxicam on
dairy cows undergoing surgical resection of the distal
interphalangeal joint due septical infection.

The hypothalamic-pituitary axis is activated as a
response to perceived pain (El-Ghoul and Hofmann,
2002) and also by release of proinflammatory cytokines
(tumor necrosis factor α, IL-1, and IL-6 from trauma-
tized tissues (Gadek-Michalska and Bugajski, 2010;
Rivest, 2010), leading to elevated cortisol plasma levels.
In the current study, as before in calves after cautery
derhorming (Heinrich et al., 2009), MEL treatment led
to reduced plasma cortisol concentrations in the post-
surgical period compared with CON cows. Also in mice,
the daily administration of meloxicam prevented an
increase in corticosterone concentrations for 3 d after
partial hepatectomy (Tubbs et al., 2011). The reduced
cortisol levels may be caused by pain reduction due to
the analgesic effect of meloxicam. However, meloxicam
is a preferential inhibitor of COX-2 (Furst, 1997) and
activation of the hypothalamic-pituitary axis may be
affected independently of pain perception by its antiin-
flammatory properties in cows with inflammatory claw
diseases. Furthermore, elevated cortisol levels alone are
unreliable indicators of pain, as surges in cortisol are
also strongly associated with handling stress, fear, and
general discomfort (Molony and Kent, 1997; Rizk et
al., 2012a). Changes in animal behavior and clinical
parameters such as heart rate are seen as more sensi-
tive indicators of pain than plasma cortisol (Grondahl-
Nielsen et al., 1999; Anil et al., 2002; Anderson and
Muir, 2005).

In the days after resection of the coffin joint dairy
cows revealed reduced heart rates compared with d 0
when treated with meloxicam but not in CON cows.
This finding is in agreement with studies in MEL calves
following dehorning (Heinrich et al., 2009; Stewart et
al., 2009). Although the findings of Heinrich et al.
(2009) were paralleled by a reduced respiratory rate,
only numerical, but no significant decreases in respira-
tory rate were found in MEL cows in the current study.
The decreased body temperature in the MEL group
on d 2 to 4 is most probably due to the antipyretic
and antiinflammatory properties of the NSAID (Furst,
1997; Heinrich et al., 2009).

Lameness is an expression of pain in cows with claw
diseases (Rushen et al., 2007) and can be semiquantita-
tively assessed by gait numerical rating scales (Whay
et al., 1998; Flower and Weary, 2006). In cows with
infected coffin joints, a quick reduction in lameness
scores can be expected after digital amputation when
inflammatory affected tissue is almost completely re-
moved. In contrast, when using more conservative and
claw-preserving techniques, such as the resection of the
coffin joint, lameness scores remain almost unchanged
for several days after the surgery (Starke et al., 2007;
Heppelmann et al., 2009a) as seen also in CON cows of
Table 3. Results of pedometry (medians with 25th and 75th percentiles in parentheses) in dairy cows on the day of surgical resection of the septic infected coffin joint (d 0) and over 7 d after surgery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Days after surgery</th>
<th>Main effect ($P$-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Standing time ($h/d$)</td>
<td>Control</td>
<td>8.9</td>
<td>8.6</td>
</tr>
<tr>
<td></td>
<td>(7.4–9.2)</td>
<td>(6.2–9.4)</td>
<td>(6.2–7.7)</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>9.1</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>(6.5–11.2)</td>
<td>(9.1–11.6)</td>
<td>(8.0–12.0)</td>
</tr>
<tr>
<td>Group difference</td>
<td>0.93</td>
<td>0.13</td>
<td>0.022</td>
</tr>
<tr>
<td>Standing bouts (no./d)</td>
<td>Control</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>12</td>
<td><strong>10</strong></td>
</tr>
<tr>
<td></td>
<td>(9–14)</td>
<td>(6–12)</td>
<td>(8–11)</td>
</tr>
<tr>
<td>Group difference</td>
<td>0.68</td>
<td>0.71</td>
<td>0.63</td>
</tr>
<tr>
<td>Duration of standing bouts (h)</td>
<td>Control</td>
<td>0.54</td>
<td><strong>1.33</strong></td>
</tr>
<tr>
<td></td>
<td>(0.53–1.18)</td>
<td>(0.57–1.05)</td>
<td>(0.57–0.86)</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>0.79</td>
<td>0.17</td>
</tr>
<tr>
<td>Steps of affected limb ($/h$)</td>
<td>Control</td>
<td>88</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>70</td>
<td>55</td>
</tr>
<tr>
<td>Steps of sound limb ($/h$)</td>
<td>Control</td>
<td>17</td>
<td><strong>11</strong></td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>29</td>
<td><strong>33</strong></td>
</tr>
<tr>
<td>Group difference</td>
<td>0.60</td>
<td>0.058</td>
<td>0.041</td>
</tr>
<tr>
<td>Step ratio</td>
<td>Control</td>
<td>4.4</td>
<td><strong>8.1</strong></td>
</tr>
<tr>
<td></td>
<td>(3.4–6.9)</td>
<td>(4.1–15.8)</td>
<td>(4.5–16.2)</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>2.5</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>(1.7–3.4)</td>
<td>(1.2–3.3)</td>
<td>(1.0–4.4)</td>
</tr>
<tr>
<td>Group difference</td>
<td>0.038</td>
<td>0.018</td>
<td>0.032</td>
</tr>
</tbody>
</table>

1All cows received regional intravenous anesthesia with 20 mL of procaine and either meloxicam (0.5 mg/kg of BW; i.v.; n = 10) or sodium chloride (control; n = 9) in an equal volume 30 min before the intervention and on d 1 to 4. Bold values differ significantly ($P < 0.05$) from the baseline.

2Analysis of variance: T = time effect; G = group effect; G × T = group × time effect.

3Recorded while cow was standing.

4$P$-value of group differences in corresponding means at specific time points.

5Ratio of recorded steps while standing on the lame and healthy limb (step ratio = stepsNlame limb/stepsNhealthy limb).
the current study. The lack of immediate improvement in gait scores after resection of the coffin joint is eminent despite the application of wooden blocks under the healthy partner claw to relieve pressure and mechanical irritation to the surgical area of the treated claw. This may be attributable to secondary hyperalgesia, which had developed around the damaged tissue before surgery (Whay et al., 1998, 2005) or pain induced by the extensive surgical procedure. This study indicated improved gait scores after surgery in MEL cows. Reduced lameness scores after MEL treatment have also been demonstrated in previous studies concerning canine and equine arthritis (Rainsford et al., 1999; Peterson and Keefe, 2004; Toutain and Cester, 2004). In an induced lameness model based on intraarticular injection of LPS in horses, meloxicam administration also led to reduced lameness within a few hours after administration (de Grauw et al., 2009). The attenuation of lameness was accompanied by reduced levels of prostaglandin E2, substance P, and bradykinin in synovial fluid, emphasizing its antiinflammatory potency. The administration of the NSAID ketoprofen in lame cows demonstrated no (Whay et al., 2005; Feist et al., 2008; Chapinal et al., 2010) or only modest (Flower et al., 2008) positive effects on gate scores. Whereas the cows in the above-named studies were diagnosed with varying degrees of lameness, all cows included in the current study suffered from septic arthritis of the coffin joint and were, therefore, severely lame. According to Flower and Weary (2006) and Flower et al. (2008) the detection of gait changes are easier at higher intensities of pain.

As a result of pain, lame cows show typical changes in daily activity patterns. To avoid weight loading on the painful limb, standing time is commonly decreased in lame cows and the duration of their individual standing bouts are shorter (Munksgaard et al., 2006; Chapinal et al., 2009, 2010). In the current study, daily standing time was significantly extended and a trend was found for duration of standing bouts in cows after MEL treatment, which is seen as an expression of reduced pain perception and improved general well being. These parameters remained unaffected in lame cows after treatment with ketoprofen (Chapinal et al., 2010). However, ketoprofen treatment revealed a significant effect on weight shifting between the lame and healthy rear legs measured by weighing platforms. This observation was interpreted as an indication for reduced restless behavior due to pain mitigation by applied treatment (Chapinal et al., 2010).

Pedometers fixed to a sound rear limb registered a reduced number of steps in lame compared with healthy cows (O’Callaghan et al., 2003), indicating that cows reduce their activity to avoid weight loading to the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Days after surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (10⁶/μL)</td>
<td>Control</td>
<td>6.23 ± 0.86</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>5.82 ± 0.76</td>
</tr>
<tr>
<td>Leucocytes (10³/μL)</td>
<td>Control</td>
<td>7.20 ± 1.99</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>6.42 ± 1.81</td>
</tr>
<tr>
<td>Platelets (10⁵/μL)</td>
<td>Control</td>
<td>6.04 ± 0.99</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>5.53 ± 0.95</td>
</tr>
<tr>
<td>Hb (g/L)</td>
<td>Control</td>
<td>9.16 ± 1.02</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>9.24 ± 0.91</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>Control</td>
<td>25.8 ± 3.0</td>
</tr>
<tr>
<td></td>
<td>Meloxicam</td>
<td>25.2 ± 3.2</td>
</tr>
</tbody>
</table>

All cows received for surgery regional intravenous anesthesia with 20 mL of procaine and either meloxicam (0.5 mg of i.v. BW; l.v.; n = 10) or sodium chloride (control; n = 9) in the current study. The lack of immediate improvement in gait scores after resection of the coffin joint is eminent despite the application of wooden blocks under the healthy partner claw to relieve pressure and mechanical irritation to the surgical area of the treated claw.
painful limb. In the current study, CON cows took a significantly lower number of steps per hour with the sound limb compared with MEL cows, indicating more active behavior in treated cows.

Lame cows tend to reduce the weight placed on the affected limb but weight shifting between the sound and affected limb occurs frequently in the standing animal (Neveux et al., 2006; Chapinal et al., 2010; Pastell et al., 2010). In the current study, pedometers were applied to both hind legs. The number of registered steps was about 2 to 7 times higher in the affected than in the sound rear limb. Weight shifting does not explain the high registered step frequency in the affected limb. In our view, most likely this finding is due to increased adduction of the affected limb as a sign of pain and discomfort, which was nonetheless counted as a step by the pedometer. Although limb lifting in the affected limb was observed by the authors during daily clinical examination, milking and feeding, it was not quantitatively recorded and no video observations were performed for retrospective analysis so that a conclusive explanation for the observed high step frequency cannot be given. In previous studies (Chapinal et al., 2011; Krebs et al., 2011), an increased step frequency in standing animals was interpreted as restless behavior and an expression of discomfort. Cows of this study were kept, fed, and milked in small individual freestall pens. Thus, in the view of the authors under these conditions an increased ratio of the step frequency in the affected and sound limb may also express restlessness and discomfort in lame cows. Control cows presented a higher step frequency ratio than cows under MEL treatment, likely indicating a higher level of discomfort in the affected limb in CON cows.

Higher degrees of lameness in cows are associated with altered feeding behavior and reduced DMI (González et al., 2008) as well as a decrease in milk yield (Green et al., 2002; Bach et al., 2007; Bicalho et al., 2008). In this study, meloxicam revealed no effect on daily DMI and milk yield. However, this may be due to the fact that cows were kept in small individual freestall pens with feed and water available in close proximity at all times. Thus, cows had only to walk a very small distance to access feed, or could even eat while recumbent.

Inflammatory alterations of the abomasal mucosa are often associated with bleeding episodes into the abomasum and, in severe cases, even with anemia (Smith et al., 1983). Generally, the use of NSAID over extended periods bear the risk of inducing gastric lesions (Grubb, 2010). However, the administration of 0.5 mg of meloxicam/kg of BW as a preferential COX-2 inhibitor (Furst, 1997; Cooper et al., 2009) over a period of 5 d revealed no adverse effects on the gastrointestinal tract in the current study, as demonstrated by consistently negative test results for occult blood in feces and no apparent changes in the red blood cell picture.

In CON cows that received no analgesics after surgery, mean lameness scores remained almost unchanged until d 6 and the step frequency ratio even increased the day following surgery. Stark et al. (2007) reported increased lameness scores for 2 d after the resection of a coffin joint. These observations suggest that in the first days after resection of a septic joint pain and discomfort appear almost unchanged or even worse in the affected limb. Thus, for ethical reasons in future studies new protocols for pain management in lame cows should be tested against an effective analgesic drug as a positive control instead of a placebo-treated negative control. Furthermore, cows should be granted analgesic treatment for at least 4 to 6 d after major claw surgeries, depending on the individual postsurgical convalescence.

CONCLUSIONS

Repeated meloxicam application indicated effective analgesia in the postsurgical period after resection of septic joints in dairy cows without indications for causing adverse effects on abomasal integrity. Meloxicam’s analgesic and anti-inflammatory properties may be used to complement local anesthesia during and after surgical intervention on the bovine digit postsurgery.

ACKNOWLEDGMENTS

The authors acknowledge the financial support given by Boehringer Ingelheim GmbH (Ingelheim, Germany). Boehringer Ingelheim GmbH exerted no influence on study design, evaluation, and interpretation of results and manuscript composition.

REFERENCES


