Analgesic efficacy of an intravenous constant rate infusion of a morphine-lidocaine-ketamine combination in Holstein calves undergoing umbilical herniorrhaphy

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OBJECTIVE
To assess the analgesic efficacy of an IV constant rate infusion (CRI) of a morphine-lidocaine-ketamine (MLK) combination in calves undergoing umbilical herniorrhaphy.

ANIMALS
20 weaned Holstein calves with umbilical hernias.

PROCEDURES
Calves were randomly assigned to receive a CRI of an MLK solution (0.11 mL/kg/h; morphine, 4.8 µg/kg/h; lidocaine, 2.1 mg/kg/h; and ketamine, 0.42 mg/kg/h) for 24 hours (MLK group) or 2 doses of flunixin meglumine (1.1 mg/kg, IV, q 24 h) and a CRI of saline (0.9% NaCl) solution (0.11 mL/kg/h) for 24 hours (control group). The assigned CRI was begun after anesthesia induction. A pain-scoring system and incisional algometry were used to assess pain, and blood samples were obtained to measure serum cortisol concentration at predetermined times for 120 hours after CRI initiation.

RESULTS
Mean pain scores did not differ significantly between the MLK and control groups at any time. Mean algometry score for the MLK group was significantly greater (calves were less responsive to pressure) than that for the control group at 4 hours after CRI initiation. Mean cortisol concentration decreased over time for both groups and was significantly greater for the MLK group than the control group at 1, 4, and 18 hours after CRI initiation.

CONCLUSIONS AND CLINICAL RELEVANCE
A CRI of MLK provided adequate postoperative analgesia to calves that underwent umbilical herniorrhaphy. However, the technical support required for CRI administration limits its use to hospital settings. Kinetic analyses of MLK infusions in cattle are necessary to establish optimal dosing protocols and withdrawal intervals. (*Am J Vet Res* 2020;81:25–32)

Identification and alleviation of pain in farm animals have garnered substantial attention in recent years owing to the ever increasing awareness of the importance of animal welfare in production animal systems.[1] The AVMA position statement on pain in animals[2] states that "animal pain is a clinically important condition that adversely affects an animal's quality of life. Drugs, techniques, or husbandry methods should be used to prevent, minimize, and relieve pain… and should be based, in part, on the species, sex, breed, age, procedure performed, degree of tissue trauma, individual behavioral characteristics, assessment of the degree of pain, and health status of the animal."

Veterinarians consider abdominal surgery to be the most painful surgical condition of cattle, and > 90% of veterinarians administer at least 1 dose of an analgesic during the perioperative period to cattle that undergo abdominal surgery.[3,4] Despite veterinarians' concerns about patient comfort following abdominal surgery, analgesic protocols for use in cattle following abdominal surgical procedures are limited.[3] According to that survey,[3] flunixin meglumine, an NSAID, is the most common drug administered to cattle during the postoperative period. Although flunixin meglumine is the only NSAID currently approved by the US FDA for use in cattle, it is approved only for the treatment of fever and endotoxemia; it is not approved as an analgesic. Few studies[5,6] have been conducted to assess analgesia in cattle following abdominal surgical procedures. Because abdominal surgical procedures are commonly performed in cattle, it is imperative that research be conducted to focus on both identification and alleviation of perioperative pain in those animals. Abdominal surgical procedures commonly performed in cattle include standing exploratory laparotomy, correction of abomasal displacements, cesarean section, and herniorrhaphy. Results of multiple studies[7–9] suggest that

ABBREVIATIONS

CRI	Constant rate infusion
HR	Heart rate
MLK	Morphine-lidocaine-ketamine
RR	Respiratory rate
TP	Total protein

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mitigation of pain and painful stimuli in cattle may lead to improved gastrointestinal tract function and return to health as well as limit production losses.

For cattle, most pain management research has focused on NSAIDs with alternative pain management modalities and analgesics only sporadically evaluated.[5,8,10,11] To our knowledge, studies to evaluate CRIs of analgesics to alleviate postoperative pain in cattle have not been performed. In our hospital, we commonly administer a CRI of MLK to cattle that undergo surgical procedures to alleviate postoperative pain and help prevent pain-induced ileus.[12–14] It is our clinical impression that those patients benefit from the CRI of MLK.

Pain management in farm animals and the benefits and risks associated with the administration of analgesics to cattle continue to be important topics of research.[8–11,15–22] The purpose of the study that is partially reported here was to describe the pharmacokinetics and analgesic efficacy of morphine, lidocaine, and ketamine associated with IV administration of an MLK combination as a CRI to calves undergoing umbilical herniorrhaphy. This article focuses solely on the analgesic efficacy aspect of the study; the pharmacokinetics aspect of the study is reported elsewhere.[23] For the portion of the study reported here, a subjective pain-scoring system and incisional algometry were used to assess surgical pain. A secondary goal was to establish a pain assessment method for cattle during the postoperative period by means of evaluation of physiologic and behavioral variables. We hypothesized that the pain scores for calves that received a 24-hour CRI of MLK would be significantly lower than those for calves that received 2 doses of flunixin meglumine.

Materials and Methods

Animals

Study procedures were reviewed and approved by The Ohio State University Clinical Research Advisory Committee and Institutional Animal Care and Use Committee. Owner consent was obtained for each animal prior to its enrollment in the study. Weaned Holstein calves that were admitted to The Ohio State University Veterinary Medical Center for surgical correction of an umbilical hernia were considered for study enrollment. Only calves that were clinically normal aside from the umbilical hernia, as determined by the results of a physical examination, were considered eligible for the study. All calves were obtained from 1 premises and examined by the same investigator (AKH) at hospital admission. Twenty calves were enrolled in the study.

Study design

The study was a prospective, blinded, case-control clinical trial. Calves were randomly assigned to 1 of 2 treatment groups (MLK and control groups; 10 calves/group) by means of a random number generator. Blood samples were collected at predetermined times before and after administration of the assigned treatment. Calves were also assigned subjective pain scores and underwent pressure algometry adjacent to the incision at predetermined times after surgery. Personnel responsible for assessing calves for signs of pain and performing pressure algometry remained unaware of (were blinded to) the assigned treatment group for all calves throughout the observation period. In fact, only 1 investigator (AJN) was not blinded to the treatment group assignment of individual calves, but that investigator was not responsible for performing any subjective assessments.

MLK group

Calves in the MLK group received a CRI of an MLK solution. The MLK solution consisted of 1,000 mL of a 2% lidocaine solution, 4 g of ketamine (concentration, 100 mg/mL; volume, 40 mL), and 45 mg of morphine (concentration, 15 mg/mL; volume, 3 mL), which resulted in a solution with a lidocaine concentration of 19 mg/mL, ketamine concentration of 3.8 mg/mL, and morphine concentration of 0.04 mg/mL. The MLK solution was administered through a jugular catheter at a rate of 0.11 mL/kg/h. Thus, the dose of lidocaine delivered was 2.1 mg/kg/h (35 µg/kg/min), the dose of ketamine delivered was 0.42 mg/kg/h (7 µg/kg/min), and the dose of morphine delivered was 4.8 µg/kg/h (0.08 µg/kg/min). The CRI was begun after anesthesia induction and orotracheal intubation and was continued for 24 hours.

Control group

Calves in the control group received 2 doses of flunixin meglumine (1.1 mg/kg, IV, q 24 h). The first dose was administered 30 minutes before the start of surgery. To ensure observers remained blinded to treatment group assignment, calves in the control group also received a CRI of sterile saline (0.9% NaCl) solution at the same infusion rate (0.11 mL/kg/h) as the CRI administered to calves in the MLK group. The CRI was begun after anesthesia induction and orotracheal intubation and was continued for 24 hours.

Anesthesia and surgical procedure

For each calf, a 14-gauge catheter[a] was aseptically placed into each jugular vein. One catheter was used for drug and fluid administration, and the other was used for collection of serial blood samples. Each calf was anesthetized and underwent an open umbilical herniorrhaphy as described.[23]

Clinical evaluation and pain assessment

One investigator (AKH) was responsible for all clinical assessments, subjective pain scoring, and pressure algometry measurements. Each calf was clinically evaluated, was assigned a pain score, and underwent pressure algometry within 30 minutes after anesthesia recovery; at 4, 8, 12, 18, and 24 hours after surgery; and at 4, 8, 12, 24, 36, 48, 60, 72, and

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96 hours after discontinuation of the assigned CRI. The pain-scoring system used was modified from those[24,25] used for research sheep undergoing orthopedic procedures. It was based on clinical assessment findings. Briefly each calf was assigned a score for each of 8 categories (mental assessment, RR, HR, recumbency, incision site, rumen, appetite, and fecal production) on a scale of 1 to 3 **(Appendix)**, where 0 was considered clinically normal and 3 was severely impaired or abnormal. For each assessment time, the individual scores for each of the 8 categories were summed. Thus, for any given assessment time, the cumulative pain score could range from 0 to 24.

A digital force algometer[b] was used to determine the peri-incisional pressure threshold (minimum force necessary to elicit a painful response; measured in N/cm^2) at each assessment time. Briefly, the algometer was applied to 4 sites adjacent to the surgical incision. The force was slowly increased until avoidance behavior was elicited, at which point the algometer was removed from the patient and the force that elicited the avoidance behavior was recorded. Avoidance behavior was defined as kicking, vocalization, or moving away from the investigator and was considered true only if it was repeatable. For each calf and each assessment time, the mean pressure threshold (algometry score) was calculated from the measurements obtained at all 4 sites and used for analysis purposes.

Blood sample collection and processing

From each calf, a blood sample (4 mL) was collected from the designated catheter at 0 (prior to anesthesia induction and initiation of CRI; baseline), 1, 2, 4, 8, 12, 18, 24 (discontinuation of CRI), 24.5, 25, 25.5, 27, 36, 48, 60, 72, 96, and 120 hours after CRI initiation. When applicable, blood samples were acquired after pain scores and algometry measurements were recorded. Blood samples were collected into blood collection tubes without any additives. The blood samples were centrifuged. The serum was harvested from each sample, divided into 2-mL aliquots, and stored in cryovials at –70°C. For each sample, the serum cortisol concentration was determined by an automated bead-based assay[c] at an accredited veterinary diagnostic laboratory.[d] The lower limit of quantitation for cortisol was 29.57 nmol/L (10 ng/mL).

Statistical analysis

For each continuous variable of interest (age, body weight, rectal temperature, HR, RR, PCV, TP concentration, pain score, algometry score, and serum cortisol concentration), the data distribution was assessed for normality by means of the Shapiro-Wilk test. Data for variables that were not normally distributed underwent a logarithmic transformation to normalize the distribution prior to analysis. Independent-sample *t* tests were used to compare age, body weight, and presurgical rectal temperature, HR, RR, PCV, and TP concentration between the MLK and control groups. The gender distribution for the 2 groups was compared by use of a Fisher exact test. For HR, RR, pain score, algometry score, and serum cortisol concentration, differences over time and between groups were assessed by use of mixed linear models. Each model included a fixed effect for treatment group (MLK or control) and sample acquisition time (time) and a random effect to account for repeated measures within calves. All analyses were performed with a commercially available statistical software program,[e] and values of $P < 0.05$ were considered significant.

Results

Calves

The calves in the MLK group did not differ significantly from the calves in the control group in terms of age, body weight, and preoperative rectal temperature, HR, RR, PCV, or serum TP concentration **(Table 1)**. The sex distribution also did not differ between the 2 groups. For all calves, the mean ± SD length of the hernia was 5.2 ± 1.3 cm (range, 3 to 8 cm). The mean HR and RR did not differ significantly within either group over time or between the MLK and control groups at any time.

Pain score, algometry score, and serum cortisol concentration

Mean pain scores, algometry scores, and serum cortisol concentrations were plotted over time **(Figure 1)**. The mean pain score did not differ significantly within either group over time or between the 2 treatment groups at any time.

A logarithmic (log) transformation was applied to the algometry data to normalize it for analysis. For both groups, the mean algometry score before surgery was greater than that after surgery. When data were aggregated over the entire observation period, the mean algometry score did not differ significantly between the MLK and control groups. However,

Table 1—Presurgical descriptive statistics for weaned Holstein calves that underwent umbilical herniorrhaphy and were randomly assigned to receive a CRI of an MLK solution (MLK group; n = 10) or 2 doses of flunixin meglumine and a CRI of saline (0.9% NaCl) solution (control group; 10).

Variable	MLK group	Control group
Age (d)	148.8 ± 29.9	160.7 ± 27.6
Weight (kg)	146.2 ± 36.7	150.5 ± 35.7
Sex		
Female	5	8
Steer	5	2
PCV (%)	32 ± 3.4	31.8 ± 2.4
TP (g/dL)	6.8 ± 0.3	7.1 ± 0.4
HR (beats/min)	88.2 ± 19.8	89.1 ± 9.4
RR (breaths/min)	52.7 ± 18.5	40.7 ± 9.9
Rectal temperature (°C)	38.8 ± 0.4	38.9 ± 0.7

Values represent the mean ± SD or number of calves. All values were obtained prior to initiation of the assigned treatment. None of the variables differed significantly ($P < 0.05$) between the 2 groups.

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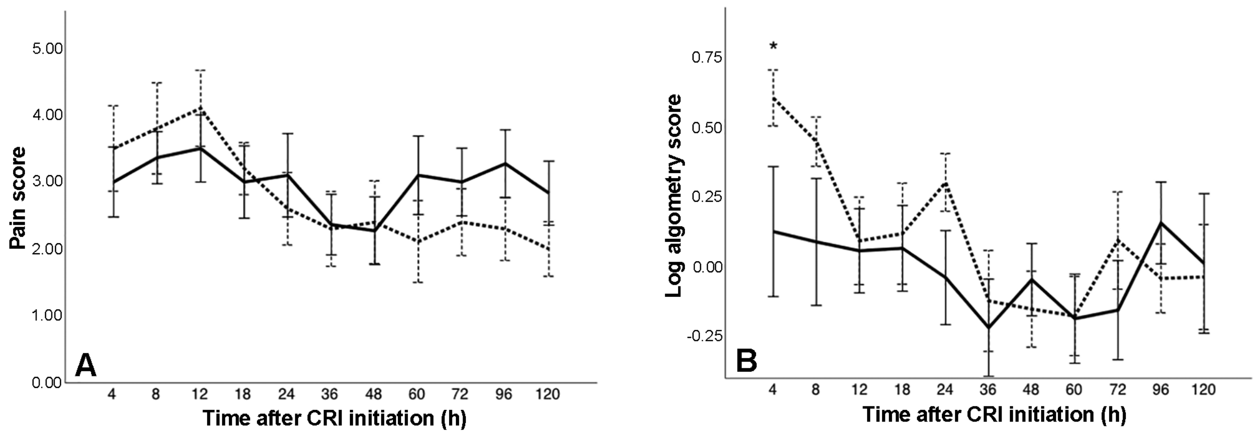

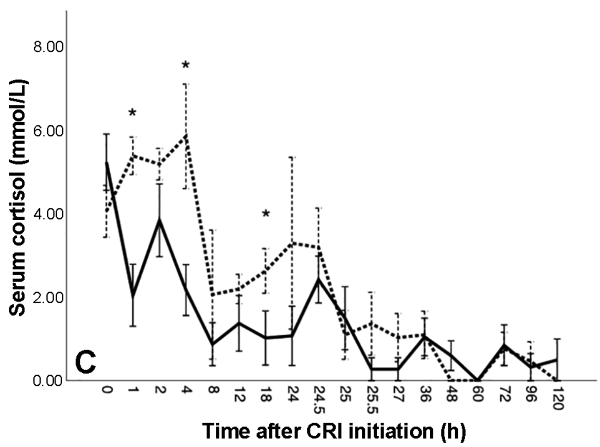

Figure 1—Mean ± SE pain score (A), algometry score (B), and serum cortisol concentration (C) for weaned Holstein calves that underwent umbilical herniorrhaphy and received a CRI of an MLK solution (MLK group; n = 10; dashed line) or 2 doses of flunixin meglumine (1.1 mg/kg, IV, q 24 h) and a CRI of saline (0.9% NaCl) solution (control group; 10; solid line). For both groups, the assigned CRI was administered through a jugular catheter at a rate of 0.11 mL/kg/h and was begun immediately after anesthesia induction and orotracheal intubation (ie, prior to surgery) and was continued for 24 hours. The MLK solution had a morphine concentration of 0.04 ng/mL, lidocaine concentration of 19 mg/mL, and ketamine concentration of 3.8 mg/mL; thus, the dose of morphine delivered was 4.8 μg/kg/h (0.08 μg/kg/min), the dose of lidocaine delivered was 2.1 mg/kg/h (35 μg/kg/min), and the dose of ketamine delivered was 0.42 mg/kg/h (7 μg/kg/min). The pain score at each assessment could range from 0 to 24. Algometry measurements were recorded in N/cm^2, and a logarithmic transformation was applied to the algometry data to normalize it for analysis. *Within a given time, mean value differs significantly ($P < 0.05$) between the 2 treatment groups.

when the algometry scores were analyzed within individual times, the mean algometry score for the MLK group was significantly greater than that for the control group (ie, the calves in the MLK groups tolerated the application of greater pressure near the incision site than did the calves in the control group) at 4 hours after initiation of the CRI (Figure 1).

The mean serum cortisol concentration decreased significantly from baseline over time for both the MLK and control groups (Figure 1). The mean serum cortisol concentration for calves in the MLK group was significantly greater than that for the calves in the control group at 1, 4, and 18 hours after initiation of the CRI.

Discussion

In the present study, indices of postoperative pain (ie, subjective pain scores and algometry scores) did not differ significantly between calves that underwent umbilical herniorrhaphy and received a 24-hour CRI (0.11 mL/kg/h) of an MLK solution (morphine, 4.8 μg/kg/h; lidocaine, 2.1 mg/kg/h; and ketamine, 0.42 mg/kg/h) and similar calves that received 2 doses of flunixin meglumine (1.1 mg/kg, IV, q 24 h) and a 24-hour CRI (0.11 mL/kg/h) of saline solution. Thus, we rejected our a priori hypothesis that calves in the MLK group would have fewer signs of pain following surgery, compared with the calves in the control group. Other variables, such as HR, RR, and serum cortisol concentration, also did not differ significantly between the 2 treatment groups when data were aggregated over the entire 120-hour observation period.

At the time this study was conducted, large animal patients with gastrointestinal tract disease or pain-induced ileus treated at The Ohio State University Veterinary Medical Center were commonly administered a CRI of MLK. Our clinical impression was that a CRI of MLK improved patient comfort by alleviating visceral pain; it also had a positive effect on gastrointestinal tract motility without causing substantial sedation or dysphoria. However, the present study was designed to evaluate the analgesic efficacy of a CRI of an MLK solution to calves undergoing umbilical herniorrhaphy, and we cannot draw any conclusions regarding the effects of the MLK solution on patient sedation or postoperative gastrointestinal tract motility. Although rumen motility and fecal production were assessed as part of the pain-scoring system used for the calves of this study, the scores for those 2 variables did not differ significantly between the MLK and control groups.

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Morphine, lidocaine, and ketamine provide effective analgesia or anesthesia in cattle undergoing surgical procedures when used alone or in combination with other drugs.[26–30] However, NSAIDs are also effective and remain the most commonly used class of analgesic to treat surgical pain in cattle.[3,31] In fact, results of the present study suggested that flunixin meglumine (an NSAID) and a CRI of an MLK solution were equally effective for providing postoperative analgesia in calves following umbilical herniorrhaphy.

Few studies have evaluated the administration of a CRI of MLK for the alleviation of perioperative pain in veterinary patients. In fact, in the 2 studies[32,33] that have been published on the topic, the CRI was administered only during the anesthetic period. Constant rate infusion of an MLK solution similar to that administered to the calves of the present study to dogs undergoing stifle joint surgery provides adequate analgesia for 24 hours after surgery.[34] Constant rate infusion of lidocaine, ketamine, or a combination of lidocaine and ketamine decreases the minimum alveolar concentration for sevoflurane in dogs.[35] In horses, a CRI of ketamine decreases the minimum alveolar concentration for halothane and induces beneficial hemodynamic effects.[36] In anesthetized calves, administration of a loading dose of lidocaine (2 mg/kg, IV) followed by a CRI of the drug (100 µg/kg/min) is associated with a decrease in HR, which may be detrimental to hemodynamically compromised patients.[37] The infusion rate (35 µg/kg/min) of lidocaine for the calves of the present study was much lower than 100 µg/kg/min and was not associated with a decrease in HR during or after the CRI.

Administration of lidocaine as a CRI infusion until the completion of surgery in horses anesthetized with isoflurane or sevoflurane is associated with an increase in ataxia and poor quality of anesthesia recovery.[38] For the calves of the present study, the CRI was discontinued briefly just prior to the discontinuation of isoflurane administration and was resumed immediately after anesthesia recovery (mean ± SD duration of CRI interruption, 15 ± 4.6 minutes). Despite the interruption in CRI, no adverse effects were observed, and all calves in the MLK group recovered from anesthesia without complications. It is difficult to compare anesthesia recovery between cattle and horses because cattle rarely develop complications during anesthesia recovery, whereas complications during anesthesia recovery are well documented for horses.[39,40] For the calves of the MLK group, the finding that all recovered from anesthesia without complications was similar to results for isoflurane-anesthetized calves of another study[41] that received a loading dose of lidocaine (2 mg/kg, IV) followed by a CRI infusion of the drug at a rate of 50 µg/kg/min. The calves of that study[41] did not continue to receive the CRI of lidocaine after surgery and were not assessed for signs of pain during the immediate postoperative period.

For calves in both the MLK and control groups, the serum cortisol concentration decreased significantly from baseline (ie, prior to initiation of the assigned treatment and surgery) over time. Serum cortisol concentrations were greatest during periods of intensive handling before and immediately after surgery. Calves were restrained in a chute for catheter placement, baseline blood sample collection, and physical examination prior to anesthesia induction. Although an attempt was made to standardize those procedures, individual calves responded differently to the restraint and handling. Additionally, the study was performed at a veterinary teaching hospital, and patient restraint and catheter placement were performed by a large number of individuals (eg, veterinary students) with variable experience handling cattle and catheter placement. The stress associated with that handling and the isolation necessary immediately after surgery owing to the ongoing CRI of the assigned treatment (MLK or saline solution) may have caused release of endogenous cortisol, thereby resulting in an increase in serum cortisol concentration regardless of the presence or absence of pain.[42,43] Results of a study[42] that assessed the effects of acute stressors in dairy cows indicate that social isolation and restraint of the head lead to increased serum cortisol concentrations, with the magnitude of that increase greatest for social isolation. In another study,[43] significant negative effects, including hypoalgesia and an increase in serum cortisol concentrations, were observed in dairy cows that underwent social isolation. For the calves of the present study, it was difficult to determine whether the changes in serum cortisol concentration over time were associated with pain or the effects of stressors. Because the mean pain scores did not decrease over time, it seemed likely that stressors were at least partially responsible for the alterations in serum cortisol concentration. Interestingly, the mean serum cortisol concentration for both the MLK and control groups decreased significantly from baseline during the first 24 hours of the observation period (ie, while the assigned CRI was administered) and then increased briefly after the CRI was discontinued. This was most likely caused by the calves being restrained for sample collection immediately after discontinuation of the CRI. Although care was taken to mitigate the effects of stressors throughout the observation period, it was not possible to eliminate all stressors in the study population.

The present study had several limitations. One was the difficulty associated with assessing pain in animals, particularly ruminants.[44–47] Even though the pain-scoring system used allowed for methodical evaluation of signs of pain in the study subjects, the pain scores were largely subjective. One investigator (AKH) was responsible for assigning all pain scores to and performing the algometry measurements on all calves to eliminate interobserver variation and bias, and that investigator was blinded to the treatment group assignment for all calves throughout the observation period. The pain-scoring system used was modified from scor-

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ing systems used to assess signs of pain in sheep following orthopedic procedures.[24,25] Most studies of pain in cattle have involved routine surgical procedures such as castration and dehorning. Only a small number of studies[5,6] have assessed visceral or incisional pain in cattle. In our opinion, the pain-scoring system used provided an adequate clinical assessment of postoperative pain for the calves of the present study. The pain-scoring system used in the present study was similar to the UNESP-Botacatu unidimensional composite pain scale that has been described and validated for use in assessing postoperative pain in cattle.[48] Measurement of the peri-incisional pressure threshold by algometry complemented the pain-scoring system used in the present study.

Other limitations of the present study included the surgical procedure performed and the lack of an untreated control group. Although open umbilical herniorrhaphy involves entry into the peritoneal cavity and some manipulation of internal organs and tissues, the calves did not appear very painful during the postoperative period regardless of treatment group. That was likely a reflection of the fact that both treatment groups received analgesics. We briefly considered including an untreated control group in the present study, but that idea was dismissed for ethical concerns. It is not appropriate to perform abdominal surgery on any animals, particularly client-owned animals, without administration of some type of analgesia.

Umbilical herniorrhaphy is an elective procedure, and cattle with umbilical hernias typically do not exhibit signs of pain during the preoperative period. Patients with other surgical conditions, such as an intestinal blockage, may be very painful prior to surgery and have an upregulation of pain responses. Administration of a CRI of MLK to cattle undergoing more invasive procedures, such as intestinal resection and anastomosis, or in clinically ill animals may yield different results from those observed in the calves of the present study. We commonly administer CRIs of MLK solutions at dosage rates similar to those used in the present study to clinical patients with enteritis, hemorrhagic bowel syndrome, severe dermal burns, or other disorders with satisfactory results, which suggested that the MLK solution administered to the calves of the present study is capable of alleviating signs of severe pain and gastrointestinal tract dysfunction. However, we have not measured serum or plasma drug concentrations in clinical patients.

Another important limitation of the present study was the fact that CRIs, particularly of analgesics and anesthetics with fairly narrow safety ranges, are not practical for all clinical situations. Although we commonly administer CRIs of MLK solutions to clinical patients, we work at a veterinary teaching hospital that has 24-hour technical support to monitor patients and maintain infusion pumps. Errors in determining flow rates or a rapid increase in the flow rate of a CRI can have detrimental effects on patients.

Results of the present study indicated that, for calves undergoing routine umbilical herniorrhaphy, the analgesic efficacy of a 24-hour CRI of an MLK solution was similar to that of 2 doses of flunixin meglumine, and both protocols provided adequate postoperative analgesia. The cost and technical support required for monitoring and maintaining a CRI makes the MLK protocol described in this study impractical for field practice. Nevertheless, a CRI of an MLK solution is a viable alternative for providing analgesia to individual patients in hospital settings. Further research and kinetic studies are necessary to assess the efficacy of a CRI of an MLK solution to clinically ill animals and establish optimal dosing protocols and withdrawal intervals for such protocols in food-producing animals.

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Footnotes

a. Abbocath-T, Abbott Ireland, Sligo, Ireland.
b. Force OneTM FDIX Force Gage, Wagner Instruments, Greenwich, Conn.
c. Immulite, Seimens Healthcare Diagnostics Inc, Tarrytown, NY.
d. The Ohio State University Clinical Chemistry Laboratory, Columbus, Ohio.
e. SPSS Statistics for Macintosh, version 22.0, IBM Corp, Armonk, NY.

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Appendix

Pain-scoring system developed to subjectively assess pain in calves before and after umbilical herniorrhaphy.

	Score			
Category	0	1	2	3
Mental assessment	Normal and alert	Lethargic, depressed appearance, ears drooping	Head down, very lethargic, ears drooping	Nonresponsive
RR	Normal (> 40 breaths/min)	Mildly increased (> 60 breaths/min)	Moderately increased	Open-mouth breathing
HR	Normal (60–80 beats/min)	Mild elevation (80–90 beats/min)	Moderate elevation (90–100 beats/min)	Severe elevation (>100 beats/min)
Recumbency	Normal	Slightly delayed rising	Requires encouragement to stand	Unwilling or unable to stand
Incision	Normal (no swelling or discharge)	Mild swelling but no discharge	Moderate swelling or serosanguinous discharge	Severe swelling or purulent discharge
Rumen	Normal	Decreased motility	—	Absent motility
Appetite	Normal	Mildly reduced interest	Moderately reduced interest	Inappetant
Fecal production	Normal	Mild decrease	Moderately decreased	Absent

At each assessment, a score was assigned to each category, then the scores for all 8 categories were summed to calculate the cumulative pain score.

— = Criteria not established for this category.

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