Safety and efficacy of preoperative administration of meloxicam, compared with that of ketoprofen and butorphanol in dogs undergoing abdominal surgery

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Objective—To compare the safety and efficacy of preoperative administration of meloxicam with that of ketoprofen and butorphanol in dogs undergoing abdominal surgery.

Animals—36 dogs undergoing laparotomy, splenectomy, or cystotomy.

Procedure—Dogs were randomly assigned to 1 of 3 groups. In the first part of the study, dogs were given a single dose of meloxicam, ketoprofen, or a placebo, and buccal mucosal bleeding times were measured. In the second part of the study, dogs were given meloxicam, ketoprofen, or butorphanol prior to surgery. Dogs in the butorphanol group received a second dose immediately after surgery. Pain scores (1 to 10) were assigned hourly for 20 hours after surgery and used to determine an overall efficacy score for each dog. Dogs with a pain score ≥3 were given oxymorphone for pain. Dogs were euthanatized 8 days after surgery, and gross and histologic examinations of the liver, kidneys, and gastrointestinal tract were conducted.

Results—Overall efficacy was rated as good or excellent in 9 of the 12 dogs that received meloxicam, compared with 9 of the 12 dogs that received ketoprofen and only 1 of the 12 dogs that received butorphanol. No clinically important hematoletic, biochemical, or pathologic abnormalities were detected.

Conclusions and Clinical Relevance—Results suggest that preoperative administration of meloxicam is a safe and effective method of controlling postoperative pain for 20 hours in dogs undergoing abdominal surgery; the analgesic effects of meloxicam were comparable to those of ketoprofen and superior to those of butorphanol. (Am J Vet Res 2001;62:882–888)

Several nonsteroidal anti-inflammatory analgesics (NSAIA) have been used successfully to control postoperative pain in dogs and cats. Before newer NSAIA are accepted in clinical practice, their efficacy and duration of action should be compared with that of established agents. In addition, because safety of NSAIA is of major concern, an assessment of potential adverse affects must be included in the overall evaluation of newer agents.

Nonsteroidal anti-inflammatory analgesics act, in part, by reducing prostaglandin (PG) synthesis via inhibition of cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), or both. Under normal circumstances, PG synthesized as a result of COX-1 activity help to maintain gastric mucosal integrity and modulate renal blood flow and platelet function. Tissue injury, on the other hand, activates COX-2, leading to production of PG that act as mediators of inflammation, causing hyperalgesia and pain. Thus, development of NSAIA that preferentially inhibit COX-2, rather than COX-1, may result in safer analgesics.

Previous studies have demonstrated that the efficacy of ketoprofen is comparable or superior to that of opioids in the management of pain following soft tissue and orthopedic procedures in dogs and ovariohysterectomy in cats. The duration of action of ketoprofen has been reported to be approximately 12 hours, which is similar to that reported for other NSAIA. Ketoprofen has been approved for use in cats and dogs in Europe and Canada.

Meloxicam, a NSAIA of the oxicam group, is a potent inhibitor of PG synthesis that has anti-inflammatory, analgesic, and antipyretic properties. It is intended for use in postoperative pain management and for the treatment of acute and chronic inflammatory musculoskeletal conditions in dogs. Meloxicam is approved for use in dogs in Europe and Canada, and currently available information suggests that meloxicam is safe and efficacious. Because meloxicam primarily inhibits COX-2, it should also be safe when used preoperatively. However, before meloxicam is used in this fashion, it would be desirable to confirm that this usage does not cause any of the adverse affects commonly associated with NSAIA administration, including inhibition of platelet function, gastric ulceration, and impaired renal function. Unlike opioids, which have immediate analgesic effects, NSAIA require 45 to 60 minutes before analgesic effects are evident. Therefore, NSAIA may have to be administered prior to surgery to control postoperative pain associated with...
surgical procedures of short duration. In addition, establishing effective blood concentrations of the NSAIA prior to any surgical stimulus may decrease nociceptive processing, which may reduce postoperative pain or wind-up.16

The purpose of the study reported here was to compare the safety and efficacy of preoperative administration of meloxicam, versus ketoprofen and butorphanol, for control of postoperative pain in dogs undergoing soft tissue surgery. The effects of ketoprofen and meloxicam on hemostasis were evaluated in dogs prior to surgery by measuring the buccal mucosal bleeding time (BMBT), essentially an in vivo test of platelet function.17,18 Subsequently, safety and efficacy of meloxicam, ketoprofen, and butorphanol were evaluated in dogs undergoing various soft tissue surgical procedures.

Materials and Methods

Study design—The study was performed in 2 parts. The first part was designed to evaluate the hemostatic effects of ketoprofen and meloxicam. The second part was patterned after a published protocol19 for assessing safety and efficacy of NSAIA. Postoperative pain and adverse effects were evaluated in dogs undergoing laparotomy (n = 12), splenectomy (12), or cystotomy (12) performed by third-year veterinary students at the Ontario Veterinary College.

Thirty-six Beagles (18 male and 18 female) between 6 and 9.5 months old and weighing between 6.5 and 12.7 kg were used in the study. Beagles were obtained from the University of Guelph Animal Care Facility. The study was conducted in accordance with guidelines of the Canadian Council on Animal Care; the study protocol was approved by the institutional animal care committee.

Evaluation of hemostatic effects—Dogs were randomly assigned to 1 of 3 groups (n = 12/group) by means of computer randomization. A single dose of meloxicam (0.2 mg/kg of body weight), ketoprofen20 (2.0 mg/kg), or a placebo (meloxicam vehicle) was given. Two individuals administered each drug and were not involved with the BMBT procedure. Buccal mucosal bleeding times were measured before (time 0) and 1, 4, 8, 24, and 48 hours after drug administration, using a spring-loaded device.21 Dogs were not sedated for determination of BMBT. Six veterinarians (2/dog) experienced with performing this technique measured the BMBT and were unaware as to which drug individual animals had been given.

Evaluation of efficacy and safety—After a washout period of at least 7 days, dogs were used to evaluate efficacy and safety of meloxicam, ketoprofen, and butorphanol.22 Dogs were assigned to the same groups as they had been for evaluation of hemostatic effects, except that for humane reasons, dogs in the placebo group were assigned to receive butorphanol.23

Dogs were sedated with acepromazine24 (0.1 mg/kg, IM) and butorphanol (0.2 mg/kg, IM), and anesthesia was induced with thiopental sodium25 (8 to 10 mg/kg, IV). Anesthesia was maintained with halothane26 in oxygen. An isotonic balanced electrolyte solution27 (10 ml/kg/h, IV) was administered throughout the procedure; fluid administration was discontinued at the completion of surgery. The electrocardiogram was monitored continuously throughout surgery, and blood pressure and heart rate were measured at frequent intervals. After induction of anesthesia, dogs were given meloxicam (0.2 mg/kg, IV), ketoprofen (2.0 mg/kg, IV), or, for dogs assigned to the butorphanol group, saline (0.9% NaCl) solution (0.2 ml/kg, IV). At the completion of surgery, dogs in the meloxicam and ketoprofen groups were given an injection of saline solution (0.2 ml/kg, IV), and dogs in the butorphanol group were given an additional dose of butorphanol (0.2 mg/kg, IV). Any dog that vocalized continuously during recovery and for which it was not possible to differentiate emergence delirium from pain was given an additional dose of butorphanol (0.4 mg/kg, IV). Because butorphanol’s duration of action is only 2 to 4 hours, it was thought that this additional dose of butorphanol would not interfere with assessments of efficacy or duration of action of ketoprofen or meloxicam beyond this period.

Postoperative assessments—Pain assessments were conducted by 1 of 3 authors (KM, GP, and WM) during the first 8 hours after anesthetic recovery. Pain assessments for the remaining 12 hours of the study were performed by 4 intensive care unit technicians experienced in pain management, all of whom had participated in previous studies.24,25 All assessors were blinded as to the analgesic assigned. Pain scores (Appendix 1) were assigned every hour for the first 20 hours after surgery, except that during the first 2 hours after surgery, pain scores were recorded every 15 minutes.26,27 Pain scores were recorded every hour, and the highest pain score obtained during each 1-hour observation period was recorded as that hour’s pain score. Oxyphenobutrate28 (0.1 mg/kg, IV, or to effect in increments of 0.05 mg/kg, IV) was given if pain score was ≥ 3 at any time. An overall evaluation of efficacy for the 24-hour postoperative period was determined by combining pain scores (Appendix 2).

Blood samples were collected from all dogs 24 hours before and 24 and 48 hours after surgery, and blood urea and serum creatinine concentration, alanine aminotransferase (ALT) activity, PCV, and total solids (TS) concentration were determined. Feces were examined for evidence of gross and occult blood or melena prior to and daily for 4 days after surgery.

Post mortem examination—One week after surgery, dogs were again anesthetized for an 8-hour surgery teaching laboratory, at the end of which dogs were euthanatized with an overdose of sodium pentobarbital. A post mortem examination was performed between 1 and 4 hours after euthanasia; all post mortem examinations were performed by a single board-certified pathologist (RF) who did not know which drug individual dogs had received. The kidneys, liver, and gastrointestinal tract were examined for gross abnormalities, and samples of each of these organs were obtained and submitted for histologic examination. One dog (butorphanol group) was not euthanatized at the end of the study but rather was adopted under the animal care guidelines for the laboratory. Prior to adoption, an endoscopic examination of the stomach was performed, and biopsy specimens of the gastric mucosa were obtained.

Data analysis—Data were analyzed by use of ANOVA for a mixed model (both random and fixed effects) for repeated-measures. The best fitting model was chosen on the basis of Akaike information criteria and comparison of log likelihood values. It is recognized that analyses of repeated measures are most robust when the time periods are of equal duration; however, it was assumed that time periods in the present study were similar enough that use of these methods was still valid. When data did not involve repeated measures, a generalized linear models ANOVA was used to compare values among groups. The number needed to treat (NNT) was calculated as a measure of how well drugs relieved pain associated with surgery during the 20-hour postoperative period. For each treatment group, paired t-tests were used to compare PCV, ALT activity, and urea, creatinine, and TS concentrations before surgery to values obtained 24
hours after surgery and to values obtained 48 hours after surgery.

The Kaplan-Meier survival method was used to analyze pain scores obtained during the first 20 hours after surgery; survival functions were compared by use of the Wilcoxon test. Failure was defined as a pain score ≥ 3. Overall efficacy scores were compared among treatment groups by means of ANOVA. All analyses were performed with computer software.* For all analyses, values of P < 0.05 were considered significant. Data are given as mean ± SD.

Results

Hemostatic effects—Buccal mucosa bleeding times were analyzed for effects of treatment, time, and the interaction between treatment and time. The interaction between treatment and time was not significant, and mean values did not differ significantly over time or among treatments. There were no significant differences in mean BMBT among the 6 time periods. Overall mean BMBT for dogs that received meloxicam (mean ± SD, 133.3 ± 38.7 seconds) was not significantly different from mean BMBT for dogs that received ketoprofen (238.4 ± 24.4 seconds) or mean BMBT for dogs that received the placebo (140.8 ± 37.2 seconds). The mean BMBT for dogs receiving ketoprofen was not significantly different from that for dogs receiving the placebo. All BMBT were within the reference range for dogs (< 300 seconds).

Physical assessments—Duration of the surgical procedure ranged from 2.5 to 3.5 hours for dogs undergoing laparotomy, from 3.5 to 5 hours for dogs undergoing splenectomy, and from 3.25 to 5 hours for dogs undergoing cystotomy. For all procedures, systolic blood pressure during surgery ranged from 80 to 120 mm Hg for dogs that received meloxicam, 85 to 120 mm Hg for dogs that received ketoprofen, and 80 to 120 mm Hg for dogs that received butorphanol. Heart rate during surgery ranged from 60 to 120 beats/min for dogs that received meloxicam, 58 to 110 beats/min for dogs that received ketoprofen, and 70 to 115 beats/min for dogs that received butorphanol. Two dogs that received meloxicam, 2 that received ketoprofen, and 3 that received butorphanol were reported to have excessive oozing at the time of closure of the abdominal incision; a compressive abdominal bandage was applied after surgery.

Evaluation of pain relief—Eleven of the 12 dogs that received butorphanol, 3 of the 12 dogs that received ketoprofen, and 2 of the 12 dogs that received meloxicam had pain scores ≥ 3 at some time after surgery and were treated with oxymorphone. Survival analysis indicated a significant difference among groups in regard to how well drugs were able to control postoperative pain (Fig 1). Treatment with butorphanol was significantly (P < 0.001) less effective in controlling postoperative pain than was treatment with ketoprofen or meloxicam; efficacy of meloxicam was not significantly different from the efficacy of ketoprofen.

Overall efficacy score for the 20-hour post-operative assessment for butorphanol (mean ± SD, 1.2 ± 0.58) was significantly less than that for ketoprofen (3.2 ± 1.3) or meloxicam (3.3 ± 1.2). No significant difference was found between overall efficacy scores for ketoprofen and meloxicam.

Eight of the 12 dogs that received meloxicam had overall efficacy scores of 4 (excellent), 1 had a score of 3 (good), 1 had a score of 2 (acceptable), and 2 had scores of 1 (inadequate). One of the 2 dogs for which overall efficacy score was 1 appeared to be in pain 3 hours after surgery. After oxymorphone was administered, however, the dog vomited, suggesting that it may not truly have been in pain; pain scores after this time were all < 3. The other dog was given oxymorphone 2 and 4 hours after surgery; pain scores were < 3 from 7 through 20 hours after surgery.

Eight of the 12 dogs that received ketoprofen had overall efficacy scores of 4, 1 had a score of 3, and 3 had scores of 1. One dog was treated with oxymorphone 2 hours after surgery; pain scores were < 3 thereafter. A second dog was treated with oxymorphone 6 hours after surgery; this dog had been very active prior to oxymorphone administration. Pain scores after oxymorphone administration were < 3. The third dog was treated with oxymorphone 5 and 10 hours after surgery.

One dog that received butorphanol had an overall efficacy score of 3; the remaining 11 all had scores of 1 and required treatment with oxymorphone. Most of these dogs required 3 or more doses of oxymorphone during the postoperative period (mean, 2.5 doses/dog).

The NNT represents the number of patients a clinician would need to treat with an analgesic for 1 patient to achieve a subjective pain score less than 3 out of 10, compared with a comparative intervention-based on the criteria of this study. For this study, the NNT for meloxicam versus butorphanol was 1.3, the NNT for ketoprofen versus butorphanol was 1.5, and the NNT for meloxicam versus ketoprofen was 12.
Biochemical changes—Baseline TS concentration was not significantly different from values obtained 24 or 48 hours after surgery for any of the treatment groups, nor were significant differences among groups detected. Significant changes in PCV were not detected for dogs in the ketoprofen (baseline, 45.3 ± 3.5%; 24 hours, 42 ± 4.7%; 48 hours, 42 ± 4.7%) or meloxicam (baseline, 45.2 ± 2.2%; 24 hours, 43.5 ± 2.6%; 48 hours, 44.3 ± 3.3%). For dogs in the butorphanol group, however, mean PCV was significantly decreased 24 hours after surgery (40.1 ± 2%), compared with the baseline value (45.4 ± 3.4%), but not 48 hours after surgery (43.2 ± 2.9%). Changes in PCV were not considered clinically important.

Serum ALT activity was within reference limits for all treatment groups at all times. There was no significant change from baseline values 24 or 48 hours after surgery for any group.

Mean serum urea and creatinine concentrations 24 and 48 hours after surgery were not significantly increased, compared with baseline values, in any treatment group. However, 1 dog that received butorphanol had a high serum creatinine concentration (154 mmol/L; reference range, 50 to 150 mmol/L) 24 hours after surgery. Two dogs that received ketoprofen had a 30 mmol/L increase in serum creatinine concentration, compared with baseline values, 24 hours after surgery, but values for these 2 dogs were still within reference limits. Similar changes in serum urea concentration were detected for these 3 dogs; however, serum creatinine and urea concentrations were similar to baseline values by 48 hours after surgery.

Gastrointestinal effects—There was no gross or occult evidence of blood in the feces of any of the dogs during the study, nor was there any difference in the prevalence of vomiting among groups. Two dogs that received ketoprofen vomited after surgery; 1 vomited 10 hours after surgery, and the other vomited 11 hours after surgery. Three dogs that received meloxicam vomited after surgery; 1 vomited 3 hours after surgery immediately after receiving oxymorphone, the second vomited 2, 4, and 5 hours after surgery, and the third vomited 12 hours after surgery. Two dogs that received butorphanol vomited after surgery; 1 vomited 9 and 13 hours after surgery, and the other vomited 13 hours after surgery. One dog that received butorphanol had intermittent diarrhea during the study; diarrhea was evident prior to administration of butorphanol.

Pathologic changes—No clinically important gross pathologic changes were evident during necropsy. Histologic examination of liver and kidney specimens did not reveal any clinically important disease or lesions that could be attributed to drug administration. Two dogs that received meloxicam had gastrointestinal tract lesions that were estimated to be > 10 days old, indicating that they had developed prior to administration of meloxicam and, possibly, prior to enrollment in the study. Results of fecal occult blood tests for this dog were negative. One dog that received ketoprofen had a focal erosion of the fundic portion of the stomach that had a bed of granulation tissue at its base. This lesion may have developed prior to or during the postoperative period. One dog that received butorphanol had chronic lymphocytic plasmacytic colitis that was assumed to be coincidental.

Discussion
Results of the present study suggest that preoperative administration of meloxicam is a safe and effective method of controlling postoperative pain for up to 20 hours in dogs undergoing abdominal surgery. The analgesic effects of meloxicam were comparable to those of ketoprofen and clearly superior to those of butorphanol in these dogs.

Pain assessments obtained immediately after surgery may be difficult to interpret because of alterations associated with general anesthesia and shivering associated with warming. Two dogs in the present study, 1 that received ketoprofen and 1 that received meloxicam, were assigned pain scores of 3 to 5 hours after surgery, because they were shivering intermittently and appeared lethargic. When handled, these animals were affectionate toward the caregiver and did not demonstrate signs of pain during palpation of the incision; however, oxymorphone was administered to ensure that the dogs were not in pain. Subsequent pain scores for these dogs were all < 3, and because oxymorphone's duration of action is usually 4 hours, analgesia after this time was a result of NSAIA administration. One of these dogs vomited immediately after oxymorphone administration, suggesting that the lethargy may have been attributable to nausea. Alternatively, the vomiting may have been associated with oxymorphone administration, which is not unusual in dogs that are not in pain. Of the 3 other dogs that received meloxicam or ketoprofen and required treatment with oxymorphone after surgery, 1 had been very active shortly after surgery, and the other 2 only required 2 doses of oxymorphone. In contrast, 11 of the 12 dogs that received butorphanol required treatment with oxymorphone, and most of these dogs received 3 or more doses.

The pain scoring system used in this study was based primarily on behavioral changes. Physiologic parameters can be altered by the use of opioids, which frequently reduce heart rate even in the presence of pain. In addition, physiologic parameters were not consistently monitored in this study; as previous reports have shown no correlation between physiologic measurements and severity of pain.22,23 In our experience, many of the obvious signs of pain, such as those described for scores ≥ 5, may indicate a state of pain that is quite advanced. By assessing subtle behavioral changes in this study, we hoped to detect signs of mild pain, so that analgesics could be administered before moderate or severe pain developed. The need for repeated administration of oxymorphone supports the usefulness of this descriptive pain assessment scale, as the expected duration of action of oxymorphone is 2 to 4 hours.

In the present study, 9 of 12 dogs that received ketoprofen were considered to be free of pain during the first 20 hours after surgery, whereas in a similar study, the duration of efficacy of ketoprofen was only
12 hours in 8 of 10 dogs. A possible explanation for this difference may be that the dogs in the previous study were premedicated with acepromazine (0.2 mg/kg) only, whereas in the present study, dogs were premedicated with butorphanol (0.2 mg/kg) in addition to acepromazine. However, it is not clear what effect, if any, butorphanol may have on the duration of effect of NSAIA. Greater than 12-hour durations of efficacy were reported for 85 and 94% of dogs in 2 previous studies (of 12-hour duration) in which ketoprofen was used to control postoperative orthopedic pain. Opioids were not administered to these dogs prior to surgery, and dogs were premedicated only with acepromazine. Thus, it is unclear whether butorphanol had a preemptive effect in the present study.

In a previous study, butorphanol alone, administered to dogs prior surgery at a dose of 0.2 to 0.8 mg/kg, did not appear to have any halothane-sparing effects, and in a separate study butorphanol administered at a dose of 0.4 mg/kg was found to have a mean duration of efficacy of 4.7 hours. Administration of butorphanol at a dose of 0.4 mg/kg has previously been reported to be adequate for control of visceral pain; however, this did not include surgical pain, and it was recommended that another dose be given after 45 to 60 minutes if continuous analgesia is needed. In the present study, butorphanol was administered at a dose of 0.2 mg/kg prior to surgery, and a second dose was administered at the end of surgery. This dosing regimen was presumably inadequate for continuous pain management, as most dogs required treatment with oxymorphone shortly after extubation. However, the duration of efficacy for butorphanol may be unpredictable, as exemplified by the 1 dog in this study for which overall efficacy of butorphanol was rated as good. An increased pain tolerance in this dog or incorrect assessments of pain severity should also be considered as possible explanations for the overall good results in this dog.

The NNT is an effective way to compare the benefits of a new treatment with those of a placebo or standard treatment, and it has been suggested that the NNT be designated as the common currency to help make the best treatment decisions for individual patients. A NNT of 1 describes an event that occurs in every patient given the treatment but in none of the patients in the comparison group. This represents a situation in which the new treatment is 100% effective, and the standard or placebo treatment is 100% ineffective, something that is extremely rare. For purposes of comparison, an NNT of 2 or 3 indicates that the intervention is effective. In the present study, the NNT for meloxicam compared with butorphanol was 1.3, meaning that for every 1.3 dogs treated with meloxicam, 1 dog obtained relief from pain during the 20-hour observation period, compared with what would have been expected if the dogs had been treated with butorphanol. Similarly, the NNT for ketoprofen compared with butorphanol was 1.5.

Because we did not detect any significant differences among groups in regard to serum creatinine or urea concentration, changes in these values cannot be attributed to NSAIA administration. Increases in serum creatinine and urea concentrations were likely caused by a combination of bradycardia, hypothermia, and hypotension associated with anesthesia and surgery.

None of the dogs in this study had clinical or histologic evidence of gastrointestinal tract disease that could be attributed to drug administration. In a previous study, several dogs receiving ketoprofen or butorphanol had weakly to strongly positive results for tests of occult blood in the feces. However, these dogs underwent anesthesia for a laboratory exercise within 18 hours after arrival on the premises, and lesions may have been a result of stress. In addition, dogs were given a second dose of ketoprofen within 12 hours after the first, resulting in a higher total dose. Dogs in the present study were on the premises for a minimum of 7 days prior to undergoing surgery.

Vomiting may be a result of gastritis secondary to NSAIA administration, manipulation of the gastrointestinal tract during surgery, or increased activity after surgery. Dogs receiving NSAIA in the present study were very active after surgery. In addition, vomiting by the dog that received meloxicam occurred immediately after oxymorphone administration and was attributed to opioid administration.

The lack of significant differences for BMBT, PCV, and TS concentration suggests that platelet function and hemostasis were not compromised by preoperative administration of meloxicam or ketoprofen. The PCV and TS concentration can be used as indirect assessments of hemostasis, in that if these values had decreased more than we typically expect for dogs undergoing abdominal surgery, we would have suspected that there had been excessive intra- or postoperative bleeding. Postsurgical hemorrhage resulting from impaired platelet function secondary to inhibition of the COX-1 product thromboxane A2 in humans and animals has been reported. In a previous study, we found a statistically but not clinically significant reduction in PCV 24 hours after surgery in dogs treated with ketoprofen. The reason for the difference between results of the present study and results of this previous study is not clear.

In this study, analgesics were administered prior to surgery to assess potential adverse affects associated with preoperative administration. Results suggest that in young dogs with no evidence of coagulopathies that receive fluids IV while anesthetized with halothane, preoperative administration of NSAIA appears to be safe. Although we did not detect any significant change in BMBT after ketoprofen administration, a recent study did find an increase in the incidence of postoperative hemorrhage after orthopedic surgery in dogs that received ketoprofen, suggesting that ketoprofen should, perhaps, be given only after surgery. Many of the dogs in the present study were extremely active after surgery, suggesting that these dogs did not have signs of pain. Obviously, activity should be restricted during the first 20 hours after any surgical procedure; however, the circumstances of this study and the nature of the dogs are not typical of clinical practice and client-owned dogs. These dogs were constantly monitored and assessed by veterinary students and

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staff, which is quite different from the usual situation in clinical practice, where dogs would be allowed to recover quietly.

For humane reasons, we elected not to incorporate a group that did not receive any analgesics as a control group when evaluating the safety and efficacy of meloxicam in this study. Rather, because duration of efficacy was an integral part of this study, we elected to use butorphanol as the control, as the duration of efficacy of butorphanol is expected to be only 1 to 2 hours. Similarly, we elected to compare meloxicam with ketoprofen as previous studies and personal experience indicate that ketoprofen has good to excellent analgesic properties for at least 12 hours.

References


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Appendix 1
System for scoring severity of postoperative pain in dogs undergoing abdominal surgery

<table>
<thead>
<tr>
<th>Score</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>0 (no pain)</td>
<td>Dog is running, playing, eating, jumping, and exuberant; sitting or walking normally; or sleeping comfortably and dreaming. Dog displays normal affectionate responses to caregiver. Heart rate is normal or high because of excitement. Dog may be grooming itself; appetite is normal. Behaviors associated with apprehension or anxiety may be seen.</td>
</tr>
<tr>
<td>1 (probably no pain)</td>
<td>Dog appears to be normal, but condition is not as clear-cut as for a score of 0. Heart rate is normal or slightly increased because of excitement.</td>
</tr>
<tr>
<td>2 (mild discomfort)</td>
<td>Dog will eat or sleep but may not dream. Dog may resist palpation of the surgical wound but otherwise shows no signs of discomfort and is not depressed. Respiratory rate may be slightly increased, heart rate may or may not be increased.</td>
</tr>
<tr>
<td>3 (mild pain or discomfort)</td>
<td>Dog will guard incision, or the abdomen may be slightly tucked up. Dog looks slightly depressed, cannot get comfortable, may tremble or shake, and appears to be interested in food but eats only a little or is some what picky. Respiratory rate may be increased, and respiration may be a little shallow. Heart rate may be increased or normal, depending on whether an opioid was given previously.</td>
</tr>
<tr>
<td>4 (mild to moderate pain)</td>
<td>Dog resists palpation of the surgical wound and abdomen. Guarding or splinting of the abdomen is apparent, or the dog may stretch all 4 legs. Dog may look or chew at the wound and may sit or lie in an abnormal position (ie, it is not curled up or relaxed) or tremble or shake. Dog may or may not appear interested in food; it may start to eat and then stop after 1 or 2 bites. Respiratory rate may be increased, and respiration may be shallow. Heart rate may be increased or normal. Pupils may be dilated. Dog may whimper or cry occasionally, be slow to rise, hang its tail, and appear somewhat depressed.</td>
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<tr>
<td>5 (moderate pain)</td>
<td>Dog may be reluctant to move, depressed, or inappetant. Dog may bite or attempt to bite when caregiver approaches the surgical wound. There is definite splinting of the abdomen, and dog may remain recumbent without moving for several hours. Heart and respiratory rates may be increased; pupils may be dilated. The dog is not interested in food, will lie down but does not really sleep, and may stand in the praying position.</td>
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<tr>
<td>6 (moderate discomfort)</td>
<td>Criteria as for a score of 5, but dog may vocalize or whine frequently, without provocation. Heart rate may be increased or normal if an opioid was administered previously. Respiratory rate may be increased with an abdominal lift. Pupils may be dilated.</td>
</tr>
<tr>
<td>7 (moderate to severe pain)</td>
<td>Same criteria as for a score of 5 or 6, but in addition, the dog is depressed and is not concerned with its surroundings. The dog may urinate or defecate without attempting to move, will cry out when moved, and will spontaneously or cont inually whimper (although some dogs may not vocalize). Heart and respiratory rates may be increased. Hypertension may also be present. Pupils may be dilated.</td>
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<tr>
<td>8 (severe pain)</td>
<td>Same criteria as for a score of 7, but vocalizing may be more of a feature, or the dog may be so consumed with pain that it will not notice the caretaker’s presence. The patient may thrash around in the cage intermittently. Tachycardia and tachypnea with increased abdominal effort and hypertension are usually present, even if an opioid was given previously, but they may not necessarily be seen.</td>
</tr>
<tr>
<td>9 (severe to excruciating pain)</td>
<td>Same criteria as for a score of 8, but the dog is also hyperesthetic. The dog will tremble involuntarily when any part of the body in close proximity to the surgical wound is touched.</td>
</tr>
<tr>
<td>10 (excruciating pain)</td>
<td>Same criteria as for a score of 9, but in addition, the dog is emitting piercing screams or almost comatose. The dog is hyperesthetic or hyperalgic. Its entire body is trembling, and signs of pain are elicited wherever the dog is touched.</td>
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Dogs with scores ≥ 3 require analgesia. When assigning scores, it is important to remember that dogs may continue to wag their tails in response to touch or commands even though they are experiencing moderate or severe pain; therefore, tail wagging should not be used as an indication that dogs are not in pain. For this scoring system, the term “depressed” means that the dog reacts slowly or reluctantly to a situation, compared with the expected response for a dog with a score of 0. In addition, they may appear tired, the palpebral fissures may be incompletely open, and the head may be carried lower than normal.

Appendix 2
Criteria for evaluating overall efficacy of analgesics used to treat postoperative pain in dogs undergoing abdominal surgery

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>4 (excellent)</td>
<td>Normal to exuberant activity within 3 hours after extubation with normal activity and behavior throughout the 20-hour period after surgery.</td>
</tr>
<tr>
<td>3 (good)</td>
<td>Dog appears to be comfortable within 3 hours after extubation; normal activity and behavior throughout the 20-hour period after surgery.</td>
</tr>
<tr>
<td>2 (acceptable)</td>
<td>Dog appears to be comfortable after recovery from anesthesia, and the dog’s behavior gradually returns to normal during the 20 hours after surgery.</td>
</tr>
<tr>
<td>1 (inadequate)</td>
<td>Analgesic was not effective in alleviating pain for the duration of the 20-hour period after surgery. Hourly pain score was ≥ 3, and oxymorphone was administered.</td>
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