Evaluation of intra-articular and subcutaneous administration of meloxicam for postoperative analgesia following stifle surgery in dogs

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Keywords
Meloxicam, intra-articular, NSAID, non-steroidal anti-inflammatory drugs, analgesia

Summary
The objective of this study was to compare the efficacy of meloxicam when given by intra-articular (IA) and subcutaneous (SC) routes of administration for postoperative analgesia versus a placebo for dogs undergoing stifle surgery. Twenty-five dogs with cranial cruciate ligament rupture (CCLR) were randomly assigned to one of three treatment groups, each with nine dogs, before surgical repair of twenty-seven stifles using a modified lateral retinacular imbrication technique. Group 1 dogs received IA administration of meloxicam and SC placebo. Group 2 dogs received IA placebo and SC meloxicam. Group 3 dogs received IA and SC administration of placebo. Dogs were assessed for pain by blinded observers using a visual analog scale (VAS), a numerical pain scoring system (NPS), and measurement of pain threshold using an algometer applied to the affected stifle. Assessments were made prior to pre-medication, postoperatively at the time of extubation, and at 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 hours following extubation. The results did not identify any significant effect of treatment between groups on the VAS data, algometer readings, or NPS data. Significantly increased VAS scores and decreased algometer readings were noted from preoperative to postoperative times. No differences were noted in early postoperative pain between dogs treated with IA meloxicam, SC meloxicam, or placebo. While intra-articular non-steroidal anti-inflammatory drug administration has shown efficacy in joint surgery for people, we did not find any evidence to support its use in dogs undergoing repair of CCLR.

Introduction
Perioperative analgesia is provided for animals undergoing joint surgery by systemic administration of opioids and non-steroidal anti-inflammatory drugs (NSAID), and by administration of local anaesthetic agents. Multimodal analgesia includes a combination of analgesic agents and techniques and can provide pain relief with fewer side effects than might occur with higher doses of a single agent (1, 2). Local administration of NSAID at the site of origin of the inflammatory process provides a more potent analgesic effect than systemic administration with a lower plasma concentration of the drug, and subsequently potentially fewer side effects (3, 4).

Intra-articular (IA) administration of analgesics, including opioids and local anaesthetic agents, has been described for dogs undergoing surgery. Intra-articular bupivacaine or morphine each provided better analgesia than IA saline in one study of 36 dogs (5). Intra-articular morphine showed analgesic effects comparable to those of epidural morphine in a controlled study of 18 dogs (6). Intra-articular administration of NSAID has not been reported for client-owned dogs, but it has been in horses and in people undergoing arthroscopic knee surgery (7–11). Adverse effects of IA NSAID administration have not been noted in any of these studies.

Meloxicam is a COX-2 selective oxicam class NSAID which is well absorbed and well tolerated after subcutaneous (SC) administration, with peak plasma concentrations attained within two to three hours (12). The serum half-life is species specific and averages 24 hours in dogs (13). Meloxicam has shown efficacy as a postoperative analgesic following surgery in dogs (14–16). An anti-inflammatory effect has been shown in an acute model of arthritis in the dog where systemic administration of meloxicam decreased both synovial fluid volume and the number of leukocytes present in the synovial fluid (17).

This study compared the effect of meloxicam administered via IA or SC routes against placebo on postoperative pain in dogs.
undergoing stifle surgery. We hypothesised that IA administration of meloxicam would significantly reduce pain when compared to SC administration of meloxicam or a placebo in the first 24 hours following arthrotomy and extra-capsular stabilisation of cranial cruciate ligament (CCL) injuries in dogs.

Materials and methods

Study design

This was a prospective, randomised, controlled, double-blinded clinical study utilising client-owned dogs. Using block randomisation, dogs were assigned to one of three treatment groups before surgery. Dogs in all groups received an opioid analgesic at the end of the surgical procedure to provide a baseline level of analgesia. In addition, dogs in Group 1 received IA administration of meloxicam and SC administration of a placebo. Dogs in Group 2 received IA administration of a placebo and SC meloxicam. Dogs in Group 3 received IA and SC administration of placebo. The surgeon (PM) was unaware of the assigned treatment group of each patient. Postoperatively, the dogs were monitored for signs of pain for 24 hours by trained observers who were unaware of the assigned treatment group of each dog.

Animals

Client owned dogs of various breeds and body weights referred for surgical repair of CCL injuries were enrolled in the study with owner consent. The study protocol was reviewed and approved by the Atlantic Veterinary College Animal Care Committee. Injuries were limited to complete or partial rupture of the CCL with or without concurrent meniscal injury. Any dog with significant metabolic disease, neurological disease, or aggressive temperament which would make monitoring difficult was excluded from the study at the discretion of the investigators. Dogs with evidence of previously treated or untreated concurrent CCL injury in the contralateral stifle were not excluded. All dogs had the same preoperative diagnostic work-up, which included physical and orthopaedic examination, complete blood count, serum chemistry, urinalysis, and radiographs of the affected stifle. All dogs were admitted to the hospital at least one day prior to surgery and were fasted for 12 hours before anaesthesia.

Anaesthetic Protocol

The anaesthetic protocol was standardised except for the required differences in analgesics between treatment groups. All dogs were pre-medicated with acepromazine maleate (0.05 mg/kg, IM) and hydromorphone hydrochloride (0.1 mg/kg, IM). General anaesthesia was induced with intravenous sodium thiopental, (approximately 10 mg/kg) to effect. Dogs were intubated and anaesthesia was maintained with isoflurane in oxygen.

Surgical procedure

Surgery consisted of a craniolateral arthrotomy of the affected stifle with debridement as needed of remnants of the torn CCL and assessment of the menisci. Any visible evidence of joint pathology was recorded. If deemed appropriate, partial meniscectomy and debridement of osteophytes were also performed. Stifles were then stabilised with a modified lateral retinacular imbrication technique using two strands of monofilament nylon leader line and a suture crimping system. No bandages were placed postoperatively. All procedures were performed by a single surgeon (PM) who was unaware of the treatment groups.

Analgesic administration

Within the final 30 minutes of the anaesthetic episode each dog received hydromorphone hydrochloride (0.05 mg/kg, IM). Following closure of the joint capsule and lateral fascia, but prior to closure of subcutaneous tissues and skin, each dog received an IA injection, and following skin closure were given a second SC injection of equal volume. Dogs in Group 1 received meloxicam (0.2 mg/kg, IA) and SC placebo. The placebo consisted of the same carrier solution used for injectable meloxicam without the active drug, coloured to match that of meloxicam to maintain blinding of the surgeon. Dogs in Group 2 received an IA placebo and meloxicam (0.2 mg/kg, SC). Dogs in Group 3 received IA placebo and SC placebo, with both placebo doses being of equal volume to a 0.2 mg/kg body weight dose of meloxicam.

Postoperative pain assessment

Dogs were assessed for signs of pain by trained observers unaware of the treatment groups. An initial baseline assessment was made prior to pre-medication. Postoperative assessments were made at the time of extubation (time 0), and at 1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 hours following extubation. At each interval, dogs were assessed by three different means: a visual analog scale (VAS), a numerical pain scoring system (NPS), and measurement of pain threshold using an algometer applied to the affected stifle. Each assessment was made in that order. For the VAS, the patient was observed without interaction for overall appearance, posture, movement, and behaviour indicative of comfort level at that time. A line 10 cm in length represented the patient’s level of pain, with one end corresponding to no pain and the other to the worst pain possible for this surgical procedure. A single mark was placed on the line to denote the patient’s apparent pain at that time. For the NPS, scores were assigned based on the dog’s movement, vocalisation, and behaviour when interacting with the assessor. The NPS was chosen for each category. These were added to produce a total NPS score for each assess-
ment time. Pain sensation near the surgical site was then tested using an algometer with a 1 cm² tip applied with steady pressure perpendicular to the skin surface over the stifle joint space just medial to the patellar tendon. The force was steadily increased and recorded at the point at which the dog consciously responded to the stimulus. Typical responses included vocalisation, turning the head and looking at the site, or pulling the leg away. The maximum applied force was limited to 4.5 Kg. Three separate algometer readings were recorded at each time interval, allowing at least 30 seconds between readings. The mean of these three readings was used for statistical analysis. Physiologic data, consisting of heart rate and respiratory rate, were collected at each interval.

**Rescue analgesic administration**

If any dog appeared to an assessor to have inadequately controlled pain, additional analgesia was provided with the administration of hydromorphone (0.05 mg/kg, IM). Guidelines for determining inadequate pain control included a VAS greater than approximately 5, an NPS score greater than 6, or an algometer pain threshold measurement of less than 1 Kg. If one or more of these guidelines were exceeded, supplemental analgesia was given at the discretion of the assessor in consultation with the surgeon. The dosage and time of administration of all supplemental hydromorphone was recorded. No further data were collected following administration of supplemental hydromorphone, but data up to and including that point were included in the analysis. Following the 24 hour observation period, analgesic administration was the responsibility of the hospital clinician in charge of the dog.

**Statistical analysis**

The VAS and algometer measurements were considered continuous and followed a normal distribution based on failure to reject the null hypothesis of normality at p < 0.05 using the Shapiro-Wilk test. The VAS and algometer measurements were summarised and reported as mean ± SD. The NPS was not considered continuous and was rank transformed, the rank NPS being the response for statistical analysis. The median and interquartile ranges were reported.

The fixed effect of treatment and time on the VAS, algometer and rank NPS responses was examined using a mixed effect linear model that included the random variance of dog nested within treatment. The models were examined for convergence, fit (Akaike’s information criterion [AIC] assessment based on altering covariance structure in the model), and normality of residuals (18). Plots of the raw and studentized residuals were examined. Significant fixed effects in the model were considered at p ≤ 0.05. Where there was a significant fixed effect or interaction, multiple comparisons were made using a Dunnet adjustment when compared to a single control (across time), or a Scheffe adjustment when compared across groups as indicated by the model analysis. The adjustment was made to maintain type I error at 0.05. Where a difference was noted, p < 0.05. The number of dogs requiring supplemental analgesia was compared between groups using Fisher’s exact test with the exact table probability reported. Significance was determined at p < 0.05. PROC FREQ, PROC UNIVARIATE, PROC MIXED and PROC NPAR1WAY were used for the analysis.

**Table 1**

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Group 1 (Intra-articular meloxicam, subcutaneous placebo)</th>
<th>Group 2 (Subcutaneous meloxicam, intra-articular placebo)</th>
<th>Group 3 (Intra-articular and subcutaneous placebo)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>Mean 3.52 ± 1.28</td>
<td>Mean 3.55 ± 0.87</td>
<td>Mean 4.09 ± 0.69</td>
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<tr>
<td>1</td>
<td>2.84 ± 1.32</td>
<td>3.30 ± 0.87</td>
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<td>2</td>
<td>2.99 ± 1.41</td>
<td>2.50 ± 1.26</td>
<td>4.08 ± 0.65</td>
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<td>4</td>
<td>2.85 ± 1.13</td>
<td>2.37 ± 1.26</td>
<td>3.43 ± 0.65</td>
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<td>6</td>
<td>3.60 ± 1.13</td>
<td>2.04 ± 1.02</td>
<td>3.07 ± 1.35</td>
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<td>8</td>
<td>3.17 ± 1.49</td>
<td>1.92 ± 1.02</td>
<td>2.92 ± 1.31</td>
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<td>10</td>
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<td>12</td>
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<td>16</td>
<td>2.12 ± 1.13</td>
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<td>20</td>
<td>2.15 ± 1.28</td>
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<td>24</td>
<td>2.77 ± 1.38</td>
<td>2.58 ± 1.28</td>
<td>2.95 ± 1.28</td>
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</table>

Shaded time points: n reduced by two dogs in Group 1 and one dog in Group 3 following administration of supplemental analgesia. * Indicates mean forces within groups that are significantly different from preoperative mean forces. a, b Within the time interval, mean forces with different superscripts are significantly different; those with the same superscript are not significantly different.
Table 2

<table>
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<tr>
<th>Preoperative time (hours)</th>
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<th>4</th>
<th>6</th>
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<th>10</th>
<th>12</th>
<th>16</th>
<th>20</th>
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<tr>
<td><strong>Group 1 (Intra-articular meloxicam, subcutaneous placebo)</strong></td>
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<td><strong>Group 2 (Subcutaneous meloxicam, intra-articular placebo)</strong></td>
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<td><strong>Group 3 (Intra-articular and subcutaneous placebo)</strong></td>
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Shaded time points: n reduced by two dogs in Group 1 and one dog in Group 3 following administration of supplemental analgesia. There were not any significant differences between pre- and postoperative scores within groups or between groups.

Results

Statistical analysis

All models converged and showed good evidence of fit with residuals following a normal distribution based on visual examination of residual plots. A mixed model using an autoregressive order one covariance structure was chosen based on the lowest AIC.

Animals

Twenty-seven surgical procedures were performed on 25 dogs. Two dogs were each enrolled a second time for cranial cruciate ligament rupture in the contralateral stifle independent of the first admission. Nine dogs were enrolled in each group. There were nine males and 18 females. Breeds included Labrador Retriever (n = 9), Golden Retriever (n = 3), Cocker Spaniel (n = 3), Beagle (n = 2), Chesapeake Bay Retriever (n = 1), American Bulldog (n = 1), English Springer Spaniel (n = 1), Bull Mastiff (n = 1), Miniature Schnauzer (n = 1), and mixed breed (n = 5). The mean ± SD body weight for all dogs was 31.8 kg ± 2.0 kg. Body weights were not significantly different between groups. Nine dogs, including three dogs in each group, were being treated with NSAID at the time of admission. Treatment was discontinued and no NSAID were given to any enrolled dog for 24 hours before surgery.

Surgery

Complete rupture of the CCL was noted in 20 stifles and partial rupture in seven stifles. Bilateral stifle disease consisting of previous CCL repair, presumed partial CCL rupture on the contralateral side, or chronic bilateral CCL rupture was noted in 14 dogs. Of these, three were in Group 1, five were in Group 2, and six were in Group 3. Meniscal injuries were noted in the caudal pole of the medial meniscus in 19 stifles, including seven in Group 1, six in Group 2, and six in Group 3. Partial meniscectomy was performed in each of these stifles. Osteophyte formation was considered significant enough to warrant debridement in 12 stifles, including three in Group 1, six in Group 2, and three in Group 3.

Pain assessment

Three dogs received supplemental postoperative analgesia. Two dogs, both in Group 1, received a single dose of additional hydromorphone 12 hours after extubation and one dog in Group 3 received a single dose of additional hydromorphone 10 hours after extubation. The frequency of supplemental analgesia was not different across groups (p = 0.11). Subsequent data from these dogs were excluded from further statistical analysis.

For the algometer measurements, there was no significant effect of treatment (p = 0.18), however there was a significant effect of time (p < 0.001) and a significant interaction of treatment and time (p = 0.01). Within Group 1, the mean forces required to provoke a pain response at all time points were not significantly different from preoperative assessment (Table 1). Within Group 2, the mean forces at times 4, 6, and 8 were significantly lower than the preoperative assessment; at all other time points mean forces were not different. Within Group 3, the mean force at time 16 was significantly lower than preoperative assessment; forces at all other time points were not different. Within time points; there was a significant difference across groups at time 1 only with the mean force for Group 3 higher than that of Group 1 and the mean force for Group 2 not different from either Group 1 or Group 3.

For the NPS, there were not any significant effects for either treatment or time (Table 2). VAS data were recorded as a measured numerical score between 1 and 10. There was not any significant effect of treatment (p = 0.22).
on the VAS data, however there was a significant effect of time (p < 0.001). Within group 1, VAS scores at all time points were significantly higher than the preoperative assessment score and time 0 score, which were not significantly different from each other (Table 3). Within group 2, VAS scores at all time points were significantly higher than preoperative assessment, time 0, and time 1 scores, which were not significantly different from each other. Within group 3, VAS scores at all time points were significantly higher than scores at the preoperative assessment, time 0, time 1, and time 2, which were not significantly different from each other.

**Discussion**

We hypothesised that IA administration of meloxicam would provide better pain control for dogs in the first 24 hours after arthroscopy and extra-capsular stabilisation of cruciate ligament injuries than either SC administration of meloxicam or placebo. Our results, however, provided no evidence to support this hypothesis. There were not any significant differences in postoperative pain assessments found between dogs receiving meloxicam by either IA or SC routes of administration using the algometer. More surprisingly, no effect on postoperative pain was noted for either route of meloxicam administration when compared with administration of placebo, except at one time point (time 1) when the pain threshold measured by the algometer was significantly greater for the placebo group than for the IA meloxicam group. Within groups, however, significant changes in pain scores were noted over time using both the algometer and the VAS. Among dogs receiving IA meloxicam, significantly lower contact pressures were required to produce pain responses 4, 6, and 8 hours after extubation than were required preoperatively or in the first two hours. Similarly, for dogs receiving the placebo, the mean algometer score at time 16 was significantly lower than the preoperative score. These results suggest that sensitivity at the surgical site increases over time regardless of treatment. The VAS results support this interpretation, with significant increases in scores within all three groups over time compared to baseline and immediate postoperative scores. Increasing postoperative pain over the first 24 hours of recovery is expected from peripheral sensitisation following tissue trauma (2). The timing of VAS increases is also consistent with a waning effect of the baseline opioid. Hydromorphone should have a duration of effect of two to four hours, and VAS scores within all three groups were increased significantly by time 4 (19).

There are several possible reasons why our findings did not show any significant improvement in postoperative analgesia using IA meloxicam. First, the provision of opioids at the end of the surgical procedure may have masked differences in signs of pain between groups. We did not, however, note any significant differences between groups using any of our assessment methods after the first four hours, at which time point the opioid effect should have dissipated. One particular challenge we encountered was to ensure adequate analgesia to dogs at all times while minimising the confounding effects of both baseline and rescue analgesics on our pain assessments. Treatment with both opioids and NSAID in the initial 24-hour postoperative period is a standard of care for dogs undergoing cruciate ligament repair in our hospital. However, the single dose of hydromorphone given near the end of the procedure may have blunted any differences between treatments. Three dogs were deemed painful enough to warrant additional administration of hydromorphone, one at 10 hours and two at 12 hours after extubation. At this point meloxicam, with an expected duration of activity of up to 24 hours, should have been providing analgesia since the observations of pain in these dogs occurred well after the expected two to four hour activity of hydromorphone. Interestingly,
two of the dogs had received IA meloxicam and one had received only placebo, however the number of dogs requiring supplemental analgesia was too low to draw any conclusions. Although supplemental analgesia may confound further readings for a treated animal, we considered inclusion of a rescue protocol necessary.

A second possibility is that our assessment methods could not detect subtle differences in postoperative pain between groups. We were, however, able to detect significant differences between preoperative and postoperative scores in all groups using theVAS, and in some groups using the algometer. Effective pain assessment methods should produce consistent results when used by different observers (20). When testing the reliability of three pain assessment scales for dogs, Holton et al found significant variability among observers (21). In an attempt to control this variability, we limited the postoperative pain evaluators to a surgeon (PM), a certified veterinary technician (AC), and a fourth year veterinary student (ER). Observers participated in a preliminary training session in the use of the algometer, VAS, and NPS. For each dog enrolled in the study, assessments were made by a single observer at each time point, although different observers made assessments over the 24 hour postoperative period. We also attempted to increase the sensitivity of our observations by evaluating patients using three separate methods, each of which has precedent in veterinary analgesic research. The use of a VAS has been described for postoperative pain assessment in dogs (5, 22). Despite its reliance on subjective observation, the VAS is considered to be a sensitive indicator (23). The numerical pain score developed for this study is loosely based upon the University of Eastern Ontario Pain Scale (20). Similar modified assessment scales have been used in other studies for postoperative pain assessment in dogs (5, 6, 24). This type of scale relies upon interpretation of behavioural cues, either with or without any interaction with an evaluator. Disadvantages of this type of scale are the subjective observation of behaviour and the reliance upon behaviours which may be stimulated by causes other than pain alone. For example, vocalisation may be a manifestation of pain in a dog, but may also represent stress, anxiety, or aggression. We attempted to minimise this effect by comparing postoperative observations to a preoperative baseline while maintaining continuity in each dog’s environment. We also chose to limit the assessment of behaviours produced during interaction with an evaluator in order to minimise responses which might be motivated more by stress, anxiety, or apprehension than by pain. In our assessment of NPS, the only interactive behaviour measured was the patient’s response to the handling around the affected limb and surgical site required for application of the algometer. Our NPS also differed from the University of Melbourne Pain Scale in that it did not incorporate any physiologic data, which has shown a poor correlation with pain severity (14, 25). Although some physiologic data was monitored (heart and respiratory rates), these were not used in assessment of pain except to provide further context if rescue analgesia was deemed necessary.

The use of a pressure algometer has precedent for postoperative pain assessment (5, 22). While many pain evaluation methods are subjective, the algometer provided quantitative data, with an accuracy within one percent. Use of the algometer may, however, have introduced some bias to our study population. There were not any body weight limits imposed for inclusion criteria. On physical examination, any dog subjectively deemed too small to allow appropriate application of the 1 cm² tip to the craniomedial aspect of the joint space was not included. One observer in this study noted mild difficulty using the algometer in one dog in this study, a beagle. However, five other dogs included in the study population had lower body weights than this dog, suggesting that imposing a weight limit would have further limited the study population. Bias produced by this type of limitation, like our choice to exclude any aggressive dog, is inherent in this type of clinical study. We also chose to establish a maximum applied limit of 4.5 Kg of force. The tip pressure produced by this force should be sufficient to provoke a pain response without producing a lasting effect, or unnecessarily sensitising the dogs, or causing apprehension. Similarly, Samm-arco et al established a maximum force limit of 50 N for the pain threshold test in dogs following stifle surgery (5).

The sample size of this study was inadequate to detect a difference between groups, as evidenced by the absence of a significant difference between SC meloxicam and placebo, despite the fact that meloxicam has previously shown benefits as a postoperative analgesic. Similar controlled analgesia studies in dogs undergoing stifle surgery have enrolled as few as six dogs in each group (6). A larger sample size could have improved detection of group differences.

Another possible reason we did not find a significant improvement in postoperative analgesia using IA meloxicam is that the NSAID dose required for local IA effect may not be equal to that used for SC administration and systemic effect. We used the highest recommended dose, based on labeling for SC or IA administration. Colbert et al gave equal doses and volumes of tenoxicam through either IA or intravenous administration to patients undergoing arthroscopic knee surgery, and found evidence for improved analgesia with the IA administration (9). However, a dose-response relationship was noted in other studies in a review of IA NSAID administration, leading to the speculation that the dose used for local administration may be important (3). The safety of a higher dose of meloxicam may, however, be of concern when the drug is administered intra-articularly. Some NSAID disrupt chondrocyte metabolism and inhibit proteoglycan synthesis, producing deleterious effects on joint cartilage (26). Meloxicam did not effect on ex vivo proteoglycan synthesis in canine cartilage explants following three doses of 0.2 mg/kg in one study (27). Further research is needed to determine the efficacy and safety of IA administration of higher doses in dogs.

Meloxicam administered IV preoperatively has demonstrated efficacy equal to ketoprofen, and is superior to butorphanol as a postoperative analgesic for dogs undergoing abdominal surgery (14). In another study, analgesia given in the first 24 hours after orthopaedic surgery was not different between dogs administered SC meloxicam or carprofen preoperatively (16). Modulation of acute IA inflammation was noted...
in one model following oral administration of meloxicam, in which both synovial fluid volume and white blood cell count were decreased in treated versus untreated dogs (17). The efficacy of preoperative administration of single-dose IV meloxicam has compared favourably with multiple perioperative doses of butorphanol for control of postoperative pain for dogs undergoing stifle surgery (15). Local infiltration with NSAID has also shown promise for postoperative analgesia. While there are no reports of clinical use of IA NSAID administration in dogs in the veterinary literature, IA administration of bupexamac has been studied in horses (7). Clinical use of IA NSAID, including ketorolac, piroxicam, and tenoxicam, is well documented in human orthopaedic surgery, particularly for use following arthroscopic surgery of the knee and shoulder (3, 8–11). One review of human literature found evidence for peripheral analgesic action for NSAID administered as IA injections, but not for those administered as components of intravenous regional anaesthesia (3). In addition, no adverse effects were noted from IA NSAID administration, although the authors note that this information was only provided in seven of 16 such studies reviewed. Postoperative analgesia following IA administration of tenoxicam, another oximac class NSAID, has been favourably compared with that of IA administration of opiates and local anaesthetics. Intra-articular tenoxicam provided longer duration of analgesia and decreased analgesic consumption than IA morphine or IA bupivacaaine following arthroscopic knee surgery in one study (8). Similarly, in another prospective study of people undergoing knee arthroscopy, IA tenoxicam, pethidine, and lidocaine produced greater postoperative consumption than IA morphine or IA bupivacaine. In people undergoing orthopaedic surgery, IA NSAID administration would seem to augment a multimodal analgesic plan, but we found no evidence to promote its use.

Acknowledgements

The authors thank Andrea Chrisholm, RVT, for technical assistance and Boehringer-Ingelheim (Canada) Ltd. for supplying the meloxicam and the placebo.

References