Endoscopic evaluation of the gastroduodenal mucosa to determine the safety of short-term concurrent administration of meloxicam and dexamethasone in healthy dogs

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Objective—To evaluate the safety, with respect to the development of gastric ulcers and erosions, of concurrent administration of meloxicam and dexamethasone for 3 days to healthy dogs.

Animals—20 conditioned purpose-bred research Beagles.

Procedure—Seven days prior to treatment, dogs were anesthetized for endoscopic evaluation of the upper portion of the gastrointestinal tract (ie, the gastric and duodenal mucosa). Five regions of the gastroduodenal area were scored by 2 investigators. Dogs were randomly assigned to 1 of 4 treatment groups as follows: saline-saline, dexamethasone-saline, saline-meloxicam, and dexamethasone-meloxicam groups. On days 1, 2, and 3, dogs received either dexamethasone or saline (0.9% NaCl) solution injections SC twice daily. On days 2, 3, and 4, dogs received either meloxicam or saline solution injections SC once daily. On day 2, dogs were anesthetized for a sham surgery (ie, electrostimulation). On day 5, the gastroduodenal area of each dog was reevaluated by use of endoscopic evaluation and histologic examination of biopsy specimens.

Results—The total endoscopic score of the dexamethasone-meloxicam group was significantly greater than the scores of the other groups. The dexamethasone-saline group had a mean cumulative score that was significantly greater than the saline-meloxicam or saline-saline groups. Endoscopic scores of the saline-meloxicam group were not significantly different from scores of the saline-saline group. No significant differences in histologic findings were found between groups.

Conclusions and Clinical Relevance—In healthy dogs, meloxicam appears to be safe with regard to adverse effects on the gastrointestinal tract. Concurrent administration of dexamethasone and meloxicam is more likely to cause gastric erosions than meloxicam administration alone. (*Am J Vet Res* 2003;63:1369–1375)

Intervertebral disc disease (IVDD) is a common neurologic disease in dogs that is treated with surgical decompression of the spinal cord. Dogs with IVDD are often treated with corticosteroids such as dexamethasone before and after surgery, and perioperative analgesia is often provided by the use of opioids. Some of the disadvantages of opioids are that they need to be administered frequently and can have a sedative effect. This sedative effect may affect the clinician's ability to evaluate the neurologic status and can make these patients less willing to perform normal behaviors.

Recently, the perioperative use of **nonsteroidal anti-inflammatory drugs (NSAIDs)** has been approved in small-animal surgery. These drugs have been shown to be safe and effective at providing postoperative analgesia. Unfortunately, it has been shown that when NSAIDs and corticosteroids were used concurrently, their negative effects on the gastrointestinal tract were additive, especially when used in instances of spinal injury.[1-3] The situation is further complicated by the observation that spinal injury alone can be associated with the formation of gastric ulcers.[4]

Although the association between the use of corticosteroids and gastric hemorrhage and enteritis is clear, the exact mechanism of action of corticosteroid-induced gastroenteritis is still poorly understood.[3,5,6] It has been suggested that corticosteroid-induced gastritis may be caused by a decrease in mucous production, an alteration of the structure of gastric mucous, and a decrease in mucosal cell renewal rate.[7-9] These effects may be mediated by inhibition of phospholipase A, resulting in reduced production of **prostaglandins (PGs)**.[9]

Endogenous PGs, such as PGE_2, normally have a protective effect on the gastric and duodenal mucosa through the stimulation of mucous and bicarbonate production and increased mucosal blood flow.[10]

The major mechanism of action of NSAIDs is to prevent the production of PGs from arachidonic acid by the inhibition of **cyclooxygenase (COX)**.[11] Along with the desired effects as an analgesic, anti-inflammatory drug, and antipyretic, the systemic inhibition of PGE_2 production inhibits the normal protective mechanisms of the gastric mucosa. In the absence of these protective mechanisms, the acidic environment of the stomach damages the mucosa, leading to gastric ulceration.[12]

Recently, 2 forms of cyclooxygenase were described, COX-1 and COX-2. The constitutive form, COX-1, is responsible for the protective effect on the gastric mucosa, platelet function, and renal blood flow, whereas the inducible form, COX-2, is responsible for the production of PGs that cause pain and inflammation.[13,14] Most of the common, traditional NSAIDs are either nonselective or preferentially selec-

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tive for COX-1.[15] Meloxicam is a COX-2 preferential NSAID that was recently licensed in Canada for use in dogs. Meloxicam is a superior analgesic and anti-inflammatory drug with minimal gastrointestinal adverse effects, compared with other commonly used NSAIDs.[15,16]

The use of NSAIDs, such as flunixin meglumine, aspirin, and phenylbutazone concurrently with high doses of corticosteroids, is associated with gastric ulceration. This is especially true for patients with spinal trauma. However, it is not known if these gastrointestinal adverse effects also occur with the use of more COX-2 specific NSAIDs and low doses of corticosteroids. Meloxicam would be a good analgesic for postoperative IVDD patients, because it has potent analgesic properties, is administered every 24 hours, and does not cause sedation or dysphoria. Although the package insert of the veterinary formulation of meloxicam lists the concurrent administration of corticosteroid anti-inflammatory drugs as 1 of the contraindications of meloxicam use, it is not known if the administration of this COX-2 preferential NSAID with corticosteroids would be safe. [17]

The purpose of the study reported here is to evaluate the gastrointestinal effects of the concurrent use of meloxicam and dexamethasone in healthy dogs for a period similar to that used for the acute management of surgical IVDD and compare them with the effects of saline (0.9% NaCl) solution, meloxicam, and dexamethasone administration alone. The null hypothesis is that meloxicam and dexamethasone used concurrently will have the same effect on the upper portion of the gastrointestinal tract (ie, the gastric and duodenal mucosa) as dexamethasone or meloxicam administered individually.

Materials and Methods

Animals—The University of Guelph Animal Care Committee approved the protocol for this study. Twenty conditioned purpose-bred research Beagles obtained through the Central Animal Facility at the University of Guelph were studied. Dogs were housed at the Central Animal Facility in separate kennels for the entire trial, except for the 2 days that endoscopy was performed. Dogs were fed a dry kibble[a] for a minimum of 14 days prior to starting the treatments. During the week preceding the trial, dogs were determined to be healthy on the basis of normal physical examination findings, CBC determination, serum biochemical analysis results, and activated clotting time. Fecal occult blood was evaluated by the use of commercially available tablets[b] for 3 consecutive days prior to the start of the trial, and the results were negative for all dogs.

Protocol—Seven days prior to drug administration, each dog had food withheld for 12 hours and was anesthetized for endoscopic evaluation of the upper portion of the gastrointestinal tract. Each dog was premedicated with acepromazine maleate[c] (0.05 mg/kg, SC) and butorphanol tartrate[d] (0.2 mg/kg, SC). An IV catheter was placed, and a balanced electrolyte solution[e] was administered at a rate of 5 mL/kg/h for the duration of anesthesia. Blood samples for PCV and total protein determinations were obtained at the time of catheter placement. General anesthetic was induced with IV administration of propofol[f] to effect and maintained with isoflurane[g] via an endotracheal tube. Blood pressure was monitored indirectly with a monitor.[h] A flexible videoendoscope[i] with a 9.5-mm-outer diameter and a 2.8-mm-diameter biopsy channel was used to assess the following 5 regions of the upper portion of the gastrointestinal tract: the cardia, angularis incisura, greater curvature, pylorus and pyloric antrum, and the proximal portion of the duodenum to the major duodenal papilla.

By the use of a grading system adapted from similar endoscopic studies in humans and dogs, each region was scored independently by 2 of the investigators (SEB and SAK).[18-20] The mucosa was graded as follows: 0 = normal in appearance; 1 = erythema or 1 to 4 punctate hemorrhages; 2 = 5 to 10 punctate hemorrhages or 1 to 4 erosions; 3 = 11 to 20 punctate hemorrhages or 5 to 9 erosions; and 4 = confluent hemorrhages, 10 to 20 erosions, or an ulcer of any size. Erosion was defined as a discontinuation of the mucosa that was < 3 mm in diameter. An ulcer was defined as a lesion producing a discontinuation of the mucosa that was > 3 mm in diameter and having a craterous center. The score for each of the 5 regions was added together to obtain cumulative score for each dog. A cumulative score of ≤ 5 and maximum score of 2 in each area were required for the dog to continue in the study.

All dogs were monitored daily for evidence of vomiting, diarrhea, depression, inappetence, or abdominal pain during the course of the study. Feces were collected daily for occult blood testing on the day of the first endoscopic evaluation until the completion of the study.

The design of the drug administration protocol was intended to simulate a clinical case of IVDD treated surgically, which typically involves the administration of corticosteroids on the day before surgery, the day of surgery, and 1 day after surgery. Surgery is performed the day after the first corticosteroid administration, and analgesia is administered after surgery. By the use of this model, the treatment protocol for this study was constructed. Dogs were randomly assigned to 1 of 4 treatment groups by use of a randomization table, with 5 dogs in each group (**Appendix**).[21] The 4 treatment groups were as follows: saline-saline group, dexamethasone-saline group, saline-meloxicam group, and dexamethasone-meloxicam group. On days 1, 2, and 3, dogs received either dexamethasone[j] or saline solution injections SC twice daily. On days 2, 3, and 4, dogs received either meloxicam[k] or saline solution injections SC once daily. The investigators, except for 1 (NMMM), were blinded to the treatment each dog received until the completion of the trial and statistical analysis of the results. The nonblinded investigator performed all of the treatments.

On day 2, following 12 hours of withholding food and the morning treatment, dogs were premedicated with oxymorphone[l] (0.05mg/kg, SC). General anesthesia was induced by the use of IV administration of thiopental[m] (5 to 15 mg/kg, given to effect) and maintained at a surgical plane with isoflurane. Blood samples for PCV and total protein determinations were obtained at the time of catheter placement. Dogs were anesthetized for 1 hour and received a balanced electrolyte solution IV at a rate of 5 mL/kg/h. During the anesthetic period and stimulation, indirect blood pressure was monitored. During the anesthetic period, dogs were electrostimulated.[n] The stimulator was connected to 1 foot for 30 seconds with a 25-gauge hypodermic needle through the interdigital web. The stimulator voltage setting was adjusted to find the lowest voltage that would create a physiologic response in the anesthetized patient that indicated sympathetic stimulation. The settings were typically 20 to 50 V at 50 cycles/s for 10 milliseconds. Responses such as an increase in the blood pressure, heart rate, or respiratory rate were considered signs of sympathetic stimulation. After a rest period of 90 seconds, the stimulator was rotated to another foot, and the process was repeated for a total of 45 minutes.

On day 5, dogs underwent endoscopic evaluation after having food withheld for 12 hours. The anesthetic protocol was identical to the previous protocol used for endoscopic evaluation in all dogs. Blood samples for PCV and total protein determination were obtained at the time of catheter placement. The endoscopic procedure and grading were identical to the previous endoscopic evaluation, except that 2 biopsy specimens were taken from each of the 5 regions of the gastoduodenum with biopsy forceps.[o] Additional biopsy specimens of gross lesions were also taken.

Biopsy specimens were fixed in formalin, and H&E stained slides were prepared. The slides were examined by the pathologist (EPS) and primary investigator (SEB). Specimens of each region were examined histologically for evidence of inflammation and erosions and scored with a grading system developed for this study. Ulceration and inflammation were scored independently. The ulceration score was as follows: 0 = normal appearing epithelium; 1 = loss of mucous, epithelial flattening, and hyperchromasia; 2 = ulceration that involved the loss of epithelial cells; and 3 = ulceration that involved the stroma. The scores for each region were added for a cumulative ulceration score. The inflammation score was 0 for normal appearance and subjectively 1, 2, and 3 for mild, moderate, and severe infiltration of inflammatory cells, respectively. The scores for each region were added to calculate a total inflammation score for each region. Artifactual separation of the epithelium and submucosal hemorrhage were noted when they occurred.

Statistical analysis—All statistical analyses, except for the interclass correlation, were performed by use of a computer software system.[22,p] The agreement in all of the cumulative endoscopic scores for all dogs between the 2 observers was evaluated by measuring the interclass correlation with an agreement of 92%.[23] Scores of the primary investigator were thus used for the rest of the statistical analysis.

A 2-factor ANOVA was used to evaluate differences in the mean total endoscopic scores of the treatment groups before and after treatment. A 3-factor ANOVA was used to assess the interactions among the areas of the stomach, time (before and after treatment), and treatment given by comparing the mean score of each region of the stomach for each of the treatment groups. A log-transformation of this data was performed prior to the 3-factor ANOVA. A 2-factor ANOVA was used to evaluate the differences between the mean PCV in each treatment group over 3 time points (first endoscopic evaluation, electrostimulation, and second endoscopic evaluation). A Kruskal-Wallis test was used to evaluate the differences in the mean total ulceration and inflammation scores among the 4 groups. A Kruskal-Wallis test was also used to evaluate the number of vascular and epithelial separation artifacts found in each group to assess whether the frequency of artifacts was significantly different in any of the 4 groups. A value of $P \leq 0.05$ was considered to be significant for all tests.

Results

None of the dogs experienced any vomiting, diarrhea, inappetence, or abdominal pain at any time during the course of the study. The mean (± SE) values for the total gross score of each group were determined (**Table 1**). Comparing the total gross score over time (before and after treatment), no significant differences were found in the mean scores before treatment among the 4 groups. Within each group, a comparison of the before- and after-treatment scores revealed no significant difference in the groups treated with saline solution or meloxicam ($P = 0.85$ in both cases). A significant difference was found between the before- and after-treatment scores in the groups treated with dexamethasone alone and dexamethasone-meloxicam ($P = 0.007$ and $P < 0.001$, respectively), with a significantly higher score given after treatment in both cases. The after-treatment score of the group treated with dexamethasone-meloxicam was significantly higher than the before-treatment scores of all groups ($P < 0.001$ in all cases). The comparison of the after-treatment scores between treatment groups also revealed that the dexamethasone-meloxicam group was significantly higher than the dexamethasone-saline, saline-saline, and saline-meloxicam groups ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively). After-treatment scores for the dexamethasone-saline group were also significantly greater than the scores for the saline-saline and saline-meloxicam groups ($P = 0.003$ and $P = 0.01$, respectively). No significant difference was found in the after-treatment scores between the saline-saline and saline-meloxicam groups.

The mean (± SE) values of the after-treatment endoscopic scores for each region of the stomach for each treatment group were determined (**Table 2**). The pylorus had a significantly larger increase in score over the treatment period, compared with all other regions of the stomach. The *P* values for the differences between the pylorus and the angularis, cardia, duodenum, and greater curvature were 0.004, 0.01, 0.002, and 0.02, respectively. No other effects of area were

Table 1—Mean (± SE) before and after treatment total endoscopic scores for each group

	Total endoscopic score	
Treatment groups	**Before treatment**	**After treatment**
Dexamethasone-saline	0.600 ± 0.400	3.800 ± 1.428
Saline-saline	0 ± 0	0.200 ± 0.200
Saline-meloxicam	0.600 ± 0.245	0.800 ± 0.583
Dexamethasone-meloxicam	0.200 ± 0.200	8.400 ± 1.568

Saline = Saline (0.9% NaCl) solution.

Table 2—Mean (± SE) after treatment endoscopic scores for each group

	Endoscopic score				
Treatment groups	**Angularis incisura**	**Cardia**	**Greater curvature**	**Pylorus & pyloric antrum**	**Duodenum**
Dexamethasone-saline	0 ± 0	0.800 ± 0.490	1.00 ± 0.316	1.80 ± 0.583	0.200 ± 0.200
Saline-saline	0 ± 0	0 ± 0	0 ± 0	0.200 ± 0.200	0 ± 0
Saline-meloxicam	0.200 ± 0.200	0 ± 0	0.200 ± 0.200	0 ± 0	0 ± 0
Dexamethasone-meloxicam	1.600 ± 0.510	1.200 ± 0.374	1.00 ± 0.548	3.00 ± 0.316	1.600 ± 0.980

See Table 2 for key.

observed. Other significant findings from this analysis were identical to those of the previous analysis for the overall effect of treatment on each dog's endoscopic scores.

The mean cumulative histologic score for inflammation ranged from 0 to 1.00 in the 4 treatment groups. The mean cumulative histologic score for ulceration ranged from 0.4 to 1.60 in the 4 treatment groups. In the evaluation of differences among the treatment groups for the histologic scoring of both the total ulceration and total inflammation scores, no significant differences were found. Also, no significant differences were found in the number of vascular or epithelial separation artifacts for any of the treatment groups.

Fecal occult blood tests were performed for a total of 12 days in each dog, from the day of the first endoscopic evaluation until the last day of the study. For 15 of the 20 dogs, the results of the fecal occult blood tests were negative for all 12 days. Three dogs from the dexamethasone-saline group had positive results for the fecal occult blood test on day 1 (2 dogs) and day 2 (1 dog) during the treatment period. The cumulative endoscopic scores after treatment in these dogs were 2, 0, and 8 respectively. One dog each from the saline-saline and saline-meloxicam groups had positive results on day 1 during the treatment period. The cumulative endoscopic scores after treatment in these dogs were 1 and 3, respectively. None of the dogs in the dexamethasone-meloxicam group had any positive results on fecal occult blood testing at any time.

Evaluation of the mean PCV in each group over time revealed no significant difference among any of the treatment groups at any period. The mean PCV was within reference range limits for all dogs.

Discussion

Endoscopy is a commonly used method to evaluate the gastroduodenal area of dogs for NSAID- and corticosteroid-induced gastric erosion or ulceration and evaluate the effects of protectant drugs, with several studies[1,6,20,24-30] using this technique published in recent years. Also, endoscopy is commonly performed in human studies[18,19,31,32] on the effects of NSAIDs on the gastroduodenal mucosa of volunteers and patients, in which full-thickness biopsy specimens and necropsy are not an option. Gross endoscopic evaluation of gastric lesions correlates well with gross lesions found at necropsy and is a reliable method to evaluate for gastric hemorrhage and ulceration.[1,5]

Endoscopic evaluation proved to be more sensitive than histologic evaluation or monitoring PCV, fecal occult blood, or clinical signs for detection of the effects of dexamethasone and meloxicam on the gastroduodenal mucosa in our study. We found that the concurrent administration of these drugs in the dexamethasone-meloxicam group had an effect on the gastrointestinal tract that was significantly different from that found for the other 3 treatment groups. Findings in our study also indicate that dexamethasone administration alone causes lesions that are significantly worse than those caused by meloxicam administration; the effects of meloxicam administration were similar to saline solution. It should be emphasized that even in the dexamethasone-meloxicam group, the lesions were mild, and the clinical importance of this finding is unknown.

The pylorus and pyloric antrum had significantly higher scores for endoscopic grading after treatment than the other 4 areas that were examined. This is consistent with findings in previous studies[5,6,24,26-28,33,34] supporting the theory that although all regions of the stomach can be affected, the pylorus and pyloric antrum appear more susceptible to the effects of NSAIDs and corticosteroids.

Results of our study confirm previous reports[3,5,6] that indicate that corticosteroids can induce erosions, gastric hemorrhage, and enteritis in dogs. It has been suggested that 1 of the mechanisms of the formation of corticosteroid-induced ulcers may be the disruption of normal protective mechanisms in the stomach mediated by PGE.[9] A study of experimentally induced gastric ulcers in rats revealed a delay in ulcer healing in rats treated with corticosteroids that was reversed by the administration of PGE_1.[9] However, results of another study by Rohrer et al[30] implied that a decrease in the production of PGE was not a primary factor in the pathogenesis of gastric hemorrhage, because the administration of synthetic PGE did not have a protective effect in dogs treated with methyl prednisilone sodium succinate. Likely, the reason for the difference seen in these 2 studies is that 1 involved ulcers that were induced with a cryoprobe prior to drug administration, and the other involved gastric hemorrhage induced with methyl prednisolone sodium succinate.

The concurrent use of corticosteroids and NSAIDs has resulted in the development of gastric ulcers. A study by Dow et al[1] evaluated the gastrointestinal effects of flunixin alone and in combination with prednisone. All treated dogs developed substantial gross lesions of the gastrointestinal tract, with the lesions in the group treated with both flunixin and prednisone being the most severe.[1] A retrospective study by Toombs et al[3] reviewed 13 instances of colonic perforation in dogs that were treated with high doses of corticosteroids. In that study, 4 dogs were concurrently treated with nonselective NSAIDs. Results of these studies support our findings that a synergistic effect exists when NSAIDs and corticosteroids are administered concurrently. In our study, dexamethasone alone had an effect on the cumulative endoscopic scores. This effect was significantly greater with the addition of meloxicam, which had no effect alone.

One problem with previous studies[3,5,33] is that they report the use of NSAIDs that are known to cause substantial gastrointestinal, adverse effects when used alone. Also, the doses of corticosteroids used in those studies were approximately 10 times higher than the dose currently recommended. Results of our study indicate that the recommendation against the concurrent use of NSAIDs and corticosteroids may still be clinically relevant, even with newer generation NSAIDs and low doses of corticosteroids.

An attempt was made in our study to approximate the sympathetic effects of surgery and anesthesia by the use of electrostimulation. Cutaneous elec-

trostimulation has been previously reported to mimic the noxious effects of surgery in dogs.[35,36] One investigator attempted to recreate the effect of spinal trauma and surgery by performing a hemilaminectomy and inducing hypotension in anesthetized research dogs.[5] Even with these efforts to recreate the clinical situation, it is unlikely to be comparable to the spinal trauma induced by extrusion of an intervertebral disc. That method, with a substantially higher morbidity, was associated with a debatable gain in authenticity.[5] In that study, the hemilaminectomy and hypotension alone did not cause substantial lesions. Electrostimulation will create sympathetic stimulation and physiologic stress that might mimic that of surgery to some extent. In our study, this was observed by an increase in heart rate, respiratory rate, and blood pressure. It is likely that the effect of the stimulator is mild in comparison to the effect of spinal trauma and hospitalization in clinical patients. However, this technique provided a humane method of inducing a level of sympathetic stimulation. There is no accurate way of mimicking the effect of spinal trauma and surgery caused by IVDD. Given that the lesions were mild in our study, a clinical trial would be the next step in assessing the safety of these medications.

Meloxicam has been shown to decrease renal PGE_2 synthesis, but this effect is weaker than that of nonselective NSAIDs.[37] Renal PGE_2 acts as a vasodilator during periods of hypotension to maintain renal perfusion.[38] This effect is primarily mediated by COX-1. However, COX-2 is induced by hypotension and does play a role in renal homeostasis.[38] If meloxicam is to be used as a postoperative analgesic in clinically affected dogs, it is important that blood pressure is monitored and supported, or if hypotension is anticipated intraoperatively, meloxicam should be administered after the pressures have normalized.

The negligible histopathologic lesions in our study did not differ significantly between treatment groups. The most likely reasons for this result are that the lesions in our study were mild overall and the number of dogs was small. Similarly, other studies[5,30] evaluating the adverse effects of NSAIDs and corticosteroids on the stomach and duodenum have failed to identify a correlation between gross and histologic lesions. One study evaluating the effects of dexamethasone, hemilaminectomy, and hypotension on the stomach found that despite the presence of gross lesions in the stomach observed by endoscopic evaluation and at necropsy, the endoscopic biopsy specimens of only 2 of the 10 dogs had mild histologic lesions at necropsy.[5] This lack of correlation between gross and histologic lesions from endoscopic biopsy specimens was supported by the study by Rohrer et al[6] evaluating the effects of high doses of methylprednisilone sodium succinate on the stomach. Another study by Dow et al[1] revealed a good correlation between the gross lesions and histologic examination of necropsy specimens.

The results of the fecal occult blood assay in our study were also consistent with results of a previous report[20] that failed to find an association between gross lesions and the presence of fecal occult blood. In our study, the lesions found in the stomach were mild with sporadic positive results on fecal occult blood testing. The results are difficult to interpret as a result of the small number of positive results. They are unlikely to be clinically important, because they were not positive during the entire treatment course in any dog. The low sensitivity of this test, mild lesions found in our study, and potential for false-positive and false-negative test results are the most plausible reasons for these findings. It is interesting to note that none of the dexamethasone-meloxicam treated dogs, which had the highest gross scores, had positive test results.

The PCV was monitored to assess whether any group of dogs had substantial blood loss. No significant difference in the PCV was found among the groups over time. Again, this is similar to results of other studies[1,20] that have shown that PCV is an unreliable monitoring tool for mild, acute gastrointestinal blood loss.

None of the dogs in our study experienced vomiting, diarrhea, inappetence, or abdominal pain. This is a similar finding to comparable studies in which gastrointestinal lesions are observed grossly and endoscopically, but clinical signs are absent or inconsistent.[1,20] Even in studies with substantial lesions of the gastrointestinal tract, clinical signs such as melena, diarrhea, and vomiting were inconsistent, and dogs had a normal amount of activity with no signs of abdominal pain.[6]

Findings in our study raise a question as to whether various endoscopic lesions are clinically relevant in the absence of clinical signs. It is our opinion that the lesions found in our study are clinically relevant for several reasons. Mild, significantly different lesions were produced among groups of healthy dogs. It is likely that additional stress in clinically affected dogs, such as pain, hospitalization, systemic disease, and spinal trauma, would have a physiologic effect that could cause more severe gastrointestinal lesions. The treatment days and times in our study were designed to simulate the medications that would be administered to a dog that was admitted to our veterinary teaching hospital for IVDD surgery. This is a short period, and it is possible that the lesions would have been more severe if the treatment times had been prolonged. Also, the dose of dexamethasone used in our study was low, compared with doses that are cited in the literature[33] or often given to dogs prior to referral to our hospital. It is likely that the lesions seen in our study are somewhat dependent on the dose and duration of treatment.

Given the potential clinical benefit of using dexamethasone and meloxicam concurrently, clinical trials to evaluate the safety of this combination may still be warranted. The lesions seen in our trial were mild, and similar lesions in a clinically affected dog would be unlikely to cause an increase in morbidity. In postoperative patients, 1 of the most substantial sources of stress is pain. It is possible that the benefits of successful pain management would outweigh the additional risk that this drug combination may pose in a clinically affected dog. Also, gastrointestinal tract protectants are often used in dogs with IVDD and were not used in

our study. It is possible that the use of gastrointestinal tract protectants would modify the lesions created by this drug combination.

The null hypothesis that meloxicam and dexamethasone used concurrently will have a similar effect on the upper portion of the gastrointestinal tract to either drug alone was rejected in our study. Our results indicate that in healthy dogs, dexamethasone and meloxicam used concurrently are more likely to cause gastrointestinal lesions than either drug used alone and suggest that this drug combination may not be safe in clinically affected dogs. Dexamethasone also appears to be more likely to cause lesions than meloxicam, and meloxicam appears to be safe with regard to the gastrointestinal tract when used alone. Results of our study indicate that the concurrent use of NSAIDs and corticosteroids continues to pose an increased risk of gastrointestinal adverse effects, even with a COX-2 preferential NSAID and low dose of dexamethasone. Fecal occult blood, PCV, and histologic examination of biopsy specimens were insensitive markers of gastrointestinal erosions in our study and should not be relied upon in a clinical situation as early markers of disease. The simultaneous use of dexamethasone and meloxicam in clinically affected dogs is not recommended at this time. However, further studies to assess this drug combination clinically and the effects of gastrointestinal tract protectants given concurrently are needed.

[a]The Iams Co, Dayton, Ohio.
[b]Hematest, Bayer Inc, Etobicoke, ON, Canada.
[c]Atravet, Ayerst Veterinary Laboratories, Guelph, ON, Canada.
[d]Torbugesic, Ayerst Veterinary Laboratories, Guelph, ON, Canada.
[e]P148, Baxter Corp, Toronto, ON, Canada.
[f]Propofol, Abbott Laboratories, North Chicago, Ill.
[g]Isoflurane, Bimeda-MTC Animal Health Inc, Cambridge, ON, Canada.
[h]Dinamap Vital Signs Monitor 8100, Critikon Inc, Tampa, Fla.
[i]Olympus, Carsen Group Inc, Markham, ON, Canada.
[j]Uni-Dex, Univet Pharmaceuticals Ltd, Milton, ON, Canada.
[k]Metacam, Boehringer Ingleheim, Burlington, ON, Canada.
[l]Numorphan, DuPont Pharma, Montreal, QC, Canada.
[m]Pentothal, Abbott Laboratories, North Chicago, Ill.
[n]Grass SD9 Stimulator, Grass Instrument Co, Quincy, Mass.
[o]Biopsy Forceps, Carsen Group Inc, Markham, ON, Canada.
[p]SAS Software, SAS Institute Inc, Cary, NC.

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Appendix

Schedule for each treatment group of dogs

	Treatment groups			
Days	**Saline-saline (5 dogs)**	**Dexamethasone-saline (5)**	**Saline-meloxicam (5)**	**Dexamethasone-meloxicam (5)**
1, 2, & 3	Saline solution (0.125 mL/kg, SC, q 12 h)	Dexamethasone* (0.25 mg/kg, SC, q 12 h)	Saline solution (0.125 mL/kg, SC, q 12 h)	Dexamethasone* (0.25 mg/kg, SC, q 12 h)
2, 3, & 4	Saline solution (0.02 mL/kg, SC, q 24 h)	Saline solution (0.02 mL/kg, SC, q 24 h)	Meloxicam† (0.1 mg/kg, SC, q 24 h)	Meloxicam† (0.1 mg/kg, SC, q 24 h)

*2 mg of dexamethasone/mL. †5 mg of meloxicam/mL. Saline = Saline (0.9% NaCl) solution.