SMALL ANIMALS

Effects of preoperative administration of ketoprofen on whole blood platelet aggregation, buccal mucosal bleeding time, and hematologic indices in dogs undergoing elective ovariohysterectomy

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Objective—To determine effects of preoperative administration of ketoprofen on whole blood platelet aggregation, buccal mucosal bleeding time, and hematologic indices in dogs after elective ovariohysterectomy.

Design—Randomized, masked clinical trial.

Animals—22 healthy dogs.

Procedure—60 minutes before induction of anesthesia, 11 dogs were given 0.9% NaCl solution (control), and 11 dogs were given ketoprofen (2 mg/kg [0.9 mg/lb], IM). Thirty minutes before induction of anesthesia, glycopyrrolate (0.01 mg/kg [0.005 mg/lb]), acepromazine (0.05 mg/kg [0.02 mg/lb]), and butorphanol (0.2 mg/kg [0.09 mg/lb]) were given IM to all dogs. Anesthesia was induced with thiopental (5 to 10 mg/kg [2.3 to 4.5 mg/lb], IV) and maintained with isoflurane (1 to 3%). Ovariohysterectomy was performed and butorphanol (0.1 mg/kg [0.05 mg/lb], IV) was given 15 minutes before completion of surgery. Blood samples for measurement of variables were collected at intervals before and after surgery.

Results—In dogs given ketoprofen, platelet aggregation was decreased 95 ± 10% and 80 ± 35% (mean ± SD) immediately after surgery and 24 hours after surgery, respectively, compared with preoperative values. At both times, mean values in dogs given ketoprofen differed significantly from those in control dogs. Significant differences between groups were not observed for mucosal bleeding time or hematologic indices.

Conclusions and Clinical Relevance—Preoperative administration of ketoprofen inhibited platelet aggregation but did not alter bleeding time. Ketoprofen can be given before surgery to healthy dogs undergoing elective ovariohysterectomy, provided that dogs are screened for potential bleeding problems before surgery and monitored closely after surgery. (*J Am Vet Med Assoc* 2002;220:1818–1822)

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Ketoprofen is a **nonsteroidal anti-inflammatory analgesic (NSAIA)** drug used to manage postoperative pain in dogs. Preoperative administration of ketoprofen may provide better analgesia than postoperative administration but may also interfere with platelet function and prolong bleeding time. Interactions between platelets and vascular endothelial cells are important in maintaining normal hemostasis.[1] Endothelial cells produce prostacyclin (prostaglandin I_2) and nitric oxide, which inhibit platelet aggregation and relax vascular smooth muscle. Adherence of platelets to exposed collagen in damaged endothelial cells initiates synthesis and release of thromboxane A_2, which stimulates platelet aggregation and vasoconstriction. The balance between vascular factors that inhibit hemostasis and platelet factors that promote hemostasis is an important determinant of bleeding time.

Thromboxane A_2 is synthesized from arachidonic acid within platelets, and the reaction is catalyzed by **cyclooxygenase (COX)**. Platelets express the constitutive form of the enzyme (COX-1) exclusively and do not express the inducible form (COX-2).[2] Inhibition of COX-1 activity by NSAIA drugs decreases formation of thromboxane A_2 and attenuates platelet aggregation.[3,4] In a canine in vitro assay system, ketoprofen inhibits the activity of COX-1 at lower concentrations than COX-2 and has a COX-1:COX-2 selectivity ratio of 0.23.[4] Ketoprofen and other NSAIA drugs with low selectivity ratios might inhibit platelet function and prolong bleeding time more than NSAIA drugs with high selectivity ratios do (eg, carprofen).

Conflicting results have been published concerning the effect of ketoprofen on **buccal mucosal bleeding time (BMBT)** in dogs. Some authors have reported that BMBT increased during orthopedic surgery[5] in dogs that received preoperative administration of ketoprofen, whereas others[6] reported that administration of ketoprofen to conscious dogs did not alter BMBT.

The effect of preoperative administration of ketoprofen on platelet aggregation in dogs after elective ovariohysterectomy has not been reported. **Whole blood platelet aggregation (WBPA)** can be used as a rapid means of screening dogs for platelet-related bleeding problems.[7] Additionally, WBPA has been used to evaluate platelet function during anesthesia and surgery and to evaluate the effect of preoperative administration of cephalosporin antibiotics in dogs.[8,9] Platelets behave differently in whole blood than in plasma, and WBPA may be a more clinically relevant method to detect changes in platelet function than techniques that use platelet-rich plasma.[10,11]

Preoperative administration of NSAIA drugs is controversial.[12-15] Presumably, administration of anti-inflammatory drugs before, rather than after, surgical trauma reduces inflammation at the surgical site, attenuates subsequent peripheral and central amplification of nociceptive input, and decreases pain after surgery. Preoperative administration of NSAIA drugs may also reduce anesthetic requirements and blunt the hypermetabolic and neuroendocrine responses that develop as a result of surgical trauma. Alternately, preoperative administration of some NSAIA drugs may inhibit platelet function and prolong bleeding time, which could lead to intraoperative as well as postoperative complications. These drugs also interfere with prostaglandin-mediated regulation of renal blood flow and tubular function, which could lead to renal failure in dogs with preexisting renal disease.[16] The purpose of the study reported here was to determine the effects of preoperative administration of ketoprofen on WBPA, BMBT, and hematologic indices in dogs that underwent elective ovariohysterectomy.

Materials and Methods

Dogs—Twenty-two client-owned dogs were enrolled in the study, which was a randomized, masked clinical trial. Personnel involved in the study were unaware of the treatment protocol. Owners were informed of the potential risks and benefits of the study before written consent was given to enroll their animals. Female dogs that were between 6 months and 3 years of age, weighed 15 to 35 kg (33 to 77 lb), and were judged to be healthy on the basis of findings of preoperative examination and diagnostic blood analyses were included in the study. Dogs that were in estrus or pregnant were excluded from the study. The study was reviewed and approved by the Animal Care Committee at the University of Prince Edward Island.

Diagnostic tests—Measurement of WBPA was performed by use of an electrical impedance aggregometer[a] as per a published technique.[7] Before surgery, samples were collected from the jugular vein via venipuncture with a 2-syringe technique, a 20-gauge needle, and 3-ml plastic syringes. After discarding the first 1 to 2 ml of blood, 2 to 3 ml of blood was collected, placed immediately into a tube containing 3.8% trisodium citrate (1:10 dilution), and mixed by gentle inversion. After surgery, samples were collected from a jugular catheter that was placed after induction of anesthesia; samples were collected by use of a 2-syringe technique and 3-ml plastic syringes, and the first 1 to 2 ml of blood was discarded. Collagen[a] (5 µg/ml) was used to stimulate platelet aggregation, and all samples were analyzed within 2 hours of collection.

Bleeding time, hematologic indices, and plasma protein concentration were determined by use of standard techniques. Measurement of BMBT was performed with a spring-loaded device[b] as per a described technique.[17] Hematologic indices (erythrocyte count, leukocyte count, Hct, hemoglobin concentration, platelet count) were determined by use of an automated cell counter,[c] and plasma protein concentration was measured by use of a temperature-compensated refractometer.[d] A manual differential count of 100 WBC was done by an experienced technologist on each sample. When errors in automated platelet counts were detected, corrected counts were estimated from blood smears.[18] Before surgery, samples were collected from the jugular vein via venipuncture with 20-gauge needles and plastic syringes, immediately placed into tubes containing sodium EDTA, and mixed by gentle inversion. After surgery, samples were collected from a jugular catheter that was placed after induction of anesthesia.

Clinical protocol—Dogs were admitted to the hospital on the day before surgery. That afternoon, initial samples for determination of WBPA and hematologic indices were collected, and BMBT was measured. The following morning, dogs were assigned at random to either the saline (0.9% NaCl) solution (control) or ketoprofen treatment group. Approximately 60 minutes before induction of anesthesia, 11 dogs (mean ± SD weight, 22 ± 6 kg [48.4 ± 13.2 lb]; mean age, 10 ± 4 months) were given saline solution, and 11 dogs (mean weight, 21 ± 4 kg [46.2 ± 8.8 lb]; mean age, 13 ± 9 months) were given ketoprofen[e] (2 mg/kg, IM). Approximately 30 minutes before induction of anesthesia, all dogs were given glycopyrrolate[f] (0.01 mg/kg [0.005 mg/lb]), acepromazine[g] (0.05 mg/kg [0.02 mg/lb]), and butorphanol[h] (0.2 mg/kg [0.09 mg/lb]) IM. Ten minutes before induction of anesthesia, a 20-gauge polytef catheter was placed aseptically into a cephalic vein. Anesthesia was induced with thiopental[i] (5 to 10 mg/kg [2.3 to 4.5 mg/lb], IV) and maintained with isoflurane[j] (1 to 3%) in oxygen (1 to 3 L/min). After induction of anesthesia, a 16-gauge polytef catheter was placed aseptically into a jugular vein to facilitate collection of blood samples during the postoperative period. Ovariohysterectomy was performed by an experienced surgeon (CLR), and butorphanol (0.1 mg/kg [0.05 mg/lb], IV) was given 15 minutes before completion of the procedure. Lactated Ringer's solution was given during surgery at a rate of 10 ml/kg/h (4.5 mg/lb/h). All surgeries were performed on the morning after admission, and total duration of anesthesia (induction with thiopental to termination of isoflurane administration) was 92 ± 33 and 78 ± 29 minutes (mean ± SD) in the saline and ketoprofen groups, respectively. Blood samples for determination of WBPA were collected immediately after surgery (time 0) and 24 hours after surgery and placed into tubes that contained citrate. Bleeding time was measured, and EDTA-anticoagulated blood samples and serum samples for determination of hematologic indices were collected before surgery, at time 0, and 12 and 24 hours after surgery. The surgeon and the veterinary technicians (SB, ER) were given the option to withdraw dogs from the study and give supplemental opioids if they believed dogs were having moderate to severe pain. Personnel involved in each trial were unaware of the treatment protocol.

Statistical analyses—Platelet aggregation, BMBT, and hematologic data were analyzed by use of ANOVA for repeated measures. A 2-way ANOVA for repeated measures was used to compare differences between treatments over time. If a significant treatment-time interaction was found, Tukey multiple comparison tests were used to compare treatments at each time period. A 1-way ANOVA for repeated measures was used to compare differences within treatments over time. If a significant time effect was found, Dunnett multiple comparison tests were used to compare times within each treatment with respective preoperative values. Platelet aggregation data are reported as percentage changes from respective preoperative values.

All data are reported as mean ± SD. For all comparisons, a value of $P < 0.05$ was considered significant.

Results

Platelet aggregation decreased in dogs given ketoprofen but not in dogs given saline solution. In the saline-treated group, mean values immediately after surgery (5 ± 40%) and 24 hours after surgery (–1.0 ± 33%) were not significantly different from preoperative values. In the ketoprofen-treated group, mean values were 95 ± 10 and 80 ± 35% less than preoperative values immediately after surgery and 24 hours after surgery, respectively. At both times, mean values in dogs given ketoprofen differed significantly from those in dogs given saline solution and from respective preoperative values. Platelet count did not change in dogs given ketoprofen or in dogs given saline solution **(Table 1)**. Mean values in dogs given ketoprofen did not differ significantly from those in dogs given saline solution at any time.

Bleeding time did not change in dogs given ketoprofen or saline solution (Table 1). Mean values in dogs given ketoprofen did not differ significantly from those in dogs given saline solution at any time. The highest mean values for BMBT were measured immediately after surgery in dogs given ketoprofen (165 ± 64 seconds) as well as in those given saline solution (163 ± 80 seconds). In dogs given ketoprofen, individual values at 0, 12, and 24 hours after surgery ranged from 70 to 245, 80 to 230, and 65 to 235 seconds, respectively. Abnormal intraoperative bleeding (150 ml) was observed in 1 dog (weight, 32 kg [70 lb]) given saline solution. Substantial bleeding was not observed in any dog during the 24-hour postoperative observation period.

Hematocrit, hemoglobin concentration, and erythrocyte count were decreased immediately after surgery, compared with preoperative values, in both treatment groups (Table 1). Mean values for all 3 indices and for both treatments were significantly less than respective preoperative values immediately after and 12 hours after surgery. Mean values 24 hours after surgery in dogs given ketoprofen remained less than preoperative values. Plasma protein concentration was decreased significantly immediately after surgery and was increased significantly 24 hours after surgery in both groups, compared with preoperative values. For all 3 erythrocyte indices and for plasma protein concentration, mean values in dogs given ketoprofen did not differ significantly from those in dogs given saline solution at any time.

Mean leukocyte count was significantly decreased immediately after surgery and was significantly increased 12 hours after surgery in both treatment groups, compared with preoperative values **(Table 2)**. Additionally, neutrophil counts were significantly greater than and eosinophil and lymphocyte counts were significantly less than respective preoperative values 12 hours after surgery. For all leukocyte indices, mean values in dogs given ketoprofen did not differ significantly from those in dogs given saline solution at any time.

Table 1—Mean ± SD platelet count, buccal mucosal bleeding time (BMBT), and erythrocyte indices in dogs that received ketoprofen (n = 11) or saline (0.9% NaCl; 11) solution before elective ovariohysterectomy

		After surgery		
Variable	**Before surgery**	**0 h**	**12 h**	**24 h**
Platelets (× 10^9/L)				
Saline solution	268 ± 50	243 ± 29	251 ± 41	272 ± 38
Ketoprofen	260 ± 64	269 ± 57	280 ± 47	263 ± 27
BMBT (s)				
Saline solution	134 ± 76	163 ± 80	123 ± 48	116 ± 36
Ketoprofen	135 ± 50	165 ± 64	139 ± 45	156 ± 53
Hct (%)				
Saline solution	42.2 ± 3.8	34.2 ± 2.7[a]	38.6 ± 3.5[a]	40.3 ± 3.7
Ketoprofen	41.6 ± 4.2	33.2 ± 2.3[a]	37.9 ± 3.9[a]	38.3 ± 3.5[a]
Hemoglobin (g/L)				
Saline solution	151 ± 12	121 ± 7[a]	137 ± 11[a]	144 ± 13
Ketoprofen	150 ± 15	117 ± 8[a]	135 ± 14[a]	138 ± 12[a]
RBC (× 10^{12}/L)				
Saline solution	6.31 ± 0.79	5.12 ± 0.64[a]	5.75 ± 0.79[a]	6.06 ± 0.83
Ketoprofen	6.19 ± 0.73	4.93 ± 0.38[a]	5.61 ± 0.73[a]	5.70 ± 0.63[a]
Plasma protein (g/L)				
Saline solution	61 ± 3	55 ± 4[a]	64 ± 4[a]	65 ± 3[a]
Ketoprofen	61 ± 3	55 ± 5[a]	63 ± 4	64 ± 4[a]

[a]Significantly ($P < 0.05$) different from preoperative value.

Table 2—Mean ± SD values for leukocyte indices in dogs that received ketoprofen or saline solution before elective ovariohysterectomy

		After surgery		
Variable	**Before surgery**	**0 h**	**12 h**	**24 h**
WBC (× 10^9/L)				
Saline solution	10.16 ± 2.72	5.57 ± 1.48[a]	15.63 ± 2.74[a]	13.04 ± 2.72[a]
Ketoprofen	10.64 ± 2.94	6.56 ± 1.74[a]	15.02 ± 4.60[a]	12.92 ± 3.77
Neutrophils (× 10^9/L)				
Saline solution	6.39 ± 2.55	3.58 ± 1.24[a]	12.62 ± 2.66[a]	9.69 ± 2.52[a]
Ketoprofen	7.03 ± 2.57	4.22 ± 1.53	11.97 ± 4.05[a]	9.44 ± 3.53
Eosinophils (× 10^9/L)				
Saline solution	0.57 ± 0.44	0.30 ± 0.26	0.16 ± 0.19[a]	0.43 ± 0.47
Ketoprofen	0.70 ± 0.65	0.38 ± 0.27	0.24 ± 0.28[a]	0.62 ± 0.55
Lymphocytes (× 10^9/L)				
Saline solution	2.55 ± 1.01	1.35 ± 0.58[a]	1.98 ± 0.88[a]	1.99 ± 0.98[a]
Ketoprofen	2.08 ± 1.35	1.33 ± 0.59	1.28 ± 0.42[a]	1.77 ± 1.03
Monocytes (× 10^9/L)				
Saline solution	0.64 ± 0.30	0.35 ± 0.27	0.82 ± 0.30	0.90 ± 0.30
Ketoprofen	0.83 ± 0.37	0.61 ± 0.17	1.03 ± 0.55	0.91 ± 0.47

[a]Significantly ($P < 0.05$) different from preoperative value.

Discussion

The most important finding of this study was that despite a decrease in WBPA, BMBT did not change after preoperative administration of ketoprofen in dogs that underwent elective ovariohysterectomy. These results are consistent with those reported for conscious dogs but differ from those reported for dogs that underwent orthopedic surgery. Mathews et al[6] reported that BMBT was unchanged 1, 4, 8, 24, and 48 hours after administration of ketoprofen to conscious dogs. Conversely, Grisneaux et al[5] reported that preoperative administration of ketoprofen to dogs undergoing orthopedic surgery increased BMBT from a preoperative value of approximately 180 seconds to intraoperative values of approximately 360 and 320 seconds. There are 2 limitations on the results of the latter study. First, the increase in BMBT is a subtle change, given the fact that values up to 300 seconds are considered within reference limits.[6] Second, these authors were not measuring the effect of administration of ketoprofen alone but were measuring the combined effect of administration of ketoprofen with a cephalosporin antibiotic. Administration of cephalosporin antibiotics before surgery inhibits WBPA and prolongs BMBT in dogs.[9] In the study by Grisneaux et al, all dogs were given cefazolin 30 minutes before the orthopedic procedure and then every 2 hours until completion of the procedure. Considering the effect of cephalosporin antibiotics on platelet function and the results of the study reported here, the conclusions reached by Grisneaux et al concerning the effect of ketoprofen on BMBT and potential for intraoperative hemorrhage should be reevaluated.

Forsyth et al[19] reported BMBT values after preoperative administration of saline solution or ketoprofen to dogs that underwent elective castration. Buccal mucosal bleeding time was determined after surgery, and a significant difference between treatments could not be detected. Furthermore, BMBT was not determined before surgery, which precludes assessment of the effects of surgery as well as those of preoperative ketoprofen administration. Considering the limitations imposed by the study design, results presented by Forsyth et al are difficult to interpret.

Preoperative administration of ketoprofen had no effect on erythrocyte indices during the 24-hour study period and did not increase the incidence of hemorrhage during or after surgery. Changes in both treatment groups were comparable to results from a previous study.[20] In that study, comparable anesthetic protocols were used, and ovariohysterectomies were performed by students, but samples for determination of erythrocyte indices were only collected before surgery and 24 hours after surgery. The authors reported that Hct, hemoglobin concentration, and erythrocyte count remained less than preoperative values 24 hours after surgery. In the study reported here, these variables were substantially less than preoperative values immediately after and 12 hours after surgery but were near preoperative values 24 hours after surgery. Discrepancies between the 2 studies may be attributable to differences in the duration of the procedures as well as the experience of the surgeon. Furthermore, in the study reported here, substantial hemorrhage was not observed during or after surgery in either group. Since substantial hemorrhage was not observed, decreases in Hct, hemoglobin concentration, and erythrocyte count, which were apparent immediately after surgery, were probably attributable to the combined effects of splenic sequestration of erythrocytes (secondary to thiopental administration), fluid shifts associated with decreases in blood pressure (secondary to acepromazine and isoflurane administration), and intraoperative fluid administration.

Preoperative administration of ketoprofen had no effect on leukocyte indices during the 24-hour study period, and apparently did not blunt the cellular stress response to surgical trauma. Changes in leukocyte indices observed in the study reported here are typical of the stress response to surgery and develop secondary to tissue trauma and increases in cortisol concentrations.[21,22] Changes in both groups were comparable to results from a previous study.[20] Again, comparable protocols and procedures were used, but samples for determination of leukocyte indices were only collected before surgery and 24 hours after surgery. The authors reported a mild leukocytosis with a concurrent neutrophilia, lymphopenia, and eosinopenia. In the study reported here, generalized leukopenia was detected immediately after surgery and became mild leukocytosis with concurrent neutrophilia, lymphopenia, and eosinopenia 12 hours after surgery.

Two important issues concerning preoperative administration of ketoprofen are not specifically addressed by the study reported here. First, perioperative administration of NSAIA drugs may interfere with renal blood flow and effective tubular function if circulating blood volume is reduced.[12,13] Typically, prostaglandins help maintain renal blood flow during hypovolemia or hypotension. Preoperative administration of NSAIA drugs may potentiate renal ischemia and interfere with tubular function in anesthetized animals, especially in those with preexisting renal disease.[16,23] Second, preoperative or preemptive administration of ketoprofen has not been shown to be more effective, in terms of postoperative analgesia, than administration of ketoprofen immediately after recovery from anesthesia.[12,13]

Preoperative administration of ketoprofen inhibited WBPA but did not alter BMBT or hematologic indices in dogs after elective ovariohysterectomy. Ketoprofen can be given before surgery to healthy dogs undergoing elective ovariohysterectomy, provided that the dogs are screened for potential bleeding problems before surgery and monitored closely after surgery.

[a]Chrono-par, Chrono-log, Havertown, Pa.
[b]Simplate II, Organon Teknika, Jessup, Md.
[c]Cell-Dyne 3500, Abbott Laboratories, Abbott Park, Ill.
[d]Reichert TS Meter, VWR Canlab, Montreal, QC, Canada.
[e]Anafen, Merial, Victoriaville, QC, Canada.
[f]Glycopyrrolate, Sabex, Voucherville, QC, Canada.
[g]Atravet, Wyest-Ayerst Canada, St Laurent, QC, Canada.
[h]Torbugesic, Wyest-Ayerst Canada, St Laurent, QC, Canada.
[i]Pentothal, Abbott Laboratories, Montreal, QC, Canada.
[j]Isoflo, Abbott Laboratories, Montreal, QC, Canada.

References

1. Schafer AI. Effects of nonsteroidal antiinflammatory drugs on platelet function and systemic hemostasis. *J Clin Pharmacol* 1995; 35:209–219.
2. Kay-Mugford PA, Benn SJ, LaMarre J, et al. Cyclooxygenase expression in canine platelets and Madin-Darby canine kidney cells. *Am J Vet Res* 2000;61:1512–1516.
3. Jones CJ, Budsberg SC. Physiologic characteristics and clinical importance of the cyclooxygenase isoforms in dogs and cats. *J Am Vet Med Assoc* 2000;217:721–729.
4. Ricketts AP, Lundy KM, Seibel SB. Evaluation of selective inhibition of canine cyclooxygenase 1 and 2 by carprofen and other nonsteroidal anti-inflammatory drugs. *Am J Vet Res* 1998;59: 1441–1446.
5. Grisneaux E, Pibarot P, Dupuis J, et al. Comparison of ketoprofen and carprofen administered prior to orthopedic surgery for control of postoperative pain in dogs. *J Am Vet Med Assoc* 1999;215: 1105–1110.
6. Mathews KA, Pettifer G, Foster R, et al. Safety and efficacy of preoperative administration of meloxicam, compared with that of

ketoprofen and butorphanol in dogs undergoing abdominal surgery. *Am J Vet Res* 2001;62:882–888.

7. Jackson ML, Searcy GP, Olexson DW. The effect of oral phenylbutazone on whole blood platelet aggregation in the dog. *Can J Comp Med* 1985;49:271–277.

8. Barr SC, Ludders JW, Looney AL, et al. Platelet aggregation in dogs after sedation with acepromazine and atropine and during subsequent general anesthesia and surgery. *Am J Vet Res* 1992;53: 2067–2070.

9. Schermerhorn T, Barr SC, Stoffregen DA, et al. Whole-blood platelet aggregation, buccal mucosa bleeding time, and serum cephalothin concentration in dogs receiving a presurgical antibiotic protocol. *Am J Vet Res* 1994;55:1602–1607.

10. Cardinal DC, Flower RJ. The electronic aggregometer: a novel device for assessing platelet behavior in blood. *J Pharmacol Methods* 1980;3:135–158.

11. Nicholson NS, Panzer-Knodle SG, Haas NF, et al. Assessment of platelet function assays. *Am Heart J* 1998;135: S170–S178.

12. Dahl JB, Kehlet H. Non-steroidal anti-inflammatory drugs: rationale for use in severe postoperative pain. *Br J Anaesth* 1991;66: 703–712.

13. Souter AJ, Fredman B, White PF. Controversies in the perioperative use of nonsteroidal antiinflammatory drugs. *Anesth Analg* 1994;79:1178–1190.

14. Mathews KA. Nonsteroidal antiinflammatory analgesics: indications and contraindications for pain management in dogs and cats. *Vet Clin North Am Small Anim Pract* 2000;30:783–804.

15. Pascoe PJ. Perioperative pain management. *Vet Clin North Am Small Anim Pract* 2000;30:917–932.

16. Forrester SD, Troy GC. Renal effects of nonsteroidal antiinflammatory drugs. *Compend Contin Educ Pract Vet* 1999;21:910–919.

17. Jergens AE, Turrentine MA, Kraus KH, et al. Buccal mucosa bleeding times of healthy dogs and of dogs in various pathologic states, including thrombocytopenia, uremia, and von Willebrand's disease. *Am J Vet Res* 1987;48:1337–1342.

18. Tvedten H, Grabski S, Frame L. Estimating platelets and leukocytes on canine blood smears. *Vet Clin Pathol* 1988;17:4–6.

19. Forsyth SF, Guilford WG, Pfeiffer DU. Effect of NSAID administration on creatinine clearance in healthy dogs undergoing anaesthesia and surgery. *J Small Anim Pract* 2000;41:547–550.

20. Millis DL, Hauptman JG, Richter M. Preoperative and postoperative hemostatic profiles of dogs undergoing ovariohysterectomy. *Cornell Vet* 1992;82:465–470.

21. Schalm OW, Jain NC, Carroll EJ. Normal values in blood morphology. In: Schalm OW, Jain NC, Carroll EJ, eds. *Veterinary hematology.* Philadelphia: Lea & Febiger, 1975;95–99.

22. Breazile JE. Physiologic basis and consequences of distress in animals. *J Am Vet Med Assoc* 1987;191:1212–1215.

23. Lobetti RG, Joubert KE. Effect of administration of nonsteroidal anti-inflammatory drugs before surgery on renal function in clinically normal dogs. *Am J Vet Res* 2000;61:1501–1507.

Correction: Use of prostaglandins and bromocriptine mesylate for pregnancy termination in bitches

In the appendix of the article "Use of prostaglandins and bromocriptine mesylate for pregnancy termination in bitches" (*JAVMA*, April 1, 2002, pp 1019), the unit of measure indicated for dinoprost tromethamine administration is incorrectly listed as µg/kg. The correct unit of measure is mg/kg. The appendix should read as follows:

Appendix

Dosage protocols for termination of pregnancy in group-1 and group-2 dogs

	Group 1 (n = 12)		Group 2 (n = 13)	
Days	Bromocriptine mesylate (PO, q 12 h)*	Dinoprost tromethamine (SC, q 24 h)†	Bromocriptine mesylate (PO, q 12 h)*	Cloprostenol sodium (SC, q 48 h)†
1	15 µg/kg (7.5 µg/lb)	0.1 mg/kg (0.05 µg/lb)	15 µg/kg (7.5 µg/lb)	1 µg/kg (0.5 µg/lb)
2	20 µg/kg (10 µg/lb)	0.15 mg/kg (0.07 µg/lb)	20 µg/kg (10 µg/lb)	None
3	20 µg/kg (10 µg/lb)	0.2 mg/kg (0.1 µg/lb)	20 µg/kg (10 µg/lb)	1 µg/kg (0.5 µg/lb)
Remaining	30 µg/kg (15 µg/lb)	0.2 mg/kg (0.1 µg/lb)	30 µg/kg (15 µg/lb)	1 µg/kg (0.5 µg/lb)

*Administered orally with food at feeding time. †Administered subcutaneously as far from feeding time as possible.