Evaluation of a modified infraorbital approach for a maxillary nerve block for rhinoscopy with nasal biopsy of dogs

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OBJECTIVE
To determine whether a maxillary nerve block via a modified infraorbital approach, applied before rhinoscopy and nasal biopsy of dogs, would decrease procedural nociception, minimize cardiorespiratory anesthetic effects, and improve recovery quality.

ANIMALS
8 healthy adult hound-type dogs

PROCEDURES
In a crossover study, dogs received 0.5% bupivacaine (0.1 mL/kg) or an equivalent volume of saline (0.9% NaCl) solution as a maxillary nerve block via a modified infraorbital approach. A 5-cm, 20-gauge over-the-needle catheter was placed retrograde within each infraorbital canal, and bupivacaine or saline solution was administered into each pterygopalatine region. Rhinoscopy and nasal biopsy were performed. Variables monitored included heart rate, systolic arterial blood pressure (SAP), mean arterial blood pressure (MAP), diastolic arterial blood pressure (DAP), plasma cortisol and norepinephrine concentrations, purposeful movement, and pain scores. After a 14-day washout period, the other treatment was administered on the contralateral side, and rhinoscopy and nasal biopsy were repeated.

RESULTS
SAP, MAP, and DAP were significantly higher for the saline solution treatment than for the bupivacaine treatment, irrespective of the time point. Plasma cortisol concentrations after saline solution treatment were significantly higher 5 minutes after nasal biopsy than at biopsy. Heart rate, norepinephrine concentration, purposeful movement, and pain score were not significantly different between treatments.

CONCLUSIONS AND CLINICAL RELEVANCE
Maxillary nerve block via a modified infraorbital approach prior to rhinoscopy and nasal biopsy reduced procedural nociception as determined on the basis of blood pressures and plasma cortisol concentrations during anesthesia. These findings warrant further evaluation in dogs with nasal disease. (Am J Vet Res 2017;78:1025–1035)

Rhinoscopy with concurrent nasal biopsy is considered to be a core component for investigation of nasal disease of dogs.1 To the authors’ knowledge, there is not a simple and effective method that provides regional anesthesia to the nasal cavity for rhinoscopy and biopsy. Sudden periods of arousal during rhinoscopy and nasal biopsy are often observed clinically and can be associated with movements such as sneezing, head shaking, and chewing. These movements have potential to cause injury to patients and damage to endoscopy equipment. To decrease the likelihood of movement, rhinoscopy patients are often maintained at a deep plane of anesthesia, which causes dose-dependent cardiorespiratory depression that can lead to hypotension and apnea.2–5 Use of multimodal anesthesia, including local anesthetics for a local or regional nerve block, may help to decrease the amount of inhalation anesthetics required, thereby decreasing the severity of complications associated with a deep plane of anesthesia.6–9

Providing regional antinociception to the nasal cavity and corresponding structures is challenging because of the complexity of innervation to the face and nose. Knowledge of the anatomy of these nerves is needed to safely and effectively provide regional antinociception. A comparison of percutaneous maxillary nerve blocks and infraorbital nerve blocks in dogs undergoing rhinoscopy revealed that the maxillary nerve block is superior to the infraorbital block for preventing adverse reactions during rhinoscopy.

ABBREVIATIONS
DAP Diastolic arterial blood pressure
MAP Mean arterial blood pressure
SAP Systolic arterial blood pressure
VAS Visual analog scale
of the caudal portion of the nasopharynx.\textsuperscript{10} However, some authors believe that the infraorbital approach is more successful than the percutaneous approach for maxillary nerve blocks when performed by inexperienced anesthetists\textsuperscript{11} and that the percutaneous approach is more difficult to perform because of its anatomic location.\textsuperscript{10} Modifying an infraorbital approach to the maxillary nerve, similar to the procedure performed in canine cadavers,\textsuperscript{11} could offer an alternative, simple method for approaching the maxillary nerve with a higher rate of success than for the traditional percutaneous approach.

The trigeminal nerve and its branches provide innervation (motor, sensory, and autonomic) to the face and nose and course through the pterygopalatine fossa. The maxillary branch of the trigeminal nerve provides sensory innervation to the nose, mucosa of the hard and soft palates, nasal vestibule, and choana via the pterygopalatine, greater palatine, lesser palatine, and caudal nasal nerves, respectively.\textsuperscript{12,13} The ophthalmic branch of the trigeminal nerve innervates most of the internal structures of the nose, including the nasal turbinates, septum and lateral walls of the nasal cavity, and portions of the nasal mucosa, and external structures of the eyes.\textsuperscript{14,15} The ophthalmic nerve of dogs is in an anatomic location that is difficult and dangerous to approach; thus, a simple approach that provides access to the maxillary nerve branches (which would partially desensitize the nasal cavity) is necessary to provide antinociception for nasal procedures such as rhinoscopy and biopsy.

The objectives of the study reported here were to investigate the feasibility of a modified infraorbital approach for a maxillary nerve block during a preliminary experiment with canine cadavers, then to conduct an in vivo study to assess the effectiveness of the modified infraorbital approach for a maxillary nerve block in dogs undergoing rhinoscopy and nasal biopsy. We hypothesized that dogs administered local anesthetic in the pterygopalatine fossa via this maxillary nerve block technique would have better anesthetic outcomes, decreased procedural nociception, and smoother recovery (as indicated by better stability of vital parameters, fewer purposeful movements, lower plasma concentrations of stress biomarkers, and lower pain scores during the recovery period), compared with results for a nonanesthetic control treatment.

**Materials and Methods**

**Animals**

Cadavers of 3 hound-type dogs were used in a preliminary experiment. Dogs were euthanized\textsuperscript{6} for reasons unrelated to the present study at the conclusion of a teaching laboratory.

Eight healthy adult (age range, 1 to 2 years) purpose-bred hound-type dogs were used in an in vivo experiment. There were 4 spayed females, 3 sexually intact females, and 1 sexually intact male. Mean ± SD body weight was 21.7 ± 2.1 kg. The dogs were deemed healthy on the basis of results of physical examination, serum biochemical analysis, and a heartworm test and evaluation of platelet count, prothrombin time, activated partial thromboplastin time, PCV, and total solids concentrations. All dogs were American Society of Anesthesiologists physical status class I. The study was approved by the Institutional Animal Care and Use Committee at the Mississippi State University College of Veterinary Medicine.

**Cadaver experiment**

An infraorbital approach to the maxillary nerve described in another study\textsuperscript{11} was replicated in each canine cadaver. A slight modification of the procedure (adjustment of the distance the catheter was inserted through the infraorbital canal into the pterygopalatine fossa) was used to determine the best method for a maxillary nerve block via the modified infraorbital approach to maximize delivery of local anesthetic to the maxillary nerve and its branches within the pterygopalatine fossa. A 1% solution of methylene blue stain\textsuperscript{6} was injected into the pterygopalatine fossa; volume of injectate was 1, 1.5, and 3 mL as determined on the basis of published regional techniques that involved the use of 0.5% bupivacaine.\textsuperscript{16} The stained and contralateral unstained pterygopalatine fossa were carefully dissected, and tissues were evaluated to detect trauma to the nerves or surrounding tissues as well as the degree of staining for each of the nerves.

**In vivo experiment**

**Experimental design**—A blinded, placebo-controlled, crossover study was performed. Each dog was randomly assigned (by a veterinary anesthesia technician who chose every other dog from a list) to receive 0.5% bupivacaine (0.1 mL/kg) or an equivalent volume of saline (0.9% NaCl) solution as a maxillary nerve block via the modified infraorbital approach. After a 14-day washout period, each dog received the alternate treatment on the contralateral side.

The number of dogs in the study was determined by use of a power analysis. It was assumed 4 dogs would be randomly assigned to initially receive the bupivacaine treatment and the saline solution treatment in a crossover design whereby differences in mean changes from baseline values for the various outcomes would be assessed with a paired \textit{t} test. Estimates of the variation anticipated for bupivacaine and saline solution treatments were based on published values for a similar study\textsuperscript{10} that was conducted to compare responses of dogs with maxillary nerve blocks with those of control dogs. The SDs reported in that study\textsuperscript{10} for control dogs for changes in heart rate (6 beats/min) and MAP (5 mm Hg) and for dogs with maxillary nerve blocks for changes in heart rate (6 beats/min) and MAP (4 mm Hg) were used in the power calculations for the study reported here. For \(\alpha = 0.05\), correlation between paired measures within a dog = 0.5, and a 1-tailed test, those SDs were used to estimate power of the study by use of available software.\textsuperscript{17c} The 8 pairs of samples would allow de-
tection of a difference in heart rate of 6 beats/min (power, 0.82) and a difference in the change in MAP of 4.5 mm Hg (power, 0.80).

Anesthesia—Food, but not water, was withheld for 12 hours before induction of anesthesia. Dogs were premedicated with acepromazine maleate\(^a\) (0.01 mg/kg, IM) and hydromorphone\(^e\) (0.1 mg/kg, IM). Twenty minutes after administration of the premedication, an 18-gauge, 5-cm catheter\(^d\) was placed in a cephalic vein. Anesthesia was induced with propofol\(^b\) (2 to 4 mg/kg, IV, to effect), dogs were endotracheally intubated, and anesthesia was maintained with isoflurane\(^h\) (calibrated vaporizer setting of 1.5 vol\%) in oxygen (1.5 L/min) by use of a partial rebreathing circuit to achieve a surgical plane of anesthesia, as evaluated by jaw tone, palpebral reflex, and eye position. Dogs were mechanically ventilated\(^l\) to maintain end-tidal partial pressure of CO\(_2\) of 35 to 45 mm Hg. Vital parameters were monitored by use of a multiparametric monitor\(^o\) and gas analyzer.\(^j\) Oscillometric blood pressures were monitored by use of an appropriately sized cuff placed on a forelimb. A 20-gauge, 3.2-cm catheter\(^d\) was placed in a dorsal pedal artery, or an 18-gauge, 5-cm catheter\(^d\) was placed in a lateral saphenous vein; catheters were used for collection of blood samples that were assayed to determine plasma cortisol and norepinephrine concentrations. A forced-air warming device\(^m\) was used to maintain body temperature between 37.2° and 38.3°C. Lactated Ringer solution\(^n\) was administered (5 mL/kg/h, IV). Heart rate, SAP, MAP, and DAP were manually recorded by the same 2 investigators (KMF and L-HK) every 5 minutes during anesthesia as well as immediately before the start of rhinoscopy (baseline), at the time of retroflexion of the endoscope in the caudal portion of the nasopharynx, at the time of nasal biopsy, 5 minutes after biopsy, and 10 minutes after biopsy. Atropine\(^e\) (0.02 mg/kg, IV) was administered as needed to resolve substantial bradycardia associated with hypotension (MAP < 60 mm Hg). Dogs that had purposeful movement (paddling, head shaking, chewing, or licking) that interfered with procedures received additional propofol (0.5 mg/kg, IV).

Maxillary nerve block via a modified infraorbital approach—The location of the infraorbital canal was determined as a small indentation dorsal to the third premolar tooth that was palpable through the oral mucosa. A 20-gauge, 5-cm over-the-needle catheter\(^d\) was placed in the infraorbital canal parallel to the maxilla and directed caudally (Figure 1). The catheter was inserted to a depth of 5 mm, after which the cannula was withdrawn until the end was just within the tip of the catheter. The catheter and cannula then were advanced until the hub of the catheter touched the gingiva or resistance was encountered, whichever came first. Once the catheter was securely within the infraorbital canal, the cannula was removed. Either 0.5% bupivacaine\(^e\) (0.5 mg/kg [0.1 mL/kg]) or an equivalent volume of saline solution\(^p\) was placed in a 3-mL syringe\(^q\) and injected into the infraorbital canal. The syringe was attached to the catheter, aspiration was performed, and if no blood was aspirated, the solution was slowly injected. If there was resistance to injection, the catheter was repositioned 2 to 3 mm to ensure it was not within the perineurium or another vital structure and aspiration was performed, and if no blood was aspirated, the volume was slowly injected. All regional nerve blocks were performed by the same investigator (KMF).

Rhinoscopy and biopsy—Dogs were allowed to remain undisturbed in sternal recumbency for 30 minutes after the maxillary nerve block to enable the local anesthetic to take effect.\(^20\) Standard rhinoscopy with nasal mucosal biopsy then was performed on the left side of the nose. An initial evaluation of the caudal portion of the nasopharynx was performed by retroflexion with a standard pediatric gastroscope.\(^5\) Direct examination of the nasal mucosa and turbinates then was performed by use of a rigid endoscope\(^e\) passed through the rostral aspect of the nares. A single pinch biopsy specimen of tissues of the nasal cavity was blindly obtained from the left side of the nose by use of an 8-mm biopsy instrument,\(^l\) placed in neutral-buffered 10% formalin,\(^a\) and submitted for histologic examination. All rhinoscopy and biopsy procedures were performed by the same investigator (TMA).
Dogs remained anesthetized until postbiopsy blood samples were obtained and bleeding from the biopsy site was controlled. After each dog had a 14-day washout period, the procedures were repeated on the right side of the nose but with injection of the alternate treatment solution for the maxillary nerve block.

**Anesthetic recovery and postoperative pain scores**—All dogs recovered from anesthesia in the intensive care unit. Vital parameters (heart rate, respiratory rate, and rectal temperature) were monitored until dogs were extubated and able to maintain sternal recumbency. Postoperative pain scores were obtained by use of the Glasgow Composite Pain Scale—Short Form (scale, 0 to 24), a VAS1 with a 10-cm scale, and the Colorado State University Canine Acute Pain Scale2 (scale, 0 to 4). Pain scores and vital parameters were recorded after extubation and 1, 2, 3, and 4 hours thereafter. Hydromorphone1 (0.1 mg/kg, IV) was used for postoperative rescue analgesia if dogs had a score > 6 of 20 or 8 of 24 for the Glasgow Composite Pain Scale—Short Form, ≥ 3 cm for the VAS, or ≥ 3 for the Colorado State University Canine Acute Pain Scale. All postoperative pain scores were assigned by 1 of 2 investigators (KMF and BET).

**Collection of blood samples**—A blood sample (3 mL) was collected immediately before the start of rhinoscopy (baseline), at the time of retroflexion of the endoscope in the caudal portion of the nasopharynx, at the time of biopsy, 5 minutes after biopsy, and 10 minutes after biopsy. Blood samples (10 arterial and 6 venous) were placed in EDTA-containing blood collection tubes.3 Plasma was harvested, and 500 µL of plasma was mixed with 25 µL of 70% perchloric acid4 and frozen at −80°C until analyzed to determine cortisol and norepinephrine concentrations.

**Cortisol analysis**—Frozen plasma samples were allowed to thaw at room temperature (20°C). Atraize mercapturate5 was added as an internal standard (final concentration, 1µM). Samples were mixed on a vortex device, placed on ice, and then centrifuged (1,300 X g at 4°C for 15 minutes) to remove protein precipitate. Supernatant was transferred to high-performance liquid chromatography vials. Samples were analyzed for cortisol by use of liquid chromatography–mass spectrometry6 as described elsewhere.7 A stock solution of cortisol (5µM) was prepared in methanol7 and used to create calibration standards in PBS solution. Concentration of calibration standards ranged from 0.1 to 100 nM. New calibration standards were prepared for each set of unknown samples. Each calibration curve yielded comparable results ($r^2 > 0.990$). The limit of quantification for cortisol was estimated as 0.25 nM.8

**Norepinephrine analysis**—Frozen plasma samples were allowed to thaw at room temperature (20°C). A 1M tris solution containing 25 ng of 3,4-dihydroxybenzylamine9 was added as an internal standard. Samples were centrifuged (1,300 X g at 4°C for 20 minutes), and then centrifugation was repeated without disruption of the pellet. The supernatant was transferred to microtubes containing 5 g of aluminum oxide10 and 500 µL of the tris–3,4-dihydroxybenzylamine solution. Samples were shaken for 30 minutes and then centrifuged (1,300 X g for 30 seconds), and the supernatant was discarded. The pellet was washed with 500 µL of reverse-osmosis water and then centrifuged (1,300 X g for 30 seconds), and the supernatant was discarded. Washing was repeated, after which the pellet was retrieved and 200 µL of 100mM citric acid11 was added. The sample was shaken for 15 minutes and then centrifuged (1,300 X g for 30 seconds), and the supernatant was harvested and analyzed. Supernatants were injected into a high-performance liquid chromatography system with an electrochemical detector12–15 by use of a mobile phase of 100mM phosphate,16 17.5% methanol,17 25µM EDTA,18 and 1mM octyl sulfate19 (pH, 3.65). The quantity of each compound was determined by comparison with known concentrations in standards of norepinephrine.9 Concentration of calibration standards ranged from 0.1 to 100 ng/µL. New calibration standards were prepared for each set of unknown samples. Each calibration curve yielded comparable results ($r^2 > 0.990$). The limit of quantification was not evaluated because all data points were within limits of the calibration standard curve.

**Histologic examination of nasal biopsy specimens**—Formalin-fixed nasal biopsy specimens were routinely processed, embedded in paraffin, and sectioned at a thickness of 5 µm. Slides were stained with H&E stain for evaluation. All histologic changes were evaluated by the same investigator (AKO). The degree of lymphoplasmacytic inflammation was scored on a scale of 0 to 3 as follows: 0 = no inflammation, 1 = mild inflammation, 2 = moderate inflammation, and 3 = severe inflammation. At least four 20X fields were evaluated for each specimen.

**Statistical analysis**—Separate linear mixed models20 were fit for heart rate, SAP, MAP, DAP, plasma cortisol concentration, plasma norepinephrine concentration, and the Glasgow Composite Pain Scale—Short Form score. First or second anesthetic event (run), order of treatment (sequence), treatment, time point, histologic score, treatment-by-time point interaction, and treatment-by-histologic score interaction were included as fixed effects with a Kenward-Rogers degrees of freedom method. Baseline measurement was also included in the model as a covariate to adjust for variation in the results among dogs prior to the start of rhinoscopy; consequently, time point included retroflexion, biopsy, 5 minutes after biopsy, and 10 minutes after biopsy. Dog was included as a random effect with a variance component covari-
ance structure. Repeated measures of dog within run for the various time points were specified in a repeated statement with an autoregressive 1-covariance structure. When sequence or run was not significant, it was sequentially removed from the model. Treatment-by-histologic score interaction, histologic score, or treatment-by-time point interaction was also removed when it was not significant. Treatment and time point were the variables of greatest interest and remained in the model regardless of significance. Differences in least squares means were determined for outcomes with significant effects. The P values were adjusted to account for multiple comparisons by use of a simulation option, which was used to estimate the critical value while incorporating the correlation structure of the model and can be an effective method for multiple comparisons for mixed models. In the case of a significant effect for the treatment-by-time point interaction, differences in least squares means between treatments were determined at each time point and among time points within each treatment by use of an estimation statement with a simulation adjustment for multiple comparisons. Distribution of the conditional residuals was evaluated for each outcome to ensure assumptions of the statistical model had been met.

Purposeful movement and Colorado State University Canine Acute Pain Scale scores were dichotomized (absent or present); VAS scores also were dichotomized (absent was ≤ 1 cm and present was > 1 cm). After dichotomization was performed, logistic regression by use of a separate generalized linear mixed model was fit for purposeful movement, Colorado State University Canine Acute Pain Scale scores, and VAS scores. Run, sequence, histologic score, and treatment were included as fixed effects. Dog was included as a random effect with a variance component covariance structure. When sequence or run was not significant, it was sequentially removed from the model. Histologic score was also removed if not significant. Values of P < 0.05 were considered significant. All data were described as mean ± SEM.

Statistical analysis of histologic results was evaluated by use of the Mann-Whitney U test. One dog was excluded from the histologic analysis because it was considered an outlier that would have skewed the results. Values of P < 0.05 were considered significant.

Results

Cadaver experiment

Results of the cadaver experiment indicated that for use of a modified infraorbital approach to the maxillary nerve block, 3 mL of methylene blue was required to stain all branches of the maxillary nerve within the pterygopalatine fossa, including the zygomatic, pterygopalatine, greater palatine, lesser palatine, caudal nasal, infraorbital, and superior alveolar nerves (Figure 2). Smaller volumes did not penetrate all the nerves. A volume of 3 mL was equivalent to 0.5 mg of 0.5% bupivacaine/kg (0.1 mL/kg) injected into each pterygopalatine fossa. Gross trauma to the nerves or surrounding structures within the infraorbital canal or pterygopalatine fossa was not detected. All nerves had > 6 mm of staining, which indicated that a complete nerve block would have resulted from the use of a 3-mL volume of local anesthetic; thus, approximately 3 mL of injectate was used for the in vivo experiment (adjusted to a volume of 0.1 mL/kg for each nerve block).

In vivo experiment

Fixed effects of sequence, run, histologic score, treatment-by-histologic score interaction, and treatment-by-time point interaction were not significant and removed from the models for SAP, MAP, heart rate, and norepinephrine concentration; treatment and time point remained in the models as fixed effects regardless of significance. The baseline value for each outcome was included in the models regardless of significance to act as a covariate to control for differences in baseline values among dogs.

Compared with results for saline solution, bupivacaine had a significant effect on blood pressures across all time points from retroflexion to 10 minutes after biopsy when the model was adjusted for baseline values (Figure 3). Bupivacaine and saline solution differed significantly with regard to mean ± SEM SAP (103 ± 2 mm Hg and 117 ± 3 mm Hg, respectively [P = 0.005]), MAP (74 ± 2 mm Hg and 93 ± 4 mm Hg, respectively [P = 0.019]), and DAP (59 ± 2 mm Hg and 81 ± 4 mm Hg, respectively [P = 0.024]). There was no significant effect of time point on SAP (P = 0.864), MAP (P = 0.542), or DAP (P = 0.788). Baseline values for each outcome were significant (all P < 0.014) in their respective models, which indicated there was variation among dogs prior to the start of rhinoscopy.

Figure 2—Photograph of structures in the right pterygopalatine fossa following injection of 3 mL of methylene blue via a 20-gauge, 5-cm over-the-needle catheter placed into the pterygopalatine fossa through the infraorbital canal by use of a modified infraorbital approach for a maxillary nerve block. There is complete staining of the maxillary nerve and its branches. Notice the maxillary nerve (m), infraorbital nerve (i), greater palatine nerve (g), pterygopalatine nerve (p), caudal nasal nerve (c), lesser palatine nerve (l), and tip of the catheter (t).
for each outcome. Including the baseline values in the model accounted for this source of variation.

Treatment did not have a significant \( (P = 0.056) \) effect on heart rate; however, there was a significant \( (P < 0.001) \) effect of time point on heart rate, when adjusted for the effect of treatment and baseline values (Figure 3). Mean \( \pm \) SEM heart rate was significantly higher at biopsy (94 \( \pm \) 5 beats/min) than at retroflexion (81 \( \pm \) 5 beats/min \( [P < 0.001]) \), 5 minutes after biopsy (84 \( \pm \) 4 beats/min \( [P < 0.001]) \), and 10 minutes after biopsy (84 \( \pm \) 4 beats/min \( [P = 0.013]) \). Three dogs (1 after administration of saline solution and 2 after administration of bupivacaine) received atropine, though there were no significant differences in heart rate between the dogs receiving atropine and untreated dogs. Significant \( (P < 0.001) \) variation in baseline heart rate among the dogs before the start of rhinoscopy was accounted for by inclusion in the model.

The treatment-by-time point interaction had a significant \( (P = 0.038) \) effect on plasma cortisol concentration (Figure 4). Mean \( \pm \) SEM plasma cortisol concentration increased significantly \( (P = 0.006) \) from biopsy (8.3 \( \pm \) 1.6nM) to 5 minutes after biopsy (17.8 \( \pm \) 4.7nM) for the saline solution treatment. There was a similar, but not significant \( (P = 0.055) \), increase between biopsy and 10 minutes after biopsy (17.8 \( \pm \) 5.4nM) for the saline solution treatment. No other significant differences were detected among time points within the saline solution treatment \( (all \ P > 0.157) \), among time points within the bupivacaine treatment \( (all \ P > 0.997) \), or between bupivacaine and saline solution treatments at any time point \( (all \ P > 0.212) \). Plasma norepinephrine concentrations did not differ significantly between bupivacaine and saline solution \( (P = 0.212) \) or among time points \( (P = 0.783) \).

In regard to clinical evaluation of dogs during rhinoscopy and nasal biopsy, 4 of 8 dogs had purposeful movement at least once during the procedure when injected with saline solution, whereas only 2 of 8 dogs had purposeful movement when injected with bupivacaine, but these proportions did not differ significantly \( (P = 1.00) \). The Glasgow Composite Pain Scale–Short Form scores for all dogs ranged from 0 to

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**Figure 3**—Mean \( \pm \) SEM values for SAP (A), MAP (B), DAP (C), and heart rate (D) for 8 dogs that underwent rhinoscopy and nasal biopsy after receiving a maxillary nerve block via a modified infratrochlear approach with 0.5% bupivacaine (gray bars) and an equivalent volume of saline (0.9% NaCl) solution (white bars). There was a 14-day washout period between treatments. Blood samples and recording of blood pressure and heart rate were performed immediately before the start of rhinoscopy (Baseline), at the time of retroflexion of the endoscope in the caudal portion of the nasopharynx (Retro), at the time of nasal biopsy (NB), 5 minutes after nasal biopsy (NB + 5), and 10 minutes after nasal biopsy (NB + 10).
there was no significant ($P = 0.24$) difference between scores for the saline solution and bupivacaine treatments. Seven of 8 dogs had a score $\geq 1$ (range, 0 to 2) for the Colorado State University Canine Acute Pain Scale when receiving saline solution, whereas 5 of 8 dogs had a score $\geq 1$ (range, 0 to 2) when receiving bupivacaine; these proportions did not differ significantly ($P = 0.264$). Three of 8 dogs had a VAS score $> 1$ cm (range, 0 to 5 cm) when receiving saline solution, whereas 1 of 8 dogs had a VAS score $> 1$ cm (range, 0 to 5 cm); these proportions did not differ significantly ($P = 0.264$). One dog required postoperative analgesia immediately after extubation when receiving bupivacaine (Glasgow Composite Pain Scale–Short Form score, 11/24; VAS score, 5 cm). No other dogs in the study required postoperative analgesia.

Histologic examination of the nasal biopsy specimens revealed that all dogs had mild to severe lymphoplasmacytic inflammation in the lamina propria. Six dogs had the same inflammation score on both sides, 1 dog had a higher score for the side when saline solution was administered, and 1 dog had a chondrosarcoma for the side when saline solution was administered. There was not a significant ($P = 0.65$) difference in the degree of inflammation between the 2 treatments.

**Discussion**

Use of the infraorbital canal to approach the maxillary nerve in the pterygopalatine fossa for administration of local anesthetic in healthy dogs undergoing rhinoscopy and nasal biopsy was associated with relatively limited changes, compared with results after the administration of saline solution. Significant differences between bupivacaine and saline solution were detected for several variables, including SAP, MAP, and DAP, when time point and baseline values were controlled for in the model. Significant changes in plasma cortisol concentrations were detected when results at biopsy were compared with results at 5 minutes after biopsy within the saline solution treatment. Similar, but not significant, changes were seen between results at biopsy versus results at 10 minutes after biopsy within the saline solution treatment. There was no significant difference between the treatments for heart rate, plasma norepinephrine concentration, purposeful movement, or postoperative pain scores. There also was no subjective clinical difference between treatments during the anesthetic or recovery periods.

In a recent study, a transorbital approach to the maxillary nerve was evaluated and compared with a

![Figure 4](image-url)

*Figure 4—Mean ± SEM values for plasma concentrations of cortisol (A) and norepinephrine (B) for 8 dogs that underwent rhinoscopy and nasal biopsy after receiving a maxillary nerve block via a modified infraorbital approach with 0.5% bupivacaine (gray bars) and an equivalent volume of saline solution (white bars). See Figure 3 for remainder of key.*
traditional percutaneous approach to the maxillary nerve. This transorbital approach, which is much more similar to maxillary nerve blocks performed in humans, can also be difficult for inexperienced anesthetists to use and can be associated with additional complications. A modified infraorbital approach to the maxillary nerve can be performed by inexperienced anesthetists, without concerns about globe rupture, maxillary artery puncture, or ocular-cardiac reflex. Both approaches, with the addition of a modified infraorbital approach to the maxillary nerve block, can provide desensitization to portions of the nasal cavity, although a modified infraorbital approach may be easier for inexperienced anesthetists to use.

In humans, maxillary nerve blocks are used for facial and nasal procedures in sedated and anesthetized patients, to help minimize anesthetic complications, and to decrease postoperative pain. The maxillary nerve and its branches are easily approached in many nerve block methods in humans. Many of these nerve block methods are similar to those performed in dogs, but the anatomic orientation of the human nose and face differs from those of dogs. The close proximity of the maxillary and ophthalmic branches to each other in humans allows for local anesthetic to travel between these nerves, likely partially blocking the ophthalmic nerve when a maxillary or infraorbital nerve block is performed. Studies in pediatric human patients have revealed a decreased opioid requirement and improved postoperative pain score when comparing maxillary blocks with a placebo, and similar results have been seen in adult patients undergoing nasal procedures who received infraorbital nerve blocks. In these same studies, 1 to 3 mL of local anesthetic was administered to adults and 0.15 mL/kg was administered to pediatric patients, which are volumes comparable to those used in dogs in the study reported here. In the present study, a modified infraorbital approach to the maxillary nerve block was tested only in mesaticephalic hound-type dogs. Use of this nerve block technique in brachycephalic dogs or in other species (eg, cats) with shorter trigeminal nerve branches has the potential to provide better antinociception. In those animals, a shorter distance for diffusion of the local anesthetic along the maxillary nerve to reach the ophthalmic nerve as well as a larger volume of local anesthetic relative to nerve length may result in a more complete blockade of the nasal mucosa and turbinates.

Blood pressures (SAP, MAP, and DAP) differed significantly between the treatments, with blood pressures generally higher during the study period for the saline solution treatment. Although heart rate increased more for the saline solution treatment than the bupivacaine treatment, this change was not significantly different between treatments. Blood pressures and heart rates typically were higher for the saline solution treatment than the bupivacaine treat-

ment, which led us to suspect that dogs receiving the saline solution treatment had a greater nociceptive stimulus. Some dogs (1 after administration of saline solution and 2 after administration of bupivacaine) were treated with atropine to resolve bradycardia associated with hypotension, which likely played a role in the blood pressure and heart rate changes, although atropine was administered prior to the start of the rhinoscopy and nasal biopsy procedures and before blood samples were collected or variables were recorded.

Cortisol and norepinephrine are biomarkers of stress and can be indicators of pain in humans and other animals. Measurement of these biomarkers can be used to indicate stress responses attributable to nociception during anesthetic procedures, postoperative pain, trauma, medication administration, and behavioral stresses. Norepinephrine is produced as an immediate response to stress, whereas cortisol can take up to 4 to 6 hours to reach peak concentrations following surgical trauma. However, changes in plasma norepinephrine concentrations were more prolonged than changes in plasma cortisol concentrations in some studies. The magnitude of change of plasma norepinephrine concentration following a nociceptive stimulus has been reported as being much smaller than that of the plasma cortisol concentration. Variability in biomarker changes in response to a stimulus can make it difficult to interpret changes in plasma norepinephrine concentrations. In the present study, plasma cortisol and norepinephrine concentrations were measured before, during, and after rhinoscopy and nasal biopsy, and we found that plasma cortisol concentrations in dogs receiving saline solution increased significantly from biopsy to 5 minutes after biopsy, which suggested that the local anesthetic blocked nociceptive stimulation of the nasal cavity to some degree. In contrast, no significant changes were seen in plasma norepinephrine concentrations at any of the measured time points. A longer postprocedure time period for measurement of plasma cortisol and norepinephrine concentrations may have provided more information regarding nociception and stress in these dogs.

The dogs used in the present study were a subjectively normal, healthy group that consisted of a sexually intact male and both sexually intact and spayed females. Sex and reproductive status did not factor into results for the study reported here because each dog served as its own control animal. Although including only dogs of the same sex and reproductive status would have provided a more uniform study population, this was not a viable option because of the dogs available for use at the time of the study.

On the basis of histologic examination of the nasal biopsy specimens, lymphoplasmacytic inflammation was seen in some dogs, but there was no difference between the 2 treatments with regard to severity of inflammation. An incidental chondrosarcoma was found

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on 1 side of 1 dog receiving saline solution. No clinical evidence of disease was noted prior to obtaining biopsy specimens in any of the dogs in this study.

A modified infraorbital approach to the maxillary nerve block in the present study did not clearly reduce the degree of purposeful movement seen clinically during rhinoscopy and nasal biopsy, compared with results for the saline solution treatment. No subjective differences were seen during recovery between dogs when receiving saline solution or bupivacaine because pain scores were not significantly different between treatments at any time point. All pain scores were assigned by 2 investigators who were well versed on pain-scoring rubrics prior to the start of the present study. One limitation of the study, especially for postoperative pain scoring, was that the subjects were relatively poorly socialized research dogs that had unpredictable behavior when placed in a cage within the intensive care facility and that were not conditioned to touching of their head and face.47,48 Therefore, a portion of the similarities and differences in pain scores between dogs for the 2 treatments could have been based on behavior and not necessarily on pain. A future study in client-owned animals that are better conditioned to human interaction may change the outcome for postoperative pain scoring, which would potentially allow for behavioral changes attributable to pain to be differentiated from changes attributable to anxiety in a stressful environment.

Results of a power analysis performed before the start of the present study suggested that significant changes in heart rate and blood pressure would be detected when a small sample size (n = 16) was used. Had the study population been larger, additional significant differences, especially in heart rate, plasma norepinephrine concentration, and pain score, may have been detected. Both cost and dog availability prohibited a larger study population, although a larger clinical study involving client-owned animals with clinically relevant nasal disease may provide additional significant differences.

On the basis of findings for the present study, there is evidence, including blood pressures and plasma cortisol concentration, that use of a modified infraorbital approach for a maxillary nerve block could decrease nociceptive and stress responses in dogs undergoing rhinoscopy and nasal biopsy. However, clinical implications for performing a maxillary nerve block via a modified infraorbital approach during the recovery period suggested that this maxillary nerve block technique may not be effective in decreasing nociception during procedures and pain during the recovery period. Further investigation of a modified infraorbital approach for a maxillary nerve block in animals with clinically relevant nasal disease undergoing rhinoscopy and nasal biopsy is indicated.

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Footnotes

b. Methylene blue 1%, Akorn Inc, Lake Forest, Ill.
e. Hospira Animal Health, Lake Forest, Ill.
f. Surflo IV catheters, Terumo Medical Corp, Elkton, Md.
g. Abbott Laboratories, North Chicago, Ill.
h. Piramal Healthcare, Bethlehem, Pa.
i. Isotec vaporizer, Smiths Medical PM Inc, Norwell, Mass.
k. Vetrends V, Systemvet, Tampa, Fla.
m. Bair Hugger, 3M, Eden Prairie, Minn.
n. Baxter Healthcare Corp, Deerfield, Ill.
o. MWI Veterinary Supply Co, Boise, Idaho.
p. B. Braun Medical Inc, Irvine, Calif.
q. Terumo Medical Corp, Somerset, NJ.
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