Ph.D. Dissertation of Veterinary Medicine

Ethmoidal-maxillary Nerve Block for Desensitization of the Nasal Cavity in Dogs

사골-상악 신경차단을 활용한 개의 비강 국소마취

August 2021

Department of Veterinary Medicine

Graduate School

Seoul National University

Major in Veterinary Clinical Sciences

Hyunseok KIM

Ethmoidal-maxillary Nerve Block for Desensitization of the Nasal Cavity in Dogs

Supervised by Professor Inhyung LEE

Submitting a Ph.D. Dissertation of
Veterinary Medicine

May 2021

Department of Veterinary Medicine
Graduate School
Seoul National University
Major in Veterinary Clinical Sciences

Hyunseok KIM

Confirming the Ph.D. Dissertation written by
Hyunseok KIM
June 2021

Chair

Vice Chair

Examiner

Examiner

Examiner

Ethmoidal-maxillary Nerve Block for Desensitization of the Nasal Cavity in Dogs

Abstract

Reflex movement and sudden changes in cardiopulmonary variables, which are induced by mechanical nasal stimulation, can cause complications during nasal procedures such as rhinoscopy, nasal biopsy or nasal surgery. To reduce the stimulation-induced responses during the procedures, ethmoidal and maxillary nerves associated with sensations of the nasal cavity should be blocked. The present study was conducted 1) to develop the technique of ethmoidal nerve block (E_{BLOCK}) in dogs and to compare an analgesic effect of the maxillary nerve block (M_{BLOCK}), E_{BLOCK} and their combination; 2) to compare the ethmoidal-maxillary nerve block (EM_{BLOCK}) and topical nasal application of lidocaine gel (L_{GEL}) for the proposal of an interchangeable technique according to clinical situations; and 3) to evaluate the clinical application of the EM_{BLOCK} in dogs.

The approach to the ethmoidal foramen was determined in canine cadavers using computed tomography with iohexol injection. The different cardiopulmonary responses under the Control, M_{BLOCK}, E_{BLOCK} or EM_{BLOCK} were evaluated during nasal stimulation in anesthetized beagle dogs. In addition, the cardiovascular responses after EM_{BLOCK} or L_{GEL} were compared during nasal stimulation in anesthetized beagle dogs. Furthermore, the clinical effect of EM_{BLOCK} was assessed in 14 client-owned dogs with scheduled rhinoscopy with or

without biopsy. The increase in cardiovascular variables (heart rate and arterial blood pressure), the anesthetic requirement and the occurrence of the reflex head movement were evaluated during rhinoscopy with EM_{BLOCK} or hydromorphone injection ($H_{INJECTION}$).

The injected iohexol was distributed around the target foramina in all cadavers. The physiologic responses were significantly attenuated with the EM_{BLOCK}. Both EM_{BLOCK} and L_{GEL} significantly attenuated the cardiovascular responses. Moreover, the increase in cardiovascular variables and the anesthetic requirements were significantly lower with EM_{BLOCK} than $H_{INJECTION}$. In addition, the occurrence of reflex head movements was more frequent with $H_{INJECTION}$.

The E_{BLOCK} technique suggested in this study can be applied to dogs. The result of the nasal stimulation experiment indicates that EM_{BLOCK} provides significant desensitization of the nasal cavity compared to either block alone. In addition, as L_{GEL} has identical potency to EM_{BLOCK}, both options can be selected interchangeably for nasal desensitization in circumstances which one of the two techniques cannot be applied. During rhinoscopy, the EM_{BLOCK} provides cardiovascular stability, attenuates adverse response movements and reduces anesthetic requirement. Therefore, EM_{BLOCK} can be suggested for stable anesthetic maintenance during nasal procedures in dogs.

Keywords: ethmoidal nerve, maxillary nerve, nasal cavity, local blockade, dog

Student Number: 2015-21829

Table of Contents

Chapter 2

Cardiovascular Responses to Nasal Stimulation under Ethmoidal-maxillary Nerve Block and Lidocaine Gel in Anesthetized Beagles

Chapter 3

Ethmoidal-maxillary Nerve Block during Rhinoscopy in Dogs: A Clinical Trial

List of Abbreviations

ASA	American society of anesthesiologists
BP	Blood pressure
CT	Computed tomography
DAP	Diastolic arterial pressure
E_{BLOCK}	Ethmoidal nerve block
EM_{BLOCK}	Ethmoidal-maxillary nerve block
Fe'Iso	End-tidal isoflurane concentration
f_R	Respiratory rate
$H_{INJECTION}$	Hydromorphone injection
HR	Heart rate
IOP	Intraocular pressure
IQR	Interquartile range
IV	Intravenous
L_{GEL}	Topical application of lidocaine gel
MAP	Mean arterial pressure
M_{BLOCK}	Maxillary nerve block
Pe'CO_2	End-tidal carbon dioxide concentration
SAP	Systolic arterial pressure

List of Abbreviations (cont'd)

SD	Standard deviation
SpO_2	Oxygen saturation
T	Temperature
TV	Tidal volume
Δ	Change

List of Figures

List of Tables

General Introduction

Mechanical stimulation of the nasal cavity during nasal procedures such as rhinoscopy, nasal biopsy or nasal surgery can induce perianesthetic instabilities, including involuntary head movement and abrupt changes in cardiopulmonary variables, even when the procedures are performed under general anesthesia (Crèmer *et al*. 2013). The head movement not only disturbs the procedures but can also damage the nasal cavity and the instrument used. In addition, the abrupt change in cardiopulmonary variables requires the veterinarians to administer additional systemic medications to deepen the anesthetic depth, resulting in cardiovascular depression.

The trigeminal nerve carries the sensation from the nasal cavity in dogs, and the nerve is further divided into the ophthalmic, maxillary and mandibular branches. After dividing into the ethmoidal nerve, the ophthalmic nerve innervates the medial parts of the nasal cavity. In addition, the maxillary nerve innervates the lateral parts of the nasal cavity (Evans and de Lahunta 2013). Hence, both nerves should be blocked to ensure desensitization of the nasal cavity.

The ethmoidal nerve block (E_{BLOCK}) has been proposed for desensitization of the nasal cavity in humans (Molliex *et al*. 1995; Sola *et al*. 2017) and horses (Caruso *et al*. 2016). Furthermore, in human medicine, the concurrent block of ethmoidal and maxillary nerves (EM_{BLOCK}) achieves optimal peri- and post-analgesia for cleft lip repair with primary rhinoplasty (Salloum *et al*. 2009). In veterinary medicine, the application of maxillary nerve block (M_{BLOCK}) has been attempted to suppress nasal stimulation-induced perianesthetic instability during

canine rhinoscopy and nasal biopsy (Crèmer *et al*. 2013; Fizzano *et al*. 2017). However, the E_{BLOCK} has not been characterized in dogs.

Therefore, this study was performed 1) to develop the technique of canine E_{BLOCK} and to compare an effect of M_{BLOCK}, E_{BLOCK} and their combination on cardiopulmonary variables during nasal stimulation (chapter 1), 2) to compare the EM_{BLOCK} and topical nasal application of lidocaine gel (L_{GEL}) as interchangeable techniques that can be applied in clinical situations where one of the two techniques cannot be applied (chapter 2), and 3) to assess the clinical application of the EM_{BLOCK} in dogs of various breeds (chapter 3).

Chapter 1

Effects of Maxillary Nerve Block, Ethmoidal Nerve Block and Their Combination on Cardiopulmonary Responses to Nasal Stimulation in Anesthetized Beagles

Abstract

This study aimed to describe an approach for ethmoidal nerve block (E_{BLOCK}) and to compare the effects of a maxillary nerve block (M_{BLOCK}), E_{BLOCK} and their combination (EM_{BLOCK}) on the heart rate (HR), systolic (SAP), mean (MAP), diastolic (DAP) arterial pressures and respiratory rate (f_R) during nasal stimulation in dogs.

The study was designed as a prospective, blinded, randomized, crossover placebo-controlled study. Fourteen beagle dogs (five cadavers, nine live dogs), with a mean ± standard deviation weight of 10.6 ± 0.5 kg, were included. The accuracy of maxillary and ethmoidal foramina injections of iohexol (each 1 mL) in cadavers was evaluated using computed tomography. Then, anesthetized dogs received four bilateral treatments separated by 1 week saline or 2% lidocaine 1 mL per injection: maxillary and ethmoidal foramina injections of saline (Control), injections of lidocaine at the maxillary foramina and saline at the ethmoidal foramina (M_{BLOCK}), injections of saline at the maxillary foramina and lidocaine at

the ethmoidal foramina (E_{BLOCK}) and injections of lidocaine at all foramina (EM_{BLOCK}). The ventral nasal meatus was bilaterally stimulated using cotton swabs, and the HR, SAP, MAP, DAP and f_R were continuously recorded. Values for each variable were compared before and after stimulation using the Wilcoxon signed-rank test. Changes in variables among treatments were analyzed using the Mann–Whitney *U* and Kruskal–Wallis tests ($p \leq 0.05$).

Computed tomography revealed iohexol distribution around the openings of the target foramina in all cadavers. In living dogs, the HR, SAP, MAP, DAP and f_R significantly increased after stimulation within each treatment ($p < 0.03$). Physiologic responses were significantly attenuated in the EM_{BLOCK} [HR ($p = 0.019$), SAP, MAP, DAP and f_R (all $p \leq 0.001$)] compared with those in the Control.

Concurrent injections of lidocaine at the maxillary and ethmoidal foramina attenuated HR, arterial pressure and f_R responses to nasal stimulation in beagle dogs.

Introduction

Mechanical stimulation of the nasal meatus mucosa during a rhinoscopy or biopsy can cause perianesthetic instabilities such as involuntary movements and changes in cardiopulmonary variables, even when the animal is anesthetized (Mazzone 2005; Crèmer *et al*. 2013; Razaq *et al*. 2015). Mechanical stimulation of the nasal meatus mucosa stimulates the maxillary and ethmoidal nerves. The caudal nasal branch of the maxillary nerve supplies the lateral mucosa of the nasal meatus via the sphenopalatine foramen. The ethmoidal nerve, a branch of the nasociliary nerve derived from the ophthalmic nerve, supplies the medial mucosa of the nasal meatus via the ethmoidal foramen (Evans and de Lahunta 2013; Kumar 2013). M_{BLOCK} has been previously used to reduce nasal stimulation-induced perianesthetic instability in dogs (Crèmer *et al*. 2013; Fizzano *et al*. 2017). The effect of E_{BLOCK} has not been evaluated in dogs; however, the E_{BLOCK} technique has been proposed for desensitization of the nasal meatus in humans (Molliex *et al.* 1995; Sola *et al*. 2017**)** and horses (Caruso *et al*. 2016). If E_{BLOCK} could be applied in dogs, the combination of E_{BLOCK} and M_{BLOCK} will complement each other and enhance nasal meatus desensitization.

This study aimed to describe the E_{BLOCK} technique in dogs and to compare the effect of M_{BLOCK}, E_{BLOCK} and EM_{BLOCK} on cardiopulmonary variables including heart rate (HR), systolic (SAP), mean (MAP), diastolic (DAP) arterial pressure and respiratory rate (f_R) during mechanical stimulation of the nasal meatus. In addition, the authors aimed to elucidate any adverse ophthalmic side-effects of the two techniques (M_{BLOCK} and E_{BLOCK}). The authors hypothesized that EM_{BLOCK} is more

effective in blunting the cardiopulmonary responses to stimulation than M_{BLOCK} alone, E_{BLOCK} alone or the saline control block.

Materials and Methods

The study comprised of two parts: Part 1, the study of cadavers using computed tomography (CT) after bilateral maxillary and ethmoidal foramina injections of iohexol (Omipaque 300; GE Healthcare, Ireland). Part 2, the study of live dogs for evaluating the effects of M_{BLOCK}, E_{BLOCK} and EM_{BLOCK} in a placebo-controlled, blinded, randomized and repeated crossover study design. All procedures were approved by the Institutional Animal Care and Use Committee of the Seoul National University (SNU-170912-4).

Animals

In part 1, five beagle cadavers, mean ± standard deviation (SD) body weight of 10.6 ± 0.4 kg, were obtained from a previous orthopedics study. In part 2, nine live beagle dogs (seven males and two females) aged 1.3 ± 0.5 years and weighing 10.6 ± 0.6 kg, were included. The dogs were part of the Laboratory Animal Resources Seoul National University research colony and were housed in individual stainless-still kennels in temperature-controlled rooms with 12 hours of light and dark cycles. All dogs were clinically healthy based on physical examination, thoracic radiographic imaging and blood analysis, including complete blood cell count and serum chemistry analysis.

Part 1

The techniques for maxillary and ethmoidal foramina injections were established in two and three cadavers, respectively. The dogs were placed in sternal

recumbency. For the maxillary foramen injection, a 23-gauge, 25-mm hypodermic needle connected to a 3 mL syringe was inserted over the palpated opening of the infraorbital foramen on the oral mucosa and advanced along the infraorbital canal up to the lateral canthus, an approximate distance of 25 mm in these beagle dogs, and the proposed site of the sphenopalatine foramen (Figure 1; Viscasillas *et al.* 2013).

For the ethmoidal foramen injection, the hair dorsal to the medial canthus was clipped. The introducer needle (26-gauge, 35-mm) of an over-the-needle catheter (24-gauge, IV Catheter; Sewoon Medical, Republic of Korea) was connected to a 3 mL syringe and inserted at the most medial point of the groove of the angularis oculi vein and advanced while maintaining contact with the medial wall of the orbit bone at a 45^{o} angle to the dorsal plane and a 30^{o} angle to the median plane (Figure 2). The tip of the needle was directed toward the ethmoidal foramen using the frontal process of the zygomatic arch in a lateral view as the landmark (Figure 2), at an approximate depth of 30 mm in these beagle dogs.

Each injection comprised of 1 mL of iohexol. Skull CT was performed before and after the injections with the following imaging conditions: 120 kVp, 150 mAs, 1 second rotation time, 0.5 mm scan slice thickness and 0.64 helical pitch (64-row multidetector, Aquillion 64; Toshiba, Japan). Iohexol distribution within the sphenopalatine and the ethmoidal foramina after maxillary and ethmoidal foramina injections, respectively, were assessed in axial, coronal and sagittal planes.

Part 2

Each live dog was anesthetized on four occasions, each separated by 1 week, with the following treatments: 1) Control treatment by injections of normal saline (0.9% NS normal saline injection; JW Pharm, Republic of Korea) bilaterally at maxillary and ethmoidal foramina; 2) M_{BLOCK} treatment by injections of 2% lidocaine (Daihan Lidocaine HCl Hydrate injection 2%; Daihan Pharm Co. Ltd, Republic of Korea) bilaterally at maxillary foramina and injections of saline bilaterally at ethmoidal foramina; 3) E_{BLOCK} treatment by injections of saline bilaterally at maxillary foramina and injections of lidocaine bilaterally at ethmoidal foramina; 4) EM_{BLOCK} treatments by injections of lidocaine at all foramina. The volume of normal saline and lidocaine injected at each site was 1 mL in all dogs. The treatment order was randomized for each dog by drawing lots.

Food was withheld for at least 12 hours with free access to water before each anesthetic episode. Intravenous (IV) catheterization was achieved with a 22-gauge catheter in the cephalic vein. Hartmann's solution (HS Hartmann's solution; JW Pharma, Republic of Korea) was infused at 10 mL/kg/hour during anesthesia. Acepromazine (0.03 mg/kg; Sedaject inj.; Samu Median Co. Ltd, Republic of Korea) was administered IV. Anesthesia was induced 5 minutes later using IV alfaxalone (2 mg/kg, Alfaxan; Jurox Pty Ltd, NSW, Australia) and maintained with isoflurane (I-Fran Liquid; Hana Pharm Co. Ltd, Republic of Korea) in oxygen (2 L/minute) at a target of 1.5% end-tidal isoflurane concentration (Fe′Iso) using a rebreathing circuit system (Multiplus; Royal Medical, Republic of Korea). A dorsal pedal artery was cannulated using a 22-gauge catheter after perivascular subcutaneous infiltration with lidocaine (0.3 mL) to measure arterial blood pressure. The arterial catheter was connected to a heparinized saline-filled

noncompliant tubing and a disposable pressure transducer (Transpac; ICU Medical, UT, USA) was placed at the level of the scapulohumeral joint, and the transducer was previously assessed against a mercury manometer and zeroed to atmospheric pressure. The dogs were allowed to breathe spontaneously. HR from an electrocardiogram, invasive SAP, MAP and DAP, f_R, oxygen saturation (SpO_2), end-tidal carbon dioxide concentration ($Pe'CO_2$) from capnometry, tidal volume (TV) from spirometry, rectal temperature (T) and Fe′Iso were continuously monitored using a multiparameter monitor (Carescape Monitor B650; GE Healthcare, Finland).

After anesthesia induction and with the dog in sternal recumbency, 30 minutes were allowed for the physiologic variables to stabilize. When MAP decreased to < 60 mmHg, the fluid infusion rate was increased to 20 mL/kg/hour until the MAP increased to 60 mmHg. Maxillary and ethmoidal foramina injections were performed using the techniques described in part 1. The oral mucosa at the needle insertion points for the maxillary foramen injections was aseptically prepared using a 0.2% chlorhexidine-soaked gauze. The hair was clipped over the insertion points for ethmoidal foramen injections, and the skin was prepared with an alcohol-soaked gauze.

Thirty minutes after anesthesia induction, the fluid infusion rate was standardized to 10 mL/kg/hour. Bilateral injections at maxillary and ethmoidal foramina were performed within 3 minutes by an experienced investigator (HK) blinded to the syringe contents. Negative pressure was applied to the syringe plunger before injections to avoid intravascular administration, and injection pressure was assessed manually to avoid intraneural injection during administration. After 10 minutes, the bilateral ventral nasal meatuses were

concurrently stimulated using two cotton swabs (Soosung cotton applicators, Soosung, Republic of Korea). The swabs were inserted and withdrawn five times within 10 seconds, and the insertion depth was at the level of the medial canthus. HR, SAP, MAP, DAP and f_R were video-recorded (iPhone 6S; Apple, CA, USA) immediately before the stimulation (baseline) until any increased values returned to baseline or video-recorded for 5 minutes when the variables did not change. Stimulation-induced changes (Δ) of the cardiopulmonary variables (ΔHR, ΔSAP, ΔMAP, ΔDAP and Δf_R) were defined as the difference between the baseline and the peak value after stimulation, and the values of the baseline and the peak were collected from the recorded video for each variable, dog and stimulation test. Subsequently, a bilateral pinching test on the nose tip was performed using mosquito hemostatic forceps (H112-22012; Hermann Medizintechnik, Germany) to verify whether M_{BLOCK} was successful. The jaw of the forceps was inserted 2 mm into the nostril, and the forceps were locked at the first ratchet for 5 seconds. The stimulation-induced cardiopulmonary changes were collected in the same manner. The vaporizer was then turned off, and the dog recovered from anesthesia. After extubation, the dog was monitored for 1 hour to identify the complications, including neurologic abnormalities.

An ophthalmic examination, including the Schirmer tear test (Schirmer tear test; MSD Animal Health, USA), rebound tonometry (Tiolat TV01; Icare, Finland), neuro-ophthalmic examination, slit-lamp biomicroscopy (SL-07; Topcon Corporation, Japan), indirect ophthalmoscopy (Pan Retinal 2.2; Volk, OH, USA) with a 20-diopter condensing lens and fluorescein staining (Fluorescein; HAAG-Streit Diagnostics, Switzerland) was performed 1 day before anesthesia and 1 week later. Intraocular pressures (IOP) were measured with rebound tonometry

immediately before and after all bilateral injections. The eyes were visually examined during recovery from anesthesia and daily for 1 week. All dogs were returned to the research colony after completing the experiments.

Statistical Analyses

Nonparametric tests were used to establish the significance of differences between treatments. The data on cardiopulmonary variables are presented as median (interquartile range, IQR). Baseline values among treatments for HR, SAP, MAP, DAP and f_R were compared using the Kruskal–Wallis test, and the values between baseline and peak measurement after nasal stimulation were compared within each treatment using the Wilcoxon signed-rank test. ΔHR, ΔSAP, ΔMAP, ΔDAP and Δf_R from M_{BLOCK}, E_{BLOCK} and EM_{BLOCK} were compared with the Control using the Mann–Whitney *U* test. Differences among M_{BLOCK}, E_{BLOCK} and EM_{BLOCK} were analyzed using the Kruskal–Wallis test, and *post hoc* comparison was performed using the Bonferroni-corrected Mann–Whitney *U* test in three pairwise multiple comparisons. IOP before and after foramina injections were compared within each treatment using the Wilcoxon signed-rank test. All analyses were conducted with SPSS version 25 (SPSS 25; IBM Corp., NY, USA). Differences in the values were deemed significant when $p \leq 0.05$.

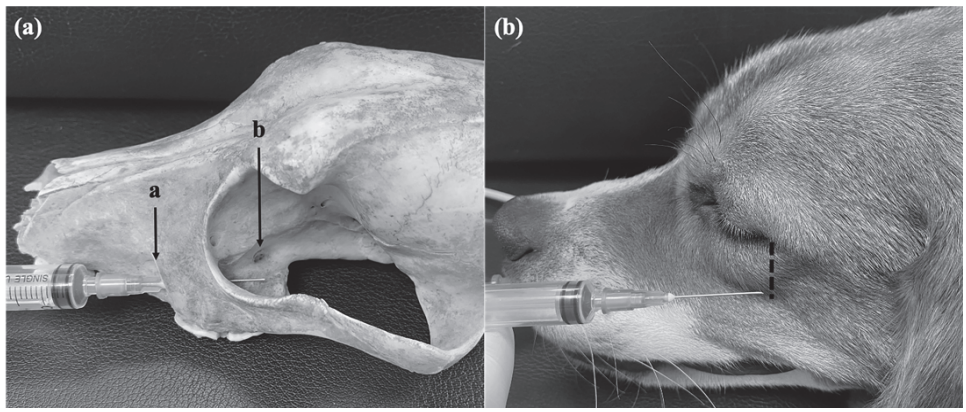

Figure 1. Skull (a) and head (b) views, illustrating the anatomy and site of needle insertion for the maxillary nerve block in a dog. The needle was inserted through the infraorbital foramen and infraorbital canal to reach the sphenopalatine foramen using the vertical line at the lateral canthus as a landmark in lateral view.

a, infraorbital foramen; b, sphenopalatine foramen.

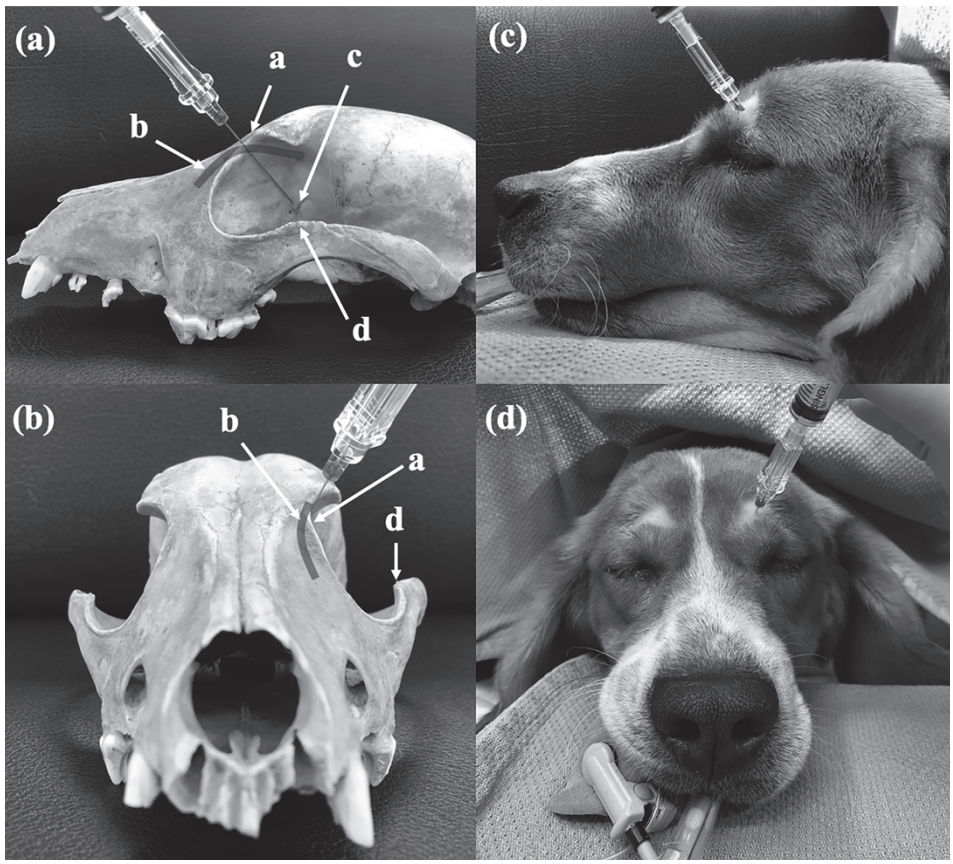

Figure 2. Skull and head views, (a, c) lateral and (b, d) rostral, illustrating the anatomy and site of needle insertion for the ethmoidal nerve block in a dog. The needle was inserted at the most medial point of the groove for the angularis oculi vein and advanced at a 45° angle to the dorsal plane and at a 30° angle to the median plane to reach the ethmoidal foramen using the zygomatic frontal process as a landmark in lateral view.

a, groove accommodating the angularis oculi vein; b, angularis oculi vein; c, ethmoidal foramen; d, zygomatic frontal process.

Results

In all cadavers, iohexol administered via maxillary and ethmoidal foramina injections created a contrast region around target openings of the sphenopalatine and ethmoidal foramina, respectively (Figures 3, 4).

At baseline, during 36 anesthetic episodes in nine live dogs, median (IQR) of SpO_2, $Pe'CO_2$, TV and T were 97 (96–97)%, 50 (46–54) mmHg [6.7 (6.1–7.2) kPa], 13.6 (13.4–13.9) mL/kg and 37.5 (37.2–37.8)°C, respectively. The Fe′Iso was maintained at 1.5% in all treatments.

Baseline values for HR, SAP, MAP, DAP and f_R did not differ among Control, M_{BLOCK}, E_{BLOCK} and EM_{BLOCK} treatments (Table 1). All variables significantly increased from baseline after nasal stimulation in all treatments, and the peak values were identified within 30 seconds (20 episodes), 1 minute (8 episodes), 2 minutes (6 episodes) and 3 minutes (2 episodes). Increased values returned to baseline within 2 minutes after reaching their respective peak values. Relative to Control measurements, the increase was smaller for ΔHR ($p = 0.019$), ΔSAP ($p < 0.001$), ΔMAP ($p < 0.001$), ΔDAP ($p < 0.001$) and Δf_R ($p = 0.001$) in the EM_{BLOCK} treatment, but not in the separate M_{BLOCK} and E_{BLOCK} treatments (Table 1, Figure 5). Among M_{BLOCK}, E_{BLOCK} and EM_{BLOCK}, significant differences were noted in ΔSAP ($p = 0.024$), ΔMAP ($p = 0.032$), ΔDAP ($p = 0.016$) and Δf_R ($p = 0.007$), but not in ΔHR. *Post hoc* analyses determined that ΔSAP ($p = 0.024$), ΔMAP ($p = 0.024$), ΔDAP ($p = 0.012$) and Δf_R ($p = 0.006$) were significantly lesser with EM_{BLOCK} than with M_{BLOCK}. The significance was not observed in the comparison between EM_{BLOCK} and E_{BLOCK} (Table 1, Figure 5).

In the nostril pinching test, the peak values were identified within 30 seconds (23 episodes), 1 minute (11 episodes) and 2 minutes (2 episodes), and increased values returned to baseline within 2 minutes after reaching their respective peak values. ΔHR (p = 0.002), ΔSAP (p = 0.003), ΔMAP (p = 0.006), ΔDAP (p = 0.006) and Δf_R (p = 0.014) were lesser in treatment with M_{BLOCK} than with the Control. ΔHR (p = 0.004), ΔSAP (p = 0.002), ΔMAP (p = 0.002) and ΔDAP (p = 0.001), but not Δf_R, were lower in treatment with EM_{BLOCK} than with the Control (Figure 6). Among M_{BLOCK}, E_{BLOCK} and EM_{BLOCK}, significant differences were noted in ΔSAP (p = 0.023), ΔMAP (p = 0.008) and ΔDAP (p = 0.005). *Post hoc* analyses determined that ΔSAP (p = 0.042), ΔMAP (p = 0.018) and ΔDAP (p = 0.009) were significantly lesser with EM_{BLOCK} than with E_{BLOCK}. In addition, ΔMAP (p = 0.024) and ΔDAP (p = 0.024) were significantly lesser with M_{BLOCK} than with E_{BLOCK} (Figure 6).

No abnormalities were observed in the ophthalmic examinations performed before the experimental procedures. In treatments with the Control, M_{BLOCK}, E_{BLOCK} and EM_{BLOCK}, there were no significant differences between the median (IQR) IOP before [19 (18–21) mmHg, 20 (18–22) mmHg, 20 (18–21) mmHg and 19 (17–22) mmHg, respectively] and after [20 (17–22) mmHg, 20 (18–22) mmHg, 20 (19–22) mmHg and 21 (18–23) mmHg, respectively] bilateral injections. During recovery from anesthesia, miosis and mydriasis were observed in the E_{BLOCK} (one and three eyes, respectively) and EM_{BLOCK} (one and six eyes, respectively) treatments, but the symptoms disappeared within 60.2 (55.4–75.3) minutes after lidocaine injection. In addition, focal subconjunctival hemorrhage around the needle insertion point for E_{BLOCK} was observed in two of 72 eyes (3%) but was not present 1 week later.

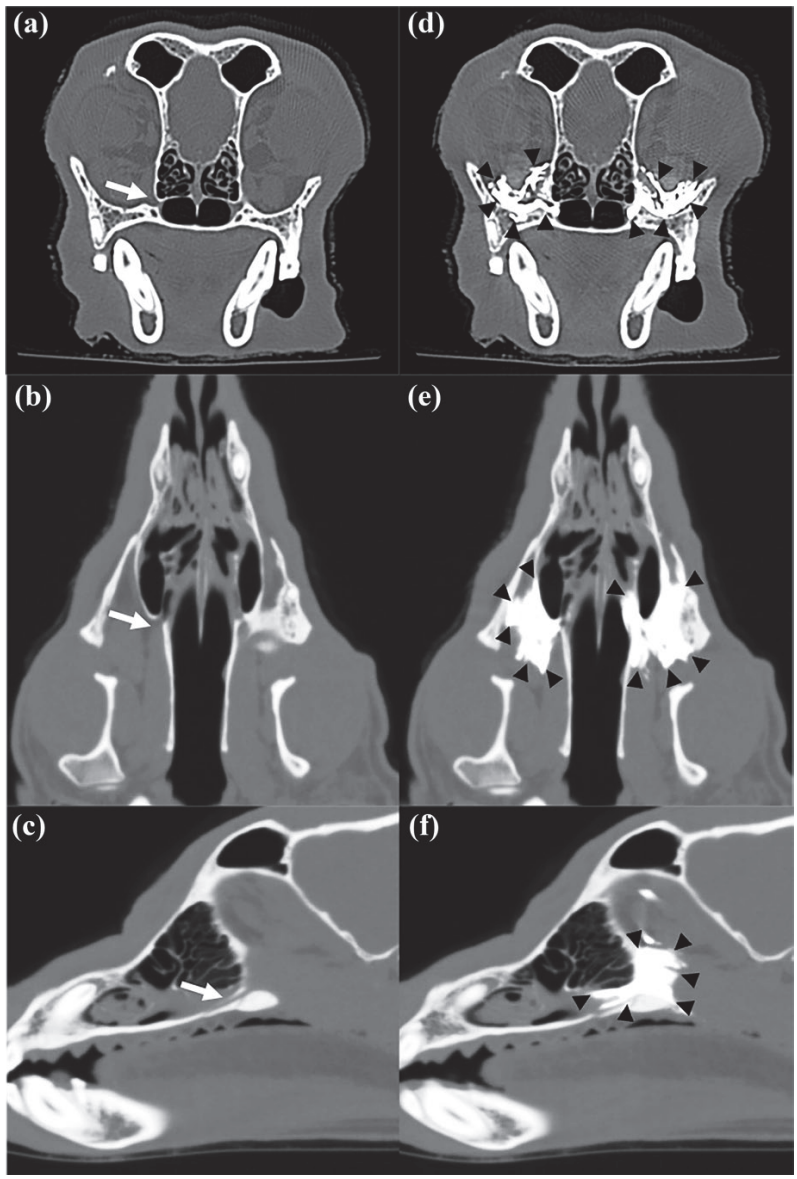

Figure 3. Axial, coronal and sagittal views of computed tomography images from canine cadavers before (a, b, c) and after maxillary injections (d, e, f) of iohexol (1 mL per site) indicating spread of contrast agent (black arrowheads) at the sphenopalatine foramen (white arrows).

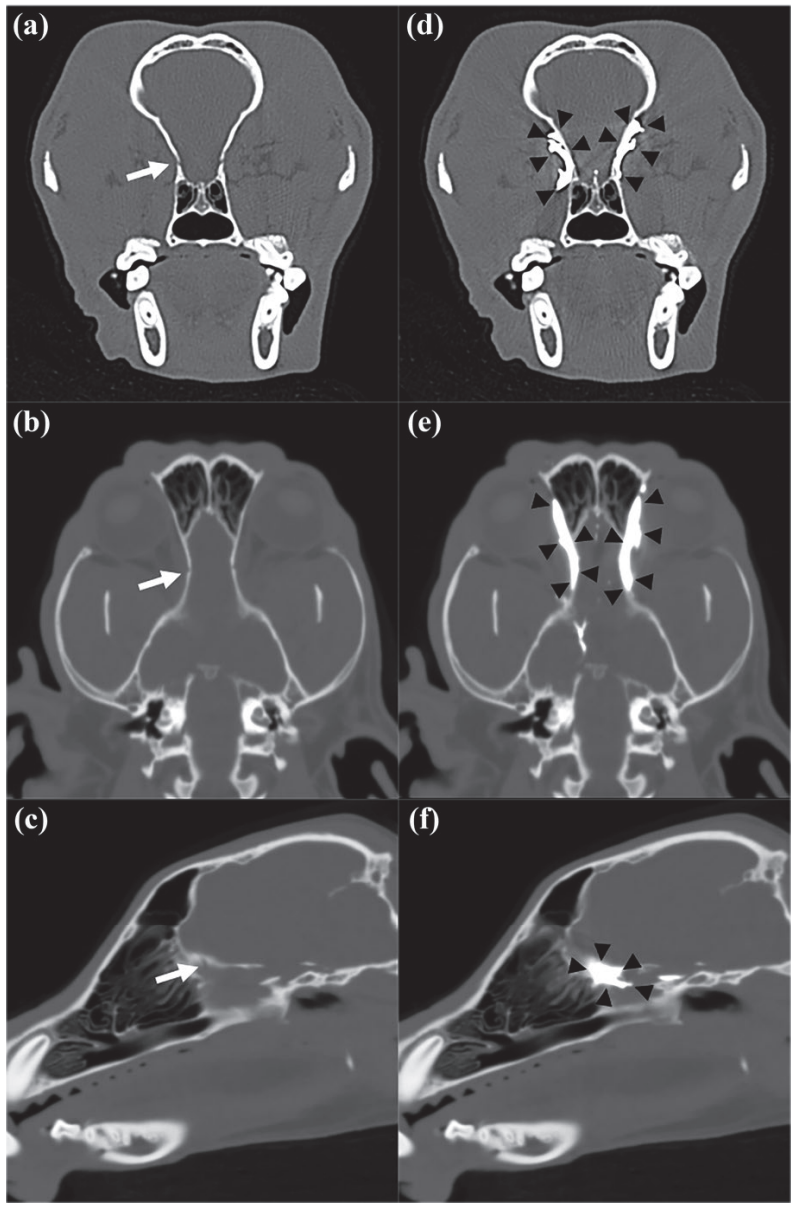

Figure 4. Axial, coronal and sagittal views of computed tomography images from canine cadavers before (a, b, c) and after ethmoidal injections (d, e, f) of iohexol (1 mL per site) indicating spread of contrast agent (black arrowheads) at the ethmoidal foramen (white arrows).

Table 1. Median (interquartile range) of the baselines and the maximum increases in cardiopulmonary variables before and after nasal stimulation with a cotton swab in nine isoflurane-anesthetized beagle dogs with four treatments

Variables	Treatments	Baselines	Increases	*p* values
HR	Control	121 (108-130)	9 (4-14)	
(beats/minute)	M_{BLOCK}	125 (117-135)	6 (3-12)	
	E_{BLOCK}	127 (119-131)	3 (2-6)	
	EM_{BLOCK}	120 (114-146)	2 (1-4) *	0.019
SAP	Control	101 (88-109)	8 (4-13)	
(mmHg)	M_{BLOCK}	98 (96-111)	6 (3-8)	
	E_{BLOCK}	100 (90-113)	5 (3-8)	
	EM_{BLOCK}	101 (94-122)	2 (1-3) *, †	0.001, 0.024
MAP	Control	60 (59-74)	5 (4-9)	
(mmHg)	M_{BLOCK}	68 (62-73)	4 (3-8)	
	E_{BLOCK}	63 (60-74)	4 (2-5)	
	EM_{BLOCK}	67 (62-76)	2 (1-2) *, †	0.001, 0.024
DAP	Control	48 (48-61)	5 (4-8)	
(mmHg)	M_{BLOCK}	55 (49-60)	4 (3-7)	
	E_{BLOCK}	50 (49-61)	4 (2-5)	
	EM_{BLOCK}	55 (53-63)	1 (1-2) *, †	0.001, 0.012
f_R	Control	8 (7-17)	12 (6-16)	
(breaths/minute)	M_{BLOCK}	8 (7-14)	9 (4-12)	
	E_{BLOCK}	9 (7-20)	5 (2-6)	
	EM_{BLOCK}	9 (8-16)	1 (0-2) *, †	0.001, 0.006

HR, heart rate; SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; f_R, respiratory rate; Control, saline injections; M_{BLOCK}, maxillary injections with lidocaine; E_{BLOCK}, ethmoidal injections with lidocaine; EM_{BLOCK}, maxillary and ethmoidal injections with lidocaine.

* Significantly different from the Control within the same variable ($p \leq 0.05$).

† Significantly different from the M_{BLOCK} within the same variable ($p \leq 0.05$).

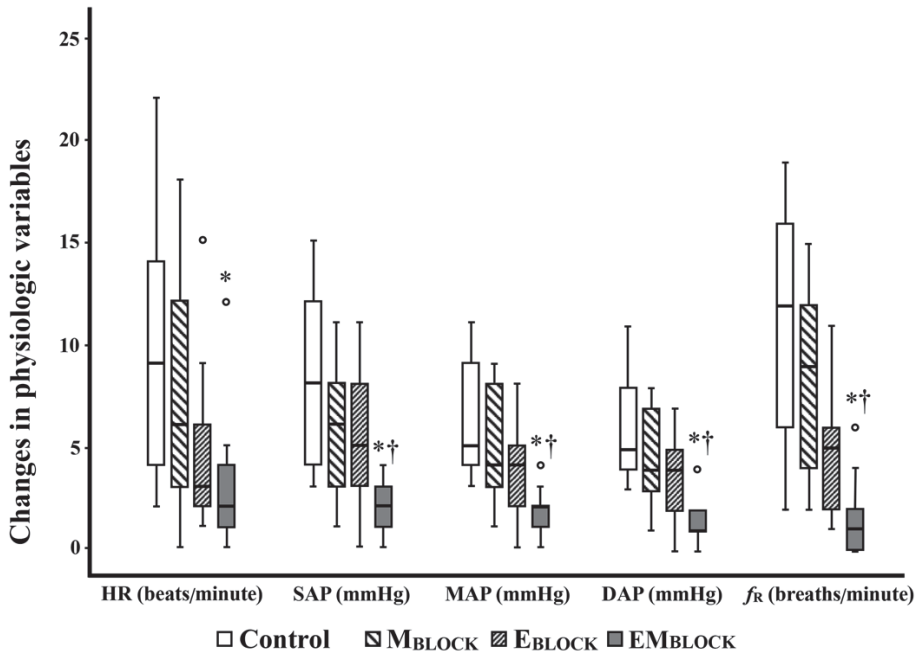

Figure 5. Histogram illustrating responses to nasal meatus stimulation on maximum increase of heart rate (HR), systolic (SAP), mean (MAP), diastolic (DAP) arterial pressures and respiratory rate (f_R), median and interquartile range, in isoflurane-anesthetized dogs administered saline (Control treatment) or 2% lidocaine over the sphenopalatine foramen (M_{BLOCK}), the ethmoidal foramen (E_{BLOCK}) or both foramina (EM_{BLOCK}).

* Significantly different from the Control within the same variable ($p \leq 0.05$).

† Significantly different from the M_{BLOCK} within the same variable ($p \leq 0.05$).

° Outlier

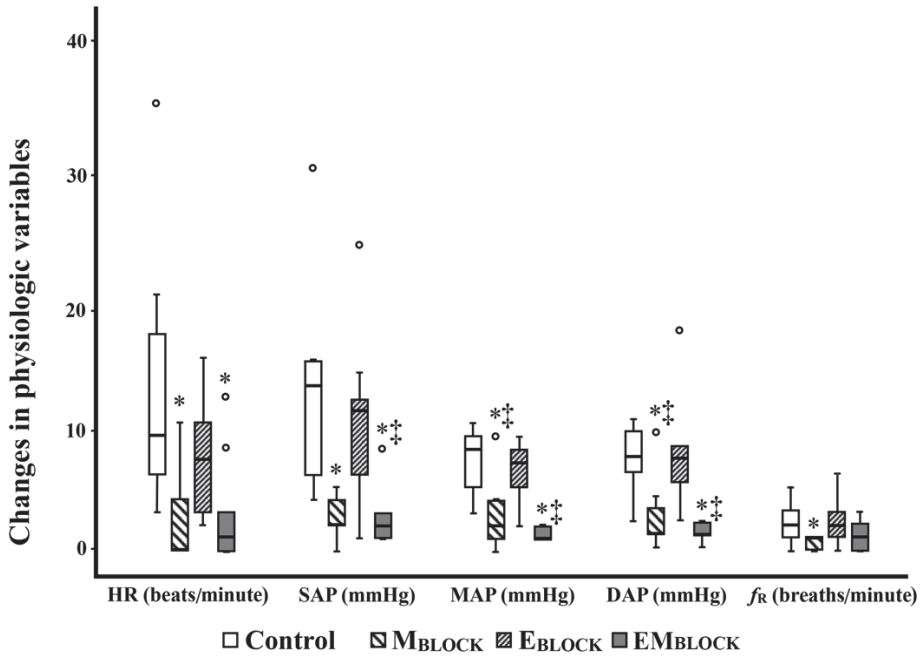

Figure 6. Histogram illustrating responses to a nose pinch on maximum increase of heart rate (HR), systolic (SAP), mean (MAP), diastolic (DAP) arterial pressures and respiratory rate (f_R), median and interquartile range, in isoflurane-anesthetized dogs administered saline (Control treatment) or 2% lidocaine over the sphenopalatine foramen (M_{BLOCK}), the ethmoidal foramen (E_{BLOCK}) or both foramina (EM_{BLOCK}).

* Significantly different from the Control within the same variable ($p \leq 0.05$).

‡ Significantly different from the E_{BLOCK} within the same variable ($p \leq 0.05$).

° Outlier

Discussion

This study proposed a technique for E_{BLOCK} in dogs and compared the effects of combining M_{BLOCK} and E_{BLOCK} on cardiopulmonary responses after nasal meatus stimulation. The results showed that EM_{BLOCK} could significantly attenuate these cardiopulmonary changes in dogs under general anesthesia.

The nasal meatus is an extremely sensitive passage of the nasal cavity. This was demonstrated in the present study by the increases in HR, blood pressure and f_R after non-noxious nasal stimulation in all anesthetized dogs. Although increased cardiopulmonary responses were observed after all treatments, the magnitude of these changes was only significantly diminished by the EM_{BLOCK} treatment. A recent study on horses suggested that the E_{BLOCK} technique would modify the incomplete nasal cavity desensitization provided by M_{BLOCK} alone (Caruso *et al.* 2016). Furthermore, a study in humans for cleft lip repair with primary rhinoplasty indicated that combining the M_{BLOCK} and E_{BLOCK} provided perianesthetic analgesia, even excluding the need for IV sedation or general anesthesia (Salloum *et al.* 2009). The results of the present study suggest that EM_{BLOCK} in dogs may provide desensitization of the entire nasal cavity allowing a decrease in anesthetic agent administration, an advantage for critically ill dogs.

The authors expected E_{BLOCK} to have a blunting effect on stimulation-induced cardiopulmonary changes considering that the ethmoidal nerve innervates the medial mucosa of the nasal meatus (Evans and de Lahunta 2013; Kumar 2013). In addition, M_{BLOCK} can reduce cardiopulmonary instability and involuntary movement during rhinoscopy in dogs (Crèmer *et al.* 2013; Fizzano *et al.* 2017). In

this study, however, a significant blunting effect was not observed in the application of the M_{BLOCK} or E_{BLOCK} alone; probably because of the difference in the diameter of the stimulation source (cotton swab *versus* rhinoscopy) relative to the nasal meatus diameter of the dogs. The diameter of a rhinoscope rarely fills the entire nasal meatus, thus avoiding damage to the nasal mucosa. Therefore, it is possible that the rhinoscope unilaterally stimulated the lateral or medial mucosa innervated by the maxillary and ethmoidal nerves, respectively. In this study, the cotton swabs tightly fit the nasal meatus, which would evenly stimulate the entire circumferential mucosa. This stimulus, which would have stimulated both the ethmoidal and maxillary nerves, resulted in similar results for treatments with Control, M_{BLOCK} and E_{BLOCK}.

In this study, the approach techniques for the E_{BLOCK} and M_{BLOCK} were applied to the beagle dogs as previously described (Salloum *et al.* 2009; Viscasillas *et al.* 2013; Caruso *et al.* 2016). A percutaneous injection technique of the E_{BLOCK} was modified from the techniques that were described for horses (Caruso *et al.* 2016) and humans (Salloum *et al.* 2009). The point of needle insertion was determined based on the palpable groove for the angularis oculi vein. The depth of needle insertion was determined with the anatomical characteristic related to the ethmoidal foramen overlapping with the frontal process of the zygomatic arch in lateral view. In addition, M_{BLOCK} was performed using the infraorbital approach (Gracis 2013) because a previous canine cadaver study reported that this approach was more successful in staining the maxillary nerve than the subzygomatic approach (Viscasillas *et al.* 2013).

Our choice of anesthetic technique in this study was based on the result of a pilot experiment. In the pilot study, nasal stimulation in the Control group caused

changes in cardiopulmonary variables, sneeze reflex and involuntary movements of the head and limbs. These movements disturbed the identical stimulation among the treatments and interrupted the accurate monitoring of cardiopulmonary variables. In the presented study, an anesthetic technique that suppressed movements to the stimulus but allowed the change in the cardiopulmonary system was achieved using isoflurane at Fe′Iso of 1.5% and administration of acepromazine (Webb and O'Brian 1988; Rankin 2015).

The volume of lidocaine was similar to that used previously for maxillary blocks (Crèmer *et al.* 2013), and the total dose of lidocaine used per dog was approximately 0, 4 and 8 mg/kg for the Control, M_{BLOCK} (or E_{BLOCK}) and EM_{BLOCK} treatments, respectively. Previous studies regarding IV lidocaine documented that increases in plasma concentrations can affect the requirement for volatile anesthetics and cardiac function in dogs (Acevedo-Arcique *et al.* 2014). Although lidocaine was not administered via the IV route in this study, systemic effects related to the administered dose could not be excluded during the stimulation test after local block. However, according to the comparison with EM_{BLOCK}, a significant difference in blood pressures and f_R was observed only with M_{BLOCK} not with E_{BLOCK}, although an equal total lidocaine dose was administrated for both M_{BLOCK} and E_{BLOCK}. In addition, considering the absorption rate from the nerve block, the systemic effect would have a minimal impact, although the measurement of plasma concentrations would be needed.

Ocular complications following periorbital injection with a local anesthetic solution, such as an increase in IOP and blockade of nerves related to the eye (Lampard and Morgan 1977), were evaluated. Changes in IOP owing to the distribution of the solution in the eye socket were not observed. Several

complications, including temporary miosis and mydriasis, may have been caused by the blockade of the oculomotor (parasympathetic) and long ciliary (sympathetic) nerves, which are in anatomic proximity to the ethmoidal nerve (Murphy *et al.* 2013; Garosi and Lowrie 2014). In addition, transient subconjunctival hemorrhage caused by needle insertion was observed in several eyes. A hypodermic or short bevel needle is clinically used for periorbital injections (Jolliffe 2016). The incidence of the subconjunctival hemorrhage may have been reduced if a short bevel needle was used for M_{BLOCK} and E_{BLOCK}.

The selection of minimally invasive stimuli was required for repeated stimulation on nasal meatus mucosa in the crossover experiment. Mechanical stimulation by rigid materials such as the rhinoscopy probe can cause mucosal damage, including swelling, inflammation and hemorrhage (Hawkins 2014), affecting the stimulation-induced cardiovascular change in the subsequent treatment. In this study, cotton swabs with a soft tip were used as noninvasive stimuli of short duration. The stimulus-induced cardiopulmonary changes may not seem clinically relevant because of the relatively lower magnitude of the experimental stimulus. Consequently, further studies are required to determine whether the autonomic and nociceptive responses from rhinoscopy are blunted in clinical patients with EM_{BLOCK}.

Conclusions

Concurrent injections of 2% lidocaine at the maxillary and ethmoidal foramina attenuated HR, arterial pressures and f_R responses to mechanical stimulation of the nasal cavity in dogs. The results indicate that combined maxillary and ethmoidal nerve blocks provide significant desensitization of the nasal cavity compared to either block alone.

Chapter 2

Cardiovascular Responses to Nasal Stimulation under Ethmoidal-maxillary Nerve Block and Lidocaine Gel in Anesthetized Beagles

Abstract

This study aimed to compare the effect of an ethmoidal-maxillary nerve block (EM_{BLOCK}) and topical application of 2% lidocaine gel (L_{GEL}) on cardiovascular variables (heart rate and arterial blood pressure) during mechanical stimulation of the nasal cavity.

Six beagles were anesthetized using alfaxalone and isoflurane on three occasions with each treatment (EM_{BLOCK}, L_{GEL} and control) in random order. The nasal cavity from the nose tip to the medial canthus was stimulated with a standard-tip cotton swab, and cardiovascular variables were recorded before and after stimulation.

The maximum increases in heart rate and blood pressure were significantly smaller with EM_{BLOCK} and L_{GEL} than with the Control. There was no significant difference between EM_{BLOCK} and L_{GEL}.

As both EM_{BLOCK} and L_{GEL} attenuated the cardiovascular response to mechanical stimulation of the nasal cavity in dogs, EM_{BLOCK} and L_{GEL} can be used for nasal desensitization.

Introduction

During canine nasal procedures, the nasal cavity mucosa is stimulated mechanically, and nasal stimulation causes tachycardia, hypertension and head movement because of nasal sensitivity, despite the procedure being performed under general anesthesia (Crèmer *et al.* 2013). The ethmoidal and maxillary nerves innervate the medial and lateral mucosa of the nasal cavity, respectively (Evans and de Lahunta 2013). Hence, both nerve blocks are required to ensure desensitization of the nasal cavity. EM_{BLOCK}, which has been applied in human medicine during nasal procedures (Salloum *et al.* 2009), has been suggested for anesthetic stabilization and reduces the complications of canine nasal procedures (Kim *et al.* 2021).

In chapter 1, for EM_{BLOCK}, the needles were inserted at four sites: the most medial points of the eye socket and the bilateral infraorbital foramina, and lidocaine was injected on the bilateral ethmoidal and sphenopalatine foramina (Figure 7; Kim *et al.* 2021). Depending on the clinical situation, these procedures may not be appropriate. For example, complications, such as neurotoxicity, can occur during local blockade in the facial region, and several such cases have been reported in veterinary and human medicine (Webber *et al.* 2001; Aprea *et al.* 2011; Dettoraki *et al.* 2015). This is caused by the direct local anesthetic inflow into the brain due to accidental intra-arterial injection, as explained in previous reports (Webber *et al.* 2001; Dettoraki *et al.* 2015). Hence, in order to present options to clinicians in situations where they are concerned about the occurrence of side-effects during EM_{BLOCK}, it is necessary to study an interchangeable technique that

does not require needle insertion. In human medicine, L_{GEL} has been suggested as topical anesthesia of nasal cavity (Webb *et al.* 1989).

This study used cardiovascular parameters as an indicator of sensation/pain (Hamaya and Dohi 2000; Crèmer *et al.* 2013; Kim *et al.* 2021) and aimed to compare the effects of EM_{BLOCK} and L_{GEL} on cardiovascular variables, including HR and arterial blood pressure, during mechanical stimulation of the ventral nasal meatus in anesthetized dogs. The authors hypothesized that both techniques would similarly blunt the cardiovascular responses to stimulation.

Materials and Methods

Animals

This study was approved by the Institutional Animal Care and Use Committee of the Seoul National University (SNU-180424-3). Six beagle dogs (four males and two females) with a mean ± SD body weight of 10.5 ± 0.3 kg and aged 1.2 ± 0.2 years were included. The dogs were housed in individual stainless-steel kennels in a temperature-controlled room with 12 hours of light and dark cycles. Before the experimental procedures, all dogs underwent a complete physical examination, complete blood cell count evaluation, blood chemistry analysis and thoracic radiography.

Study Design

This study was conducted as a placebo-controlled, blinded, randomized and repeated crossover study design. Each dog was anesthetized on three occasions, with each instance separated by more than 7 days, as follows: 1) EM_{BLOCK} by injections of 2% lidocaine bilaterally at the ethmoidal and maxillary foramina; 2) L_{GEL} by topical application of 2% lidocaine gel (Korea Pharma Lidocaine Hydrochloride Jelly 2%; Korea Pharma, Republic of Korea) bilaterally in the nasal cavity; and 3) Control. The treatment order for each dog was determined by drawing lots for randomization.

Anesthesia and Physiologic Variable Measurement

Before each anesthetic procedure, food was withheld for at least 8 hours with free access to water. IV catheterization was performed with a 22-gauge

catheter in the cephalic vein. Hartmann's (sodium lactate) solution was infused at 5 mL/kg/hour, and acepromazine (0.01 mg/kg) was injected IV. After 5 minutes, anesthesia was induced using IV alfaxalone (2 mg/kg). General anesthesia was maintained with isoflurane in oxygen (2 L/minute) using a rebreathing circuit system, and the vaporizer was adjusted with a target of 1.5% Fe′Iso. To maintain a Pe'CO_2 of 40 mmHg, the dogs were ventilated using a volume-controlled ventilator (VENT-V; Royal Medical, Republic of Korea) with the following ventilator settings: TV of 10–13 mL/kg, a peak inspiratory pressure of 10–12 cmH_2O, and inspiration time of 1 second. A warm-water blanket (HTP-1500; Adroit Medical Systems, Loudon, USA) was used to keep the body temperature at a target of 37.5°C. Arterial catheterization was achieved with a 22-gauge catheter in the dorsal pedal artery to measure arterial blood pressure. The arterial catheter was connected to heparinized saline-filled noncompliant tubing, and the tubing was connected to a disposable pressure transducer placed at the heart level. The transducer was zeroed to atmospheric pressure before measuring arterial blood pressure. After preparing for vital sign monitoring, the dogs were left in sternal recumbency for 30 minutes to stabilize the physiologic variables. During anesthesia, the HR, SAP, MAP, DAP, Fe′Iso, Pe'CO_2, SpO_2 and T were continuously monitored using a multiparameter monitor.

Local Anesthesia of the Nasal Cavity

Local anesthesia of the nasal cavity was performed by the same investigator in all dogs. For the EM_{BLOCK}, four syringes were readied to use at each site. The short bevel needles (BD Spinal needle; BD Caribe Ltd., Republic of Korea) were connected to 3 mL syringes filled with 2% lidocaine solution. During

E_{BLOCK}, the hair dorsal to the medial canthus was clipped, and the needle was inserted at the angularis oculi vein groove after disinfection of the skin with an alcohol-soaked gauze (Figure 7; Kim *et al.* 2021). The needle was advanced at a 45° angle to the dorsal plane and a 30° angle to the median plane while maintaining contact with the medial part of the orbit, and the needle tip was placed at the target point, which was identified using the frontal process of the zygomatic arch in a lateral view (Figure 7; Kim *et al.* 2021). During M_{BLOCK}, the needle was inserted at the infraorbital foramen after disinfection of the oral mucosa with 0.2% chlorhexidine-soaked gauze (Figure 7; Kim *et al.* 2021). In addition, the needle was advanced along the infraorbital canal, and the needle tip was placed at the target point, which was identified using the lateral canthus (Figure 7; Kim *et al.* 2021). To avoid intravascular administration, negative pressure was applied to the syringe plunger before the injections, and 1 mL of lidocaine was injected at each site (total 4 mL per dog). During lidocaine administration, injection pressure was assessed manually to avoid intraneural injection, and the needle was reinserted if high injection pressure was felt.

For L_{GEL}, two syringes were readied to use at each nostril, and 8-Fr feeding tubes (HMS feeding tubes 8-Fr; Hankook Medical, Seokjeok-eup, Republic of Korea) were connected to 3 mL syringes (3 Kovax-syringe; Koreavaccine, Ansan-si, Republic of Korea) filled with 2% lidocaine gel. The depth of the nasal cavity, from the nose tip to the level of the medial canthus, was quartered, and 0.5 mL of lidocaine gel was applied at each depth level (total 4 mL per dog). In addition, the lidocaine gel was gently spread on the nasal cavity mucosa with a cotton swab. In order to minimize irritation, the nasal insertion of a cotton swab was limited to once.

Nasal Cavity Stimulation and Cardiovascular Responses

Stimulation of the nasal cavity was started 10 minutes after local anesthesia to ensure the peak effect of lidocaine had been achieved (Duke-Novakovski 2016). Two standard-tip cotton swabs were inserted into the bilateral ventral nasal meatuses concurrently to stimulate the nasal cavity mucosa. The insertion depth was at the level of the medial canthus, and the cotton swab was inserted and extracted five times by the blinded investigator within 10 seconds. To obtain the values of cardiovascular parameters such as HR, SAP, MAP and DAP, the multiparameter monitor was video-recorded from immediately prior to stimulation (baseline) until any increased values returned to the baseline or recorded for 5 minutes when the values did not change. After recording, the fluid infusion and isoflurane vaporizer were terminated. During the anesthesia recovery period, the dog was visually monitored for 1 hour after extubation to check for complications associated with the local blockade.

Statistical Analyses

Δcardiovascular variables (ΔHR, ΔSAP, ΔMAP and ΔDAP) were calculated as the difference between the peak value after stimulation and the baseline for each variable in each dog. Baseline values of the cardiovascular variables were compared using the Kruskal-Wallis test among the treatments. Differences among EM_{BLOCK}, L_{GEL} and the Control were analyzed using the Kruskal-Wallis test. Furthermore, a *post hoc* comparison was performed with the Bonferroni-corrected Mann-Whitney *U* test. All analyses were performed using SPSS version 25, and the differences were considered significant when $p \leq 0.05$.

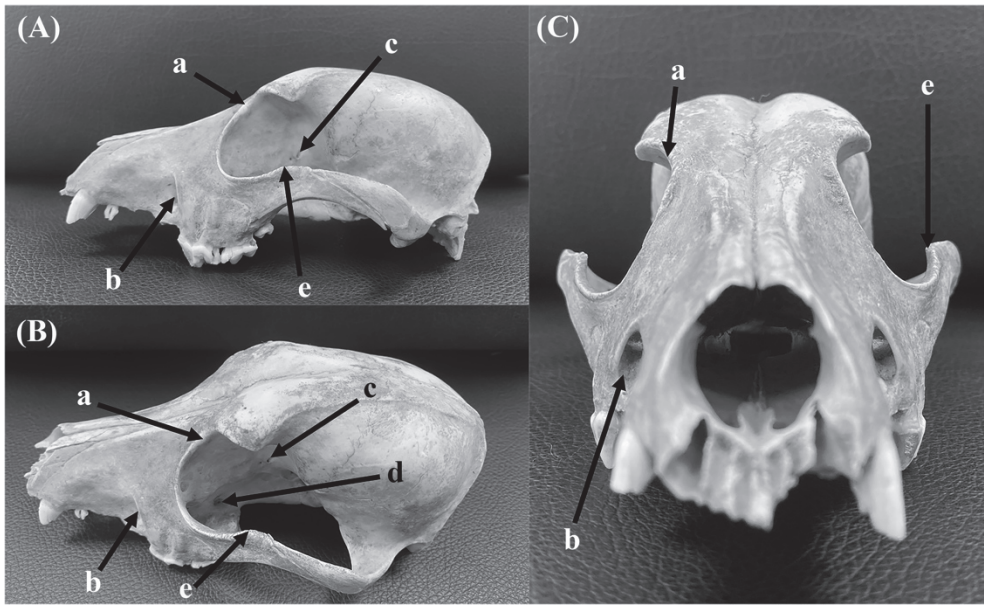

Figure 7. Canine skull views: lateral (A), oblique (B) and rostral (C), including anatomical landmarks for the ethmoidal-maxillary nerve block such as angularis oculi vein groove (a), infraorbital foramen (b), ethmoidal foramen (c), sphenopalatine foramen (d) and frontal process of zygomatic arch (e).

Results

Pre-anesthetic examinations showed that all dogs were clinically healthy based on physical examinations, laboratory tests and thoracic radiography. At baseline, the Fe′Iso and $Pe'CO_2$ were established at 1.5% and 40 mmHg, respectively, in all treatments. In addition, the median (IQR) of SpO_2 and T were 98% (97–98%) and 37.5°C (37.4–37.6°C), respectively, during the 18 anesthetic occasions in six dogs.

Baseline values for HR, SAP, MAP and DAP did not differ among EM_{BLOCK}, L_{GEL} and Control treatments (Table 2). Significant differences of Δ cardiovascular variables were noted among EM_{BLOCK}, L_{GEL} and Control treatments. In *post hoc* analyses, significant differences were identified with EM_{BLOCK} and L_{GEL} compared with the Control (Table 2). Relative to the Control treatments, the increase was smaller for ΔHR, ΔSAP, ΔMAP and ΔDAP (all $p = 0.006$) with EM_{BLOCK}, and the increase was smaller for ΔHR ($p = 0.006$), ΔSAP ($p = 0.027$), ΔMAP and ΔDAP (all $p = 0.006$) with L_{GEL} (Table 2). There was no significant difference between EM_{BLOCK} and L_{GEL}.

During recovery from anesthesia, mydriasis was observed in 3 of 12 eyes (25.0%) with EM_{BLOCK}, and the mydriasis disappeared within 1 hour after lidocaine injection, whereas mydriasis was not observed with L_{GEL}.

Table 2. Median (interquartile range) of the baselines and the maximum increases in cardiovascular variables before and after nasal stimulation with a cotton swab in six isoflurane-anesthetized beagle dogs with three treatments

Variables	Treatments	Baselines	Increases	*p* value
HR	EM_{BLOCK}	115.0 (97.3–132.5)	4.0 (0.0–5.3) *	0.006
(beats/minute)	L_{GEL}	111.0 (97.5–126.5)	6.0 (3.3–7.3) *	0.006
	Control	96.0 (87.8–111.3)	35.0 (20.8–46.8)	
SAP	EM_{BLOCK}	97.5 (94.3–117.3)	1.5 (0.0–2.3) *	0.006
(mmHg)	L_{GEL}	99.5 (97.0–113.5)	2.0 (1.8–3.5) *	0.027
	Control	108.5 (96.0–119.0)	11.0 (4.0–21.5)	
MAP	EM_{BLOCK}	63.5 (61.3–79.5)	1.5 (0.8–2.3) *	0.006
(mmHg)	L_{GEL}	68.0 (63.5–75.8)	2.5 (2.0–3.3) *	0.006
	Control	63.0 (59.0–69.0)	10.0 (6.8–23.0)	
DAP	EM_{BLOCK}	54.0 (51.3–68.0)	1.5 (0.8–2.0) *	0.006
(mmHg)	L_{GEL}	57.0 (53.3–61.8)	3.0 (2.0–3.3) *	0.006
	Control	50.0 (48.5–57.0)	9.0 (6.8–21.5)	

HR, heart rate; SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; EM_{BLOCK}, ethmoidal-maxillary nerve block with lidocaine; L_{GEL}, topical application of lidocaine gel at nasal cavity; Control, no local anesthesia treatment.

* Significantly different from the Control within the same variable ($p \leq 0.05$).

Discussion

This study showed that EM_{BLOCK} could significantly attenuate the cardiovascular responses during nasal cavity stimulation. The application of L_{GEL} to the nasal cavity had the same effect as that of EM_{BLOCK}, which was consistent with the authors' hypotheses. Nerve signal transmission initiated by nasal cavity stimulation was blocked by EM_{BLOCK} treatment, and the activation of mechanoreceptors in the nasal cavity mucosa was blocked by L_{GEL} treatment (Hamaya and Dohi 2000; Kim *et al.* 2021). Although the mechanisms of the two treatments were different, an equal desensitization effect of the nasal cavity with both methods was identified.

Immediately after irritation of the nasal cavity mucosa, sudden changes in patient parameters can occur. When the reaction is severe, involuntary movements can occur, interfering with the procedure and can cause nasal mechanical injury (James and Daly 1972; Crèmer *et al.* 2013). To suppress the responses to nasal passage stimulation, options such as deepening the level of anesthesia, administration of additional sedatives, or application of local anesthesia can be considered.

When referring to the results of this study, EM_{BLOCK} and L_{GEL} can both be considered for local anesthesia of the nasal cavity. Each of these methods has advantages and disadvantages. For EM_{BLOCK}, in the case of neoplastic lesions at the local anesthetic drug administration sites, there is a possibility of causing metastasis from drawing neoplastic cells along the needle tract. In addition, systemic side-effects can be caused by accidental intravascular or intraneural

injection. For L_{GEL}, if the nasal cavity is obstructed it may not be possible to apply the gel appropriately. In addition, intranasal lidocaine gel can interfere with visualization during rhinoscopy or intranasal surgery. In human medicine, according to the judgment of the clinician, EM_{BLOCK} or L_{GEL} is used to implement effective analgesic treatment during nasal procedures (Webb *et al.* 1989; Johnson *et al.* 2003; Salloum *et al.* 2009). Since the effects of EM_{BLOCK} and L_{GEL} were equivalent in this study, either technique can be proposed equally during canine nasal procedures and can be selected by clinicians according to the clinical situation.

Before the application of EM_{BLOCK} and L_{GEL}, the volume of local anesthetic should be discussed. Depending on the size of the dog, the required dose of local anesthetic may differ. In the present study, 4 mL of 2% lidocaine (80 mg) was used per dog. As all dogs weighed more than 10 kg, the dose of lidocaine used for each dog was 8 mg/kg or less, within the range of the maximum safe dose (10 mg/kg; Duke-Novakovski 2016). When applying EM_{BLOCK} and L_{GEL} in the clinic, dose adjustment is necessary in small breed dogs. Furthermore, for EM_{BLOCK}, since the diameter of the ethmoidal and maxillary nerves are different, appropriate volume division of local anesthetic drugs at four injection sites should be ensured for effective nerve blockade. Since the maxillary nerve is thicker in diameter than the ethmoidal nerve, a relatively higher volume of local anesthetic is likely to be required for M_{BLOCK}. For L_{GEL}, because of the rapid absorption rate of the respiratory mucosa (Wu *et al.* 1993), local anesthetic agents may be absorbed before the onset of local anesthesia if a small amount of local anesthetic is applied. The volume of the gel that can contact the nerves until the onset of local anesthesia should be studied.

As a temporary complication, mydriasis was observed during anesthetic recovery in EM_{BLOCK}. The mydriasis was caused by blockade of the oculomotor nerve, which is a parasympathetic nerve located near the ethmoidal nerve (Murphy *et al.* 2013; Garosi *et al.* 2014). However, temporary complications were resolved within 1 hour, and by analogy, the nasal local anesthesia in this study might also be effective for approximately 1 hour (Duke-Novakovski 2016).

The cardiovascular system is influenced by hypercarbia and hypothermia. Hypercarbia increases blood pressure (Rothe *et al.* 1990), and hypothermia initially induces tachycardia and elevation of blood pressure but induces bradycardia and a decrease of blood pressure as it worsens (Prec *et al.* 1949). For response evaluation using the cardiovascular variables, all dogs were ventilated, and $Pe'CO_2$ was maintained at 40 mmHg. In addition, body temperature was maintained within the range of 37.4–37.6°C. Hence neither of these factors should have had any impact on the results of this study.

The limitations of this study were that saline injection or topical application of saline was not performed in Control subjects. In addition, the systemic action of lidocaine, such as analgesic effects or cardiovascular suppression, could not be excluded. However, the lidocaine used for local blockade did not have a significant systemic effect in a previous similar study (Hamaya and Dohi 2000).

Conclusion

In conclusion, EM_{BLOCK} and L_{GEL} attenuated the cardiovascular response, specifically HR and blood pressure, to mechanical stimulation of the nasal cavity in dogs. Hence, EM_{BLOCK} and L_{GEL} can be applied alone or in combination to provide significant desensitization of the nasal cavity for nasal procedures.

Chapter 3

Ethmoidal-maxillary Nerve Block during Rhinoscopy in Dogs: A Clinical Trial

Abstract

This study aimed to evaluate the clinical effects of an ethmoidal-maxillary nerve block (EM_{BLOCK}) during rhinoscopy in dogs.

This study was conducted on 14 dogs that underwent rhinoscopy. Under general anesthesia with isoflurane, EM_{BLOCK} was applied bilaterally using 2% lidocaine before rhinoscopy in eight dogs (EM_{BLOCK} group). Six dogs were premedicated with hydromorphone ($H_{INJECTION}$) as a substitute for the local nerve block ($H_{INJECTION}$ group). During rhinoscopy, the heart rate (HR), arterial blood pressure (BP), and end-tidal isoflurane concentration (Fe'Iso) were recorded. When there were reflex movements caused by nasal stimulation, the vaporizer setting was adjusted to increase the Fe'Iso. Increases in the cardiovascular values upon endoscope insertion and the Fe'Iso at the end of procedures were analyzed between groups using the Mann-Whitney *U* test ($p \leq 0.05$). Binary scores for head movement were analyzed using the chi-square test ($p \leq 0.05$).

Median (interquartile range) increases in HR, systolic, mean and diastolic BP, and Fe'Iso in the EM_{BLOCK} group were significantly lower than those in the

$H_{INJECTION}$ group. Head movements were more frequently observed in the $H_{INJECTION}$ group.

Concurrent block of ethmoidal and maxillary nerves can reduce the cardiovascular response, reflex movement and anesthetic requirement during rhinoscopy in dogs, and could be a useful analgesic technique for nasal procedures.

Introduction

Rhinoscopy facilitates the visual assessment of the nasal cavity using an endoscope (Hawkins 2014). However, mechanical stimulation of the nasal cavity by inserting the endoscope can trigger adverse reactions during rhinoscopy, including head movement and variability of cardiovascular parameters (Crèmer *et al*. 2013). The movement not only interferes with the procedure but can also cause nasal injury and damage to the instrument. In addition, the instability of cardiovascular variables can lead to the practitioner injecting additional systemic medications to deepen the anesthetic depth, resulting in cardiovascular depression. The adverse reactions are caused by stimulation of one or both nerves between the ethmoidal and maxillary nerves, which are related to the sensation of the medial nasal mucosa and the lateral nasal mucosa, respectively (Evans and de Lahunta 2013).

In chapters 1 and 2, the nasal desensitization effect of EM_{BLOCK} was demonstrated in beagle dogs (Kim *et al*. 2021). Thus, to assess the clinical effects of EM_{BLOCK}, this study evaluated the cardiovascular responses, head movement, and general anesthetic sparing effect during rhinoscopy under EM_{BLOCK} or systemic analgesic injection in dogs of various breeds. The authors hypothesized that the reduction in cardiovascular responses, head movement and general anesthetic requirement would be higher with EM_{BLOCK} than with a systemic analgesic.

Materials and Methods

Animals

The present study was approved by the Institutional Animal Care and Use Committee of the Seoul National University (SNU-190924-3). All owners of patients consented to the academic use of patient information. This study was conducted between October 2019 and February 2020 at the Veterinary Medical Teaching Hospital of Seoul National University and on client-owned 14 patients that underwent rhinoscopy. Patients were excluded if they had severe cardiovascular instability requiring treatment in perianesthetic periods or a nasal mass on the ethmoidal or maxillary foramen.

Anesthesia Procedures

In all patients, physical examination, blood analysis (complete blood count and serum chemistry), urinalysis and thoracic radiography were performed as pre-anesthetic examinations. The dogs were classified according to the American Society of Anesthesiologists (ASA) score based on the underlying diseases and the results of the pre-anesthetic examination. Before anesthesia, food and water were withheld for 8 hours and 2 hours, respectively. An IV catheter was placed in the cephalic vein to inject Hartmann's solution (5 mL/kg/hour) and sedative, analgesic and induction agents. Seven dogs that were included in ASA I or II were sedated with acepromazine (0.01 mg/kg, IV), and the other dogs that were included in ASA III were sedated with midazolam (0.2 mg/kg, IV, Bukwang Midazolam Inj.; Bukwang Pharma, Republic of Korea). Anesthesia was induced

with alfaxalone (IV), and the doses were titrated to effect. Following endotracheal intubation, the patients were connected to a circle rebreathing anesthesia circuit, and anesthesia was maintained with isoflurane in 98% oxygen. A catheter was placed in the dorsal pedal artery and connected to a heparinized saline-filled uncompliant tube of a pressure transducer placed at the level of the scapulohumeral joint. The direct arterial blood pressure was measured after zeroing the transducer to atmospheric pressure.

During anesthesia, the HR, SAP, MAP, DAP, f_R, SpO_2, $Pe'CO_2$, TV, T and Fe'Iso were monitored continuously with a multiparameter monitor. The patients were mechanically ventilated to maintain a $Pe'CO_2$ of 40 mmHg with the following ventilator settings: TV ranging from 10 to 13 mL/kg, a peak inspiratory pressure of 12–13 cmH_2O and inspiration time of 1 s. The T was maintained within the range of 36.5–37.5°C using a warm air blanket (Bair Hugger; 3M, USA), and the Fe'Iso was maintained at a target of 1.3%. CT scan of the head was performed in all patients before rhinoscopy with the following imaging conditions: 120 kVp, 150 mAs, 1-s rotation time, 0.5-mm scan slice thickness and 0.64 helical pitch.

Analgesic Treatments

After the CT scan, analgesic treatment was performed at least 40 minutes after induction of anesthesia. The analgesic technique for each individual patient was determined by client preference between EM_{BLOCK} application and hydromorphone (Dilid Inj.; Hana Pharm, Republic of Korea) injection ($H_{INJECTION}$).

Bilateral EM_{BLOCK} was applied prior to rhinoscopy in eight dogs (EM_{BLOCK} group) by the same investigator. For E_{BLOCK}, after hair clipping and aseptic preparation with alcohol-soaked gauze, a short bevel needle was inserted

transcutaneously at the angularis oculi vein groove and was then advanced while maintaining contact with the medial wall of the orbit bone until the previously documented target point, which was the depth level of the frontal process of the zygomatic arch in a lateral view (Kim *et al*. 2021). For the M_{BLOCK}, after aseptic preparation of the oral mucous membrane with a 0.2% chlorhexidine-soaked gauze, a short bevel needle was inserted transmucosally at the opening of the infraorbital foramen and was then advanced until the previously documented target point, which was the depth level of the lateral canthus in a lateral view (Viscasillas *et al*. 2013, Kim *et al*. 2021). The injection volume of 2% lidocaine was 1 mL at each site in dogs weighing more than 10 kg, and a total of 8 mg/kg lidocaine was equally divided and injected at the four sites (0.1 mL/kg per site) in dogs weighing less than 10 kg. Bilateral EM_{BLOCK} were completed within 3 minutes in each individual dog. In six dogs ($H_{INJECTION}$ group), hydromorphone (0.05 mg/kg, IV) was administered as a substitute for EM_{BLOCK}.

Rhinoscopy Procedures and Data Collection

The patients were allowed to remain undisturbed in sternal recumbency for 10 minutes after analgesic treatments to ensure peak analgesic effects. Before insertion of the endoscope, values of the cardiovascular variables (HR, SAP, MAP and DAP) were recorded for the baseline. Rhinoscopy was performed using a small-diameter rigid endoscope (Karl Storz rhinoscope, 0° angle, 3 x 70 mm, model 64301AA; Karl Storz, China) connected to a standard endoscopic tower (Karl Storz-endoskope; Karl Storz, China). The examination was conducted on normal side of the nostril and was then conducted on the suspected side of the lesion. The endoscope was passed through rostral aspect of the nostril and no

further, and the cardiovascular parameters were measure after 30 seconds. As occasion demanded, the vaporizer was adjusted 0.25% by an anesthetist blinded to the analgesic technique. When there was a head movement caused by nasal stimulation, the rhinoscopy was interrupted for 5 minutes to increase Fe'Iso under an adjusted vaporizer setting. During the procedures, isoflurane administration decreased when a progressive decrease in cardiovascular variables was noted. A biopsy was performed as necessary for the diagnosis. The Fe'Iso value was recorded when all the procedures were terminated. The patients' responses were qualitatively evaluated by the endoscopist using a binary scoring system: 0, no reaction; and 1, movement of the head-pulling back while shaking. During recovery from general anesthesia, the patients' eyes were visually examined to check for complications of the local anesthesia, such as conjunctival hemorrhage, mydriasis or miosis.

Statistical Analyses

Due to the small sample size, nonparametric methods were used for data description and statistical analyses, wherein data were presented as medians (IQR). The increase in cardiovascular variables caused by stimulation was defined as the difference between the values before and after endoscope insertion. The baseline values of the cardiovascular variables, increases in cardiovascular values within the groups and values of Fe'Iso at the end of the procedures were analyzed between groups using a Mann-Whitney *U* test. Binary scores for head movements of the patients were analyzed using a chi-square test. In addition, the data were also analyzed according to the breed (brachycephalic or non-brachycephalic), weight (≤ 10 kg or > 10 kg), ASA grade, type of sedatives used (acepromazine or midazolam)

and whether biopsy was conducted. All analyses were conducted using SPSS version 25, and the results were deemed significant when $p \leq 0.05$.

Results

The breeds, body weight, age, ASA, total endoscopy time of both groups and biopsy are described in Table 3. There were no significant differences among the values obtained for the various type of breed, weight, ASA, type of sedatives used and whether the biopsy was conducted.

There was no significant difference in the baseline values for HR, SAP, MAP and DAP between the groups (Table 4). Stimulation-induced increases in HR (p = 0.001), SAP (p = 0.003), MAP (p = 0.005) and DAP (p = 0.029) in the EM_{BLOCK} group were significantly lower than those in the $H_{INJECTION}$ group (Table 5).

Adverse movement reactions were more frequently observed in the $H_{INJECTION}$ group (p = 0.008). Head movement due to endoscope insertion was observed in 5/6 dogs (83.3%) within the $H_{INJECTION}$ group and in 1/8 dogs (12.5%) within the EM_{BLOCK} group.

The value of Fe'Iso (p = 0.001) at the end of the procedure in the EM_{BLOCK} group was significantly lower than that of the $H_{INJECTION}$ group (Table 5). No complications caused by local anesthesia were observed during recovery.

Table 3. Characteristics of dogs included in the study by group

Groups	Breeds (n)	Body weight (kg) *	Age (months) *	ASA grade (n)		Total endoscopy time (minutes) *	Biopsy (n)	
				1-2	3		O	X
EM_{BLOCK} (n = 8)	Border collie (1) Dachshund (3) Pomeranian (2) Welsh corgi (2)	9.8 ± 7.5	115.5 ± 36.2	4	4	46.8 ± 13.4	5	3
$H_{INJECTION}$ (n = 6)	Cocker spaniel (1) Maltese (3) Poodle (1) Schnauzer (1)	6.4 ± 3.2	76.0 ± 44.0	3	3	43.0 ± 9.3	5	1

* Data was expressed as mean ± standard deviation.

ASA grade, American society of anesthesiologist grade; O, performed; X, not performed; EM_{BLOCK}, the group applied ethmoidal and maxillary nerve blocks; $H_{INJECTION}$, the group applied hydromorphone injection.

Table 4. Median (interquartile range) of cardiovascular variables before and 30 seconds after rhinoscopy probe insertion

Variables	Groups	Before	After
HR (beats/minute)	EM_{BLOCK}	117.5 (111.3-128.8)	117.5 (115-132.5)
	$H_{INJECTION}$	125.0 (98.8-131.3)	145.0 (113.8-158.8)
SAP (mmHg)	EM_{BLOCK}	105.0 (96.3-113.8)	115.0 (102.5-115.0)
	$H_{INJECTION}$	112.5 (107.5-120.0)	137.5 (131.3-151.3)
MAP (mmHg)	EM_{BLOCK}	74.5 (70.0-78.8)	81.5 (76.0-85.0)
	$H_{INJECTION}$	72.5 (69.5-75.8)	96.5 (79.5-105.0)
DAP (mmHg)	EM_{BLOCK}	60.0 (52.0-63.8)	65.0 (59.8-68.0)
	$H_{INJECTION}$	57.5 (53.8-61.3)	78.5 (60.0-85.0)

HR, heart rate; SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; EM_{BLOCK}, the group applied ethmoidal and maxillary nerve blocks; $H_{INJECTION}$, the group applied hydromorphone injection.

Table 5. Median (interquartile range) increases in cardiovascular variables from baseline and end-tidal isoflurane concentration at the end of procedures

Variables	Groups	Results	*p* value
HR (beats/minute)	EM_{BLOCK}	0.0 (0.0-5.0)*	0.001
	$H_{INJECTION}$	20.0 (10.0-32.5)	
SAP (mmHg)	EM_{BLOCK}	7.5 (1.3-10.0)*	0.003
	$H_{INJECTION}$	27.5 (17.5-38.8)	
MAP (mmHg)	EM_{BLOCK}	5.0 (1.3-9.5)*	0.005
	$H_{INJECTION}$	20.0 (10.0-31.3)	
DAP (mmHg)	EM_{BLOCK}	5.0 (1.3-9.5)*	0.029
	$H_{INJECTION}$	16.0 (8.8-26.3)	
Fe'Iso (%)	EM_{BLOCK}	1.20 (1.03-1.28)*	0.001
	$H_{INJECTION}$	1.55 (1.38-1.73)	

HR, heart rate; SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; Fe'Iso, end-tidal isoflurane concentration; EM_{BLOCK}, the group applied ethmoidal and maxillary nerve blocks; $H_{INJECTION}$, the group applied hydromorphone injection.

* Statistically significant difference from the $H_{INJECTION}$ within the same variable ($p \leq 0.05$).

Discussion

This study was conducted to determine the effect of EM_{BLOCK} in clinical settings. Based on these findings, there were significantly lower stimulation-induced changes in cardiac variables with EM_{BLOCK} than $H_{INJECTION}$. There were significantly fewer head movements with EM_{BLOCK} than $H_{INJECTION}$. In addition, the application of EM_{BLOCK} decreased the requirement for a general anesthetic agent. These results support the hypotheses.

The cardiovascular response attenuation effect of EM_{BLOCK} was identified in clinical situations with various breeds of dogs in the present study, while the effectiveness of EM_{BLOCK} was only mentioned within the experimental setting with beagles in chapters 1 and 2. Since the stimulation-induced cardiovascular response was lesser with EM_{BLOCK} than $H_{INJECTION}$, compared to systemic analgesic administration, EM_{BLOCK} could be preferentially recommended for cardiovascular stabilization during rhinoscopy in dogs.

As the mucosa of the nasal cavity is exceedingly sensitive to touch, violent sneezing and head shaking are induced by rhinoscopy probe insertion into the nose (Noone 2001). Strong mechanical stimulation such as a biopsy procedure is more likely to cause reflex movements, and the movements should be prevented because they may cause damage to the nasal mucosa or equipment. In this study, biopsy was performed in 5/8 dogs in the EM_{BLOCK} group and 5/6 dogs in the $H_{INJECTION}$ group. There was lesser patient movement in the EM_{BLOCK} group than in the $H_{INJECTION}$ group, regardless of the biopsy procedure. Considering that EM_{BLOCK} prevented head movement more effectively than systemic analgesic treatment

under strong mechanical stimulation like biopsy, the application of the EM_{BLOCK} in canine nasal surgery can be effective, although additional corroborating studies are needed.

The surgical plane of anesthesia is required during rhinoscopy to prevent reflex responses (Noone 2001, Weil 2009) without local anesthesia. The minimum dose of volatile inhalation anesthetics should be applied to critically ill patients because all volatile inhalation anesthetics can decrease cardiac output (Steffey *et al*. 2015). Local anesthesia application is one of the methods to reduce the requirement of volatile inhalation agents (Mosing *et al*. 2010), which can be safely applied to critically ill patients. In the present study, EM_{BLOCK} reduced the isoflurane requirement more than systemic analgesics regardless of the ASA grade, making it useful for applications of EM_{BLOCK} in critically ill dogs that require nasal procedures.

In E_{BLOCK}, the angle of needle insertion to the dorsal plane tended to be larger in the brachycephalic breed than in the non-brachycephalic breed. The tendency was due to the anatomical difference of the skull, and to explain additional technical differences, further studies about the differences between breeds are required.

Complications, such as hemorrhage of the conjunctiva, mydriasis and miosis, identified in chapters 1 and 2, were not found in the present study. A short bevel needle was used instead of a hypodermic needle; thus, the occurrence of hemorrhage would decrease. In addition, the total rhinoscopy time was approximately matched with the lidocaine acting time. Hence, the mydriasis and miosis may not have been identified during the recovery period because the

lidocaine effects would have terminated at anesthetic recovery even if the non-target nerve blockade occurred.

At first, this experiment was planned for the L_{GEL} group as well. However, this group was excluded because the lidocaine gel applied to the nasal cavity interfered with rhinoscopy vision.

The limitation of this study was that the procedure was not used during surgery or in critically ill dog patients. Further research is necessary to establish practical guidelines for its use in canine clinical procedures.

Conclusions

EM_{BLOCK} provides stabilization of cardiovascular values and reduces head movement reactions and isoflurane requirement during rhinoscopy with or without biopsy in dogs. Therefore, the clinical application of EM_{BLOCK} can be suggested for anesthetic stabilization during rhinoscopy in dogs. In addition, it is expected that EM_{BLOCK} would be especially useful in canine nasal surgeries and critically ill dogs.

General Conclusions

This study was designed to develop a local blockade technique for nasal desensitization in dogs and evaluate the technique's clinical application during canine nasal procedures.

In chapter 1, concurrent injections of 2% lidocaine at the maxillary and ethmoidal foramina attenuated cardiopulmonary responses to mechanical stimulation of the nasal cavity in dogs. The results indicated that combined maxillary and ethmoidal nerve blocks provided significant desensitization of the nasal cavity compared to either block alone.

In chapter 2, the ethmoidal-maxillary nerve block and nasal topical application of lidocaine gel equally attenuated the cardiovascular response to mechanical stimulation of the nasal cavity in dogs. Hence, according to the veterinarians' judgments, both local block techniques could be applied alone or in combination to provide significant desensitization of the nasal cavity for nasal procedures depending on the situation.

In chapter 3, the ethmoidal-maxillary nerve block provided stabilization of cardiovascular values and reduced head movement reactions and isoflurane requirement during rhinoscopy with or without biopsy in dogs.

The present study demonstrated that the ethmoidal-maxillary nerve block is a reliable and useful technique for nasal desensitization. Therefore, the clinical application of the ethmoidal-maxillary nerve block can be suggested for anesthetic stabilization during nasal procedures in dogs. The topical application of lidocaine gel could be considered an additional or alternative option depending on the

clinical situations. In addition, it is expected that these techniques would be especially useful in canine nasal surgeries and critically ill dogs.

References

Acevedo-Arcique CM, Ibancovichi JA, Chavez JR *et al*. Lidocaine, dexmedetomidine and their combination reduce isoflurane minimum alveolar concentration in dogs. PLoS One 2014; 18, e106620.

Aprea F, Vettorato E, Corletto F. Severe cardiovascular depression in a cat following a mandibular nerve block with bupivacaine. Vet Anaesth Analg 2011; 38: 614-618.

Berry SH. Injectable anesthetics. In: Grimm KA, Lamont LA, Tranquilli WJ *et al*., editors. Veterinary Anesthesia and Analgesia. 5th edn. Ames, IA: Wiley-Blackwell; 2015, pp. 277-96.

Caruso MI 3rd, Schumacher J, Henry R. Perineural injection of the ethmoidal nerve of horses. Vet Surg 2016; 45: 494–498.

Crèmer J, Sum SO, Braun C *et al*. Assessment of maxillary and infraorbital nerve blockade for rhinoscopy in sevoflurane anesthetized dogs. Vet Anaesth Analg 2013; 40: 432–439.

Dettoraki M, Dimitropoulou C, Nomikarios N *et al*. Generalized seizures and transient contralateral hemiparesis following retrobulbar anesthesia: a case report. BMC Anesthesiol 2015; 15: 108.

Duke-Novakovski T. Pain management II: local and regional anaesthetic techniques. In: Duke-Novakovski T, Vries M, Seymour C, editors. BSAVA Manual of Canine and Feline Anaesthesia and Analgesia. 3rd edn. British Small Animal Veterinary Association, UK, 2016, pp. 143-158.

Evans HE, de Lahunta A. Cranial nerve. In: Evans HE, de Lahunta A. editors. Miller's Anatomy of the Dog. 4th edn. St. Louis, MO: Elsevier; 2013, pp. 708-730.

Fizzano KM, Claude AK, Kuo L *et al*. Evaluation of a modified infraorbital approach for a maxillary nerve block for rhinoscopy with nasal biopsy of dogs. Am J Vet Res 2017; 78: 1025–1035.

Garosi L, Lowrie M. Neuro ophthalmology. In: Gould D, McLellan GJ, editors. BSAVA Manual of Canine and Feline Ophthalmology. 3rd edn. British Small Animal Veterinary Association, UK, 2014, pp. 357–383.

Gracis M. The oral cavity. In: Campoy L, Read MR, editors. Small Animal Regional Anesthesia and Analgesia. Ames, IA: Wiley-Blackwell; 2013, pp. 119–140.

Hamaya Y, Dohi S. Differences in cardiovascular response to airway stimulation at different sites and blockade of the responses by lidocaine. Anesthesiology 2000; 93: 95-103.

Hawkins EC. Respiratory system disorders. In: Nelson RW, Couto CG, editors. Small Animal Internal Medicine. 5th edn. St. Louis, MO: Elsevier; 2014, pp. 217–366.

James JEA, Daly MEB. Reflex respiratory and cardiovascular effects of stimulation of receptors in the nose of the dog. J Physiol 1972; 220: 673-696.

Johnson PE, Belafsky PC, Postma GN *et al*. Topical nasal anesthesia for transnasal fiberoptic laryngoscopy: a prospective, double-blind, cross-over study. Otolaryngol Head Neck Surg 2003; 128: 452-454.

Jolliffe C. Ophthalmic surgery. In: Duke-Novakovski T, Varies M, Seymour C, editors. BSAVA Manual of Canine and Feline Anesthesia and Analgesia. 3rd edn. British Small Animal Veterinary Association, UK, 2016, pp. 258–271.

Kim HS, Jang M, Shin CW *et al*. The effects of maxillary nerve block, ethmoidal nerve block and their combination on cardiopulmonary responses to nasal stimulation in anesthetized Beagle dogs. Vet Anaesth Analg 2021; 48: 92-100.

Kumar MSA. Clinically Oriented Anatomy of the Dog and Cat. Ronkonkoma, NY: Linus Learning; 2013, pp. 511–595.

Lampard DG, Morgan DL. Intraocular pressure during retrobulbar injection. Aust Vet J 1977; 53: 490–491.

Mazzone SB. An overview of the sensory receptors regulating cough. Cough 2005; 1: 2–9.

Molliex S, Navez M, Baylot D *et al*. Regional anaesthesia for outpatient nasal surgery. Br J Anaesth 1995; 76: 151–153.

Mosing M, Reich H, Moens Y. Clinical evaluation of the anaesthetic sparing effect of brachial plexus block in cats. Vet Anaesth Analg 2010; 37: 154-161.

Murphy CJ, Samuelson DA, Pollock RVH. The eye. In: Evans HE, de Lahunta A, editors. Miller's Anatomy of the Dog. 4th edn. St. Louis, MO: Elsevier Saunders; 2013, pp. 746–785.

Noone KE. Rhinoscopy, pharyngoscopy, and laryngoscopy. Vet Clin North Am Small Anim Pract 2001; 31: 671-689.

Prec BO, Rosenman R, Braun K *et al*. The cardiovascular effects of acutely induced hypothermia. J Clin Invest 1949; 28: 293-300.

Rankin DC. Sedatives and tranquilizers. In: Grimm KA, Lamont LA, Tranquilli WJ *et al*., editors. Veterinary Anesthesia and Analgesia. 5th edn. Ames, IA: Wiley-Blackwell; 2015, pp. 196–206.

Razaq ASA, Mohamad I, Salim R. Mechanoreceptors in the nose. Egyptian J Ear Nose Throat Allied Sci 2015; 16: 9–12.

Rothe CF, Maass-Moreno R, Flanagan AD. Effects of hypercapnia and hypoxia on the cardiovascular system: vascular capacitance and aortic chemoreceptors. Am J Physiol-Heart C 1990; 259: H932-9.

Salloum ML, Eberlin KR, Sethna N *et al*. Combined use of infraorbital and external nasal nerve blocks for effective perioperative pain control during and after cleft lip repair. Cleft Palate Craniofac J 2009; 46: 629–635.

Sola C, Dadure C, Choquet O *et al*. Nerve blocks of the face. In: Hadzic A, editor. Hadzic's Textbook of Regional Anesthesia and Acute Pain Management. 2nd edn. New York, NY: McGraw-Hill Education; 2017, pp. 535–551.

Steffey EP, Mama KR, Brosnan RJ. Inhalation anesthetics. In: Grimm KA, Lamont LA, Tranquilli WJ, *et al*., editors. Veterinary Anesthesia and Analgesia. 5th edn. Ame, IA: Wiley Blackwell; 2015, pp. 297-331.

Viscasillas J, Seymour CJ, Brodbelt DC. A cadaver study comparing two approaches for performing maxillary nerve block in dogs. Vet Anaesth Analg 2013; 40: 212–219.

Webb AI, O'Brian JM. The effect of acepromazine maleate on the anesthetic potency of halothane and isoflurane. J Am Anim Hosp Assoc 1988; 24: 609–613.

Webb AR, Woodhead MA, Dalton HR *et al*. Topical nasal anaesthesia for fibreoptic bronchoscopy: patients' preference for lignocaine gel. Thorax 1989; 44: 674-675.

Webber B, Orlansky H, Lipton C *et al*. Complications of an intra-arterial injection from an inferior alveolar nerve block. J Am Dent Assoc 2001; 132: 1702-1704.

Weil AB. Anesthesia for endoscopy in small animals. Vet Clin North Am Small Anim Pract 2009; 39: 839-848.

Wu F, Razzaghi A, Souney PF. Seizure after lidocaine for bronchoscopy: case report and review of the use of lidocaine in airway anesthesia. Pharmacotherapy 1993; 13: 72-78.

국 문 초 록

사골-상악 신경차단을 활용한 개의 비강 국소마취

지도교수 이 인 형

김 현 석

서울대학교 대학원

수의학과 임상수의학 전공

본 연구의 목적은 1) 개에서의 사골 신경차단 기법을 개발하고 상악 신경차단, 사골 신경차단, 그리고 두 신경차단의 병용 시 그 효과를 비교하며, 2) 상호보완적인 기법을 제시하기 위해 사골-상악 신경차단과 리도카인 젤의 비강 국소 적용을 비교하고, 3) 개에서 사골-상악 신경차단의 유용성을 임상적으로 평가하는 것이다.

제1장에서는 개 사체에서 조영제 투여와 함께 컴퓨터단층촬영을 통하여 사골공 접근법을 설정하고, 전신마취된 비글견에서 대조군, 상악 신경차단, 사골 신경차단, 그리고 두 신경차단의 병용에 따라 비강 자극 시 심폐관계의 반응을 비교하였다. 자극에 대한 반응은 두 신경차단을 병용하였을 때 유의적으로 감소하였고, 이 결과로부터 사골 신경과 상악

신경을 모두 차단하는 것이 각 신경차단을 단독적으로 적용하는 것보다 효과적으로 비강 감각을 차단하는 것을 확인하였다.

제2장에서는 전신마취된 비글견에서 사골-상악 신경차단 실시, 또는 리도카인 젤을 비강에 국소 적용한 후, 비강 자극 시 심맥관계의 반응을 비교하였다. 두 기법 모두에서 유의적으로 심맥관계 반응이 감소하였으며, 그 결과로부터 두 가지 기법은 서로 상호보완적으로 비강 감각차단을 위해 선택 가능하다는 것을 확인하였다.

제3장에서는 비강 내시경을 진행했던 14마리의 환견에서 사골-상악 신경차단의 임상적용을 평가하였다. 비강 내시경을 진행하는 중에 심맥관계 수치의 상승, 전신 마취제 요구량, 그리고 자극에 대한 반사 움직임을 사골-상악 신경차단을 적용한 그룹과 전신 진통제를 투여한 그룹으로 나누어 평가하였다. 심맥관계 수치의 상승과 전신 마취제 요구량이 국소마취를 진행한 그룹에서 유의적으로 낮았다. 또한, 자극에 대한 반사 움직임이 전신 진통제를 투여한 그룹에서 유의적으로 빈번하였다. 실험 결과에 따라, 사골-상악 신경차단이 개의 비강 시술에 대한 효과적인 진통 기법이라는 것을 확인하였다.

본 연구들의 결과를 통하여, 상악 신경과 사골 신경을 모두 차단하는 것은 비강의 감각을 효과적으로 차단하는 것을 확인할 수 있었다. 비강 감각차단을 통해 사골-상악 신경차단은 비강 자극 시 심폐관계의 안정성 증진, 반사 움직임의 감소, 그리고 전신 마취제 요구량의 감소 효과를 보이기 때문에 개의 비강 시술 시 안정적인 마취 유지를 위해 적용을 고려해 볼 수 있을 것으로 판단된다. 또한, 리도카인 젤의 비강

국소 적용은 사골-상악 신경차단과 동일한 효과를 보이기 때문에 두 가지 국소마취 기법 중 특정 방법을 적용하지 못하게 되는 상황에서 소동물 임상가의 판단 하에 상호보완적인 적용이 가능할 것으로 사료된다.

주요어: 사골 신경, 상악 신경, 비강, 국소마취, 개

학번: 2015-21829