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Authors

Shilo-Benjamini, Yael
Pascoe, Peter J
Maggs, David J
et al.

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ORIGINAL ARTICLE

Retrobulbar vs peribulbar regional anesthesia techniques using bupivacaine in dogs

Yael Shilo-Benjamini¹ | Peter J. Pascoe² | David J. Maggs² | Steven R. Hollingsworth² | Ann R. Strom² | Kathryn L. Good² | Sara M. Thomasy² | Philip H. Kass³ | Erik R. Wisner²

¹Koret School of Veterinary Medicine, The Robert H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot, Israel

²Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA, USA

³Department of Population Health and Reproduction, School of Veterinary Medicine, University of California, Davis, CA, USA

Correspondence

Y. Shilo-Benjamini

Email: shilo.yael@gmail.com

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Abstract

Objective: To compare the effectiveness of retrobulbar anesthesia (RBA) and peribulbar anesthesia (PBA) in dogs.

Animal studied: Six adult mixed-breed dogs (18–24 kg).

Procedures: In a randomized, masked, crossover trial with a 10-day washout period, each dog was sedated with intravenously administered dexmedetomidine and administered 0.5% bupivacaine:iopamidol (4:1) as RBA (2 mL via a ventrolateral site) or PBA (5 mL divided equally between ventrolateral and dorsomedial sites). The contralateral eye acted as control. Injectate distribution was evaluated by computed tomography. Following intramuscularly administered atipamezole, corneal and periocular skin sensation, intraocular pressure (IOP), and ocular reflexes, and appearance were evaluated for 24 hours. Comparisons were performed with mixed-effects linear regression (IOP) or the exact Wilcoxon signed rank test (scores). Significance was set at $P \leq .05$.

Results: Injectate distribution was intraconal in 2/6 RBA- and 4/6 PBA-injected eyes. Eyes undergoing PBA had significantly reduced lateral, ventral, and dorsal periocular skin sensation for 2–3 hours, and significantly reduced corneal sensitivity for 4 hours, relative to control eyes. Chemosis and exophthalmos occurred in 33%–40% of eyes undergoing RBA and 83%–100% eyes undergoing PBA but resolved within 14 hours. Anterior uveitis developed in 2/6 and 1/6 eyes of RBA and PBA, respectively, of them corneal ulcer developed in one eye of each treatment. Both resolved 1–3 days following medical treatment.

Conclusions: Peribulbar injection produced notable anesthesia more reliably than did retrobulbar injection. Both techniques may produce adverse effects, although the uveitis/ulcer could have resulted from the contrast agent used.

KEYWORDS

analgesia, bupivacaine, dogs, ophthalmic regional anesthesia, peribulbar anesthesia, retrobulbar anesthesia

1 | INTRODUCTION

Ocular regional anesthetic techniques provide analgesia, akinesia,^{1,2} and may protect against the oculocardiac reflex

during ocular surgeries in humans^{3,4} and horses.⁵ Retrobulbar anesthesia (RBA) involves administration of a relatively small volume of local anesthetic into the extraocular muscle cone (ie, intraconal injection), whereas peribulbar

anesthesia (PBA) involves administration of a larger volume of local anesthetic outside the cone (ie, extraconal injection), which then diffuses into the cone and eyelids.²

Retrobulbar anesthesia provides excellent perioperative analgesia for dogs undergoing ocular surgery,⁶⁻¹⁰ and PBA was effective in an experimental setting.¹¹ However, to the authors' knowledge, there are no studies comparing the effectiveness of RBA and PBA in dogs. Therefore, the goals of this study were to evaluate injectate distribution and clinical effects of PBA in comparison with RBA, and to describe adverse events potentially associated with these techniques in dogs. Our hypothesis was that PBA would provide intraconal injectate distribution and clinical effects comparable to the RBA technique.

2 | MATERIALS AND METHODS

2.1 | Animals

The study was approved by the University of California Davis Animal Care and Use Committee. Six intact female mixed-breed dogs were used in this study. Their mean $\pm$ SD body weight and age were 21.3 ± 2.4 kg and 1 ± 0.2 years, respectively. No abnormalities were detected on physical examination, and complete blood count and blood urea nitrogen concentration were within the reference ranges for dogs.

Complete neuro-ophthalmic examination was performed by a board-certified veterinary ophthalmologist, and included assessment of direct and consensual pupillary light reflex (PLR), menace response, palpebral reflex, corneal sensitivity using the Cochet-Bonnet aesthesiometer (Luneau Ophtalmologie, Chartres Cedex, France), aqueous tear production using the Schirmer tear test 1, and intraocular pressure (IOP) using applanation tonometry (Tono-Pen Vet™, Reichert Technologies, Depew, NY, USA) following administration of one drop of 0.5% proparacaine hydrochloride (Falcon Pharmaceuticals, Fort Worth, TX, USA). Slit lamp biomicroscopy before and after pupil dilation with tropicamide, indirect ophthalmoscopy following pupil dilation, and topical application of fluorescein stain were also performed. No ophthalmic abnormalities were detected in any dog before this study was undertaken.

2.2 | Evaluation of corneal sensitivity

Corneal sensitivity was measured in the central cornea using the standard Cochet-Bonnet monofilament nylon fiber of 0.12-mm diameter held perpendicular to the cornea. The aesthesiometer was advanced until the tip touched the cornea, producing a slight bend in the fiber. This was performed 3-5 times while observing for reflexive eyelid closure. The initial stimulation used a 4-cm filament, which

was decreased by 0.5-cm increments until a blink reflex was seen. Decreased filament length required to stimulate a blink reflex reflected decreased corneal sensitivity. The longest filament length in centimeters that induced a blink reflex on at least 3 of 5 stimulations was recorded as the corneal sensitivity, and a lack of blink reflex using a 0.5-cm filament was defined as complete loss of corneal sensation (ie, corneal sensitivity of zero).¹²⁻¹⁵ Environmental conditions were kept the same between measurements in an effort to standardize the aesthesiometer data collection.

2.3 | Regional anesthesia injection techniques

The dogs were randomly (www.randomizer.org) assigned to receive one of two treatments: RBA or PBA. A combination of bupivacaine 0.5% (Bupivacaine HCl 0.5%; Hospira Inc., Lake Forest, IL, USA) and a contrast agent (Iopamidol 76%; Isovue-370, Bracco Dx, Princeton, NJ, USA) 4:1 was used as the injectate solution. The contralateral eye was not injected and served as a control. After a 10-day washout period, the dogs were administered the second treatment in the contralateral eye.

Dogs were fasted but provided free access to water for 12 hours before each treatment. Prior to RBA or PBA, each dog underwent bilateral baseline assessment of horizontal pupil diameter (HPD; measured in millimeters) using a Jameson caliper, direct and consensual PLRs, palpebral reflex, and menace response. The periocular skin sensation was tested using a "pin-prick" technique with pressure applied to the periocular skin using the tip of a ballpoint pen at the mid-dorsal eyelid, mid ventral eyelid, and lateral and medial canthi. The response was considered positive when the dog closed the eyelids or moved the head.¹⁶ Lastly, corneal sensitivity and then IOP were assessed as described earlier.

Following baseline assessment, dogs were sedated with 15 μ g/kg of dexmedetomidine administered intravenously (Dexdomitor, Orion Pharma, Espoo, Finland), and were positioned sternally, with their head elevated on a triangular foam pad. During sedation, heart rate and blood pressure were monitored noninvasively, and all dogs received supplemental flow-by oxygen. Prior to RBA or PBA, the periocular skin was aseptically prepared using povidone-iodine solution diluted 1:20 in sterile saline.

Retrobulbar anesthesia was performed in accordance with guidelines described by Accola et al 2006. Briefly, a 2.5-inch (6.4 cm), 22-gauge spinal needle (BD spinal needle, BD Medical, Franklin Lakes, NJ, USA) was bent to form an angle of approximately 20°. The needle was then inserted through the inferior eyelid at the junction of its middle and temporal thirds, and advanced until a slight popping sensation was detected. The needle was then directed slightly dorsally and nasally toward the apex of the

orbit and advanced approximately 3–5 mm, and 2 mL of injectate was delivered.

Peribulbar anesthesia was performed using two 1-inch (2.5 cm), 22-gauge hypodermic needles (Monoject, Covidien, Mansfield, MA, USA) inserted through the eyelids and advanced in close proximity to the bony orbit. One needle was inserted through the lateral portion of the inferior eyelid (ie, into the ventrolateral orbit), and the second needle was inserted through the medial portion of the superior eyelid (ie, into the dorsomedial orbit); 2.5 mL of injectate was administered at each site. The needle was held against the skin to ensure that it would not be repulsed during injection.

For both techniques, negative pressure was applied to the syringe plunger before injections to avoid intravascular administration, and the bevel of the needle was oriented toward the globe. The same board-certified veterinary anesthesiologist (PJP), who has over 20 years of experience performing RBA, performed all injections.

2.4 | Injectate distribution assessment

Computed tomography (CT) (LightSpeed 16 slice helical CT scanner, General Electric Co., WI, USA) was performed immediately before and 10 minutes following injections. Imaging parameters included 0.625 mm image collimation, 120 kVp, 200 mA and image reconstruction using bone (edge enhancing) and soft tissue (edge smoothing) algorithms. The same board-certified veterinary radiologist (ERW), who was masked to injection technique, assessed distribution of the injectate in all dogs. DICOM images (digital imaging and communication in medicine) were reviewed on a workstation with medical imaging software (eFilm v4.0, Merge Healthcare, IL, USA). Transverse images were reformatted to enable assessment of regions of interest in dorsal and oblique anatomic planes.

Intraconal injectate distribution volume was scored as described: 0 = none, 1 = moderate, and 2 = large. The extent of contact between the injectate and the optic nerve was scored as: 0°, 90°, 180°, 270°, or 360°. ¹⁶ Injectate distribution likely to produce partial anesthesia was defined as moderate intraconal distribution and optic nerve contact of 90–180°, and distribution likely to produce successful anesthesia was defined as large intraconal distribution volume and optic nerve contact of 270–360°.

2.5 | Clinical assessment of regional anesthesia techniques

Measurements of IOP and HPD were performed following sedation (but prior to injections), and immediately ($T_{1 \text{ min}}$), 5 ($T_{5 \text{ min}}$), and 10 minutes ($T_{10 \text{ min}}$) after RBA or PBA injections, while still under sedation. On these

times, the IOP was measured without the use of topical anesthetic.

After completion of imaging, sedation was reversed with atipamezole (Antisedan, Orion Pharma, Espoo, Finland) administered intramuscularly at 10 times the dexmedetomidine dose. Neuro-ophthalmic evaluation was repeated as soon as dogs were able to walk appropriately ($T_{0.5}$), then once hourly for 12 hours (T_{1-12}), and then every 2 hours ($T_{14, 16...}$) until complete recovery. The same investigator (YSB), who was masked to the injection technique, performed all clinical assessments bilaterally. Assessment included evaluation of globe and conjunctival appearance, HPD, menace response, palpebral reflex, direct and consensual PLRs, periocular skin sensation, and corneal sensitivity (all performed as described at baseline). The duration of corneal insensitivity was calculated as the time from injection to the time when the corneal sensitivity was ≤ 0.5 cm. The reflexes and skin sensitivity were scored as: 0 = no response; 1 = partial response; and 2 = normal response. Sterile isotonic buffered solution (Eye wash, OCUSOFT, Inc., Richmond, TX, USA) was applied once every 2 hours to lubricate the cornea. An Elizabethan collar was placed if the dog attempted to rub its ocular or periocular structures.

To assess for adverse effects 24 hours following each injection and 4 weeks following the second injection, complete neuro-ophthalmic and ophthalmic examinations (as performed at study entry) were repeated by a board-certified ophthalmologist masked to the injection technique.

2.6 | Statistical analyses

Statistical analyses were carried out using commercial software (Stata IC/12.1, StataCorp, College Station, TX, USA). The exact Wilcoxon signed rank test for paired data was used to compare data from control and injected eyes, and the treatments at each time with regard to the qualitative data (eg, injectate distribution scores, neuro-ophthalmic reflexes, periocular skin sensitivity, and corneal sensitivity). Mixed-effects linear regression was performed to compare quantitative variables (eg, IOP and HPD). Post-hoc Bonferroni contrast adjustments for multiple comparisons were applied when indicated. For all analyses, P -values $\leq .05$ were considered significant.

3 | RESULTS

On the first session, three dogs were administered RBA (2 OD, 1 OS) and three dogs PBA (2 OS, 1 OD). On the second session, three dogs were administered RBA (2 OD, 1 OS) and three dogs PBA (2 OS, 1 OD). Administration of the injection at the second location of PBA was made more

difficult by exophthalmos produced following the first injection. No significant differences in intraconal injectate distribution score or extent of optic nerve contact were detected between RBA and PBA techniques ($P = .5$ for all parameters; Table 1). Computed tomography confirmed intraconal injectate distribution in 2/6 RBA-injected eyes and 5/6 PBA-injected eyes. In the 4 remaining RBA-injected eyes, the injectate was all extraconal. In the one remaining PBA-injected eye, the injectate was distributed largely within the eyelids.

No significant difference in baseline values of IOP and HPD was detected between eyes randomly assigned to RBA or PBA, or between treated and control eyes within each treatment. Sedation resulted in ventral globe rotation in all dogs, making evaluation of IOP and HPD impossible unless the globe was gently rotated to a more central position using forceps; therefore, measurements were recorded approximately 1-2 minutes following injections and not immediately afterward. The mean IOP following sedation but prior to periocular injection was significantly higher than at baseline ($P < .001$ in both treatments and control). This significant difference persisted at $T_{5 \text{ min}}$ and $T_{10 \text{ min}}$ ($P < .001$ in both treatments and control; Figure 1) following injection. However, a significant difference was not detected between treated and control eyes for either treatment ($P = 1.000$ for RBA, and $P = .360$ for PBA) or between treatments ($P = .404$). Intraocular pressure measured 24 hours following injection tended to be lower than baseline; this difference approached significance $P = .051$; Figure 1).

Following sedation but prior to periocular injection, there was a significant decrease in HPD in control eyes and eyes scheduled for RBA or PBA ($P < .001$; Table 2).

TABLE 1 Number of eyes assigned an intraconal distribution volume score (0 = none, 1 = moderate, and 2 = large) and optic nerve contact score (90°, 180°, 270°, or 360° of optic nerve circumference) following retrobulbar (RBA; 2 mL) or peribulbar (PBA; 5 mL) injection of bupivacaine 0.5% and iopamidol (4:1) followed by computed tomography (CT) in 6 dogs with normal eyes

Parameter	Score	RBA	PBA
Intraconal	0	4	1
	1	0	3
	2	2	2
	Median (range)	0 (0-2)	1 (0-2)
Optic nerve contact (degrees)	0	4	2
	90-180	0	3
	270-360	2	1
	Median (range)	0 (0-360)	90 (0-360)

Median (range) values for each score are also provided.

Mean $\pm$ SD time to first measurement after reversal of sedation ($T_{0.5}$) was 30 ± 3 minutes for RBA and 32 ± 2 minutes for PBA at which point HPD returned to values similar to baseline in RBA-injected eyes, but increased significantly in PBA-injected eyes (Table 2); at $T_{0.5}$ ($P = .007$) and at T_1-T_2 ($P < .001$). The HPD of the PBA-injected eyes was also significantly higher from the control eyes at $T_{0.5-2}$ ($P < .001$), T_3 ($P = .020$), and T_5 ($P = .013$). In two dogs (one from each treatment group), HPD in the treated eye decreased from 10-11 to 3 mm relative to the contralateral control eyes, in which HPD was more stable; 7-10 mm. This occurred at T_3-T_4 in the PBA-injected dog and at T_2-T_4 in the RBA-injected dog, during which the PLR and consensual PLR (from the control to the injected eye) were still absent/reduced in these eyes. These two dogs had later developed anterior uveitis.

Menace response was present from the first measurement following recovery from sedation ($T_{0.5}$) in all treated and control eyes. Palpebral reflex was reduced from normal in only one dog—a dog that was administered a “successful” RBA based on CT scoring of intraconal injectate distribution. Median (range) direct and consensual PLRs at $T_{0.5}-T_3$ were significantly lower in PBA-injected eyes 0 (0-1) than in control eyes 2 (2) ($P = .0313$). Direct and consensual (from the control to the injected eye) PLRs were absent or reduced in PBA-injected eyes for 4-12 (mean $\pm$ SD = 8 ± 3) hours and absent or reduced for 4-9 hours in the two successful RBA-injected eyes.

Periocular skin sensitivity scores during the first 6 hours after injections are presented in Table 3. A significant decrease in periocular skin sensitivity of PBA-injected eyes vs control eyes was observed at the dorsal region at T_2 , at the ventral region from $T_{0.5}-T_2$, and at the lateral region from $T_{0.5}-T_3$ ($P = .0313$ for all). Corneal sensitivity was significantly decreased in the PBA-injected eyes vs control eyes from $T_{0.5}-T_4$ ($P = .0313$; Figure 2). Mean $\pm$ SD (range) duration of complete corneal sensitivity loss in the PBA-injected eyes was 4.7 ± 4.1 (1-11) hours.

Adverse effects associated with RBA and PBA are presented in Table 4. Ophthalmic examinations performed 24 hours following injections revealed that two dogs from the RBA treatment and one dog from the PBA treatment had complications, all were considered successful based on CT scoring of intraconal injectate distribution. A total of two dogs were affected on three events; one of the dogs developed anterior uveitis after both RBA and PBA injections, and a corneal ulcer after the PBA injection; the other RBA-injected dog developed anterior uveitis and a corneal ulcer. An Elizabethan collar was required in these dogs to prevent scratching of the eye at 4-5 hours following injection. Affected dogs were treated with ophthalmic ointment containing neomycin sulfate, polymyxin B sulfate, and bacitracin zinc (Akorn, Inc., Lake Forest, IL, USA; dogs with

FIGURE 1 Mean $\pm$ SD (error bars) intraocular pressure (mm Hg) of noninjected eyes (Control; $n = 12$ eyes) and contralateral eyes before and following retrobulbar (RBA; 2 mL; $n = 6$ eyes) or peribulbar (PBA; 5 mL; $n = 6$ eyes) injection of bupivacaine 0.5% and iopamidol (4:1) in 6 dogs with normal eyes. *Intraocular pressure significantly different from baseline for RBA, PBA, and control ($P \leq .05$)

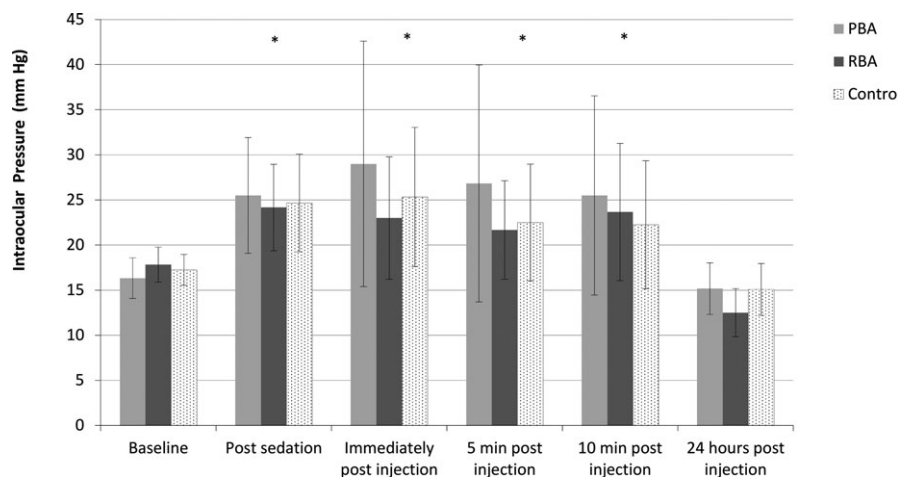


TABLE 2 Mean $\pm$ SD (range) horizontal pupil diameter (mm) in noninjected eyes (Control; $n = 12$ eyes), and contralateral eyes before and following retrobulbar (RBA; 2 mL; $n = 6$ eyes) or peribulbar (PBA; 5 mL; $n = 6$ eyes) injection of bupivacaine 0.5% and iopamidol (4:1) in 6 dogs with normal eyes

Time	RBA	PBA	Control
Baseline	8 $\pm$ 1 (6-8)	8 $\pm$ 1 (7-8)	8 $\pm$ 1 (6-8)
Following sedation	2 $\pm$ 0 (2-3) ^a	3 $\pm$ 1 (2-5) ^a	3 $\pm$ 3 (2-5) ^a
T _{1 min}	2 $\pm$ 1 (1-4) ^a	4 $\pm$ 2 (2-6) ^a	2 $\pm$ 1 (1-5) ^a
T _{5 min}	3 $\pm$ 3 (1-9) ^a	4 $\pm$ 3 (2-9) ^a	2 $\pm$ 1 (1-5) ^a
T _{10 min}	4 $\pm$ 3 (2-8) ^a	6 $\pm$ 4 (2-11)	3 $\pm$ 1 (2-6) ^a
T _{0.5}	8 $\pm$ 2 (6-11)	11 $\pm$ 1 (9-12) ^{a,b}	7 $\pm$ 3 (5-9)
T ₁	8 $\pm$ 2 (6-11)	12 $\pm$ 1 (10-13) ^{a,b}	7 $\pm$ 1 (6-9)
T ₂	7 $\pm$ 3 (3-12)	12 $\pm$ 1 (10-13) ^{a,b}	8 $\pm$ 1 (6-10)
T ₃	7 $\pm$ 3 (2-11)	10 $\pm$ 4 (3-13) ^b	7 $\pm$ 1 (6-9)
T ₄	6 $\pm$ 2 (3-7)	9 $\pm$ 4 (3-13)	7 $\pm$ 1 (6-8)
T ₅	6 $\pm$ 1 (5-8)	10 $\pm$ 2 (5-12) ^b	7 $\pm$ 1 (5-9)
T ₆	7 $\pm$ 1 (6-8)	10 $\pm$ 2 (6-12)	7 $\pm$ 1 (6-9)

T_{1-10 min} = Time from injections in minutes.

T_{0.5-6} = Time from injections in hours.

^aSignificantly different from baseline values ($P \leq .05$).

^bSignificantly different from control eyes ($P \leq .05$).

corneal ulceration) or ophthalmic ointment containing neomycin sulfate, polymyxin B sulfate, and dexamethasone (Alcon laboratories Inc., Novartis, Fort Worth, TX, USA; dog without corneal ulceration) four times daily, 1% atropine sulfate ophthalmic ointment (Bausch & Lomb Inc., Tampa, FL, USA) twice daily, and 75 mg carprofen (Rimadyl Chewable Tablets, Zoetis, Lincoln, NE, USA) twice daily. Dogs were examined daily until resolution of these complications, which occurred 1-3 days following initiation of medical treatment. At the ophthalmic examination conducted 4 weeks after the second injection, there were no abnormal findings in any dog.

4 | DISCUSSION

In the present study, PBA was more reliable than RBA in introducing injectate into the extraocular muscle cone, and in inducing anesthesia of the cornea and periocular skin. The stimulus for performing this study arose from the clinical impression that RBA had a low success rate during enucleation surgeries, that is, observation of autonomic responses to surgical stimulation at a light plane of anesthesia when a complete block of nerve transmission would remove these responses. However, the success rate for RBA reported in the literature is quite high: 82%-100%.^{6,8,10} In these three clinical studies, evaluation of analgesia was performed only following surgery, and not during eye removal. As our ability to assess analgesia in companion animals is limited, the success rate of RBA may be lower than reported. For example, there were control dogs in one of these studies that were administered saline injections and were not identified as painful following surgery, suggesting a low sensitivity of the assessment method.⁶ In humans, assessing the success of RBA (and other regional anesthesia techniques) relies on regional anesthetic administration to alert or sedated patients who can provide feedback, and receive additional local anesthetic injections when needed.^{17,18}

Successful RBA requires intraconal administration of the anesthetic agent.⁹ Data from the present study support this as no change in corneal sensitivity was observed in those eyes, in which extraconal administration occurred. This was also reported in cats, where success rate of RBA was 50% (3 of 6).¹⁶ The two successful RBA injections in the present study abolished corneal sensitivity for several hours following injection, which implies that when administered intraconally, 2 mL of bupivacaine is sufficient to produce corneal anesthesia in dogs up to (and maybe in excess of) 25 kg.

In contrast to RBA, PBA does not require administration of anesthetic into a specific compartment but relies on

TABLE 3 Median (range) periocular skin sensitivity scores (0 = no response; 1 = partial response; and 2 = normal response) measured in 4 regions (dorsal, ventral, lateral, and medial) of noninjected eyes (Control; n = 12 eyes) or contralateral eyes before and following retrobulbar (RBA; 2 mL; n = 6 eyes) or peribulbar (PBA; 5 mL; n = 6 eyes) injection of bupivacaine 0.5% and iopamidol (4:1) in 6 dogs with normal eyes

	Dorsal			Ventral		Lateral		Medial	
	Control	RBA	PBA	RBA	PBA	RBA	PBA	RBA	PBA
Baseline	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)
$T_{0.5}$	2 (2)	2 (0-2)	0.5 (0-2)	1 (0-2)	0 (0-1) ^a	1.5 (0-2)	0 (0-1) ^a	2 (0-2)	2 (2)
T_1	2 (2)	2 (0-2)	0.5 (0-2)	1 (0-2)	0 (0) ^a	0.5 (0-2)	0 (0) ^a	2 (0-2)	2 (1-2)
T_2	2 (2)	1.5 (1-2)	0.5 (0-1) ^a	1 (0-2)	0 (0-1) ^a	1 (0-2)	0 (0) ^a	1.5 (0-2)	2 (1-2)
T_3	2 (2)	1 (0-2)	0.5 (0-2)	2 (1-2)	0 (0-2)	2 (0-2)	0 (0-1) ^a	1.5 (1-2)	2 (2)
T_4	2 (2)	1.5 (1-2)	1.5 (0-2)	2 (2)	0 (0-2)	2 (2)	0 (0-2)	2 (1-2)	2 (2)
T_5	2 (2)	2 (1-2)	2 (0-2)	2 (2)	0.5 (0-2)	2 (2)	1 (0-2)	2 (1-2)	2 (2)
T_6	2 (2)	2 (1-2)	2 (0-2)	2 (2)	1 (0-2)	2 (2)	2 (0-2)	2 (1-2)	2 (2)

$T_{0.5-6}$ = Time from injections in hours.

^aSignificantly different from baseline/control ($P \leq .05$).

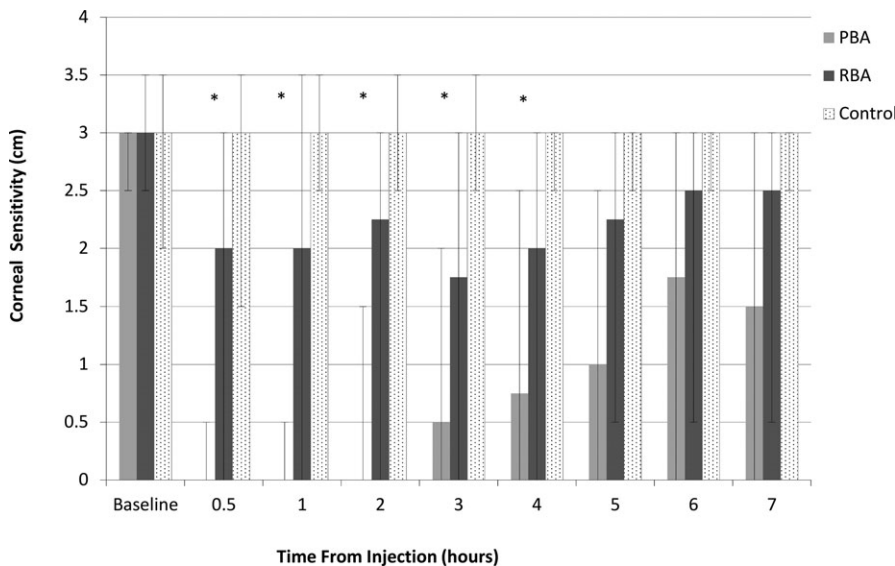


FIGURE 2 Median and range (error bars) corneal sensitivity (cm of aesthesiometer filament) before and following retrobulbar (RBA; 2 mL; n = 6 eyes) or peribulbar (PBA; 5 mL; n = 6 eyes) injection of bupivacaine 0.5% and iopamidol (4:1), or contralateral noninjected eyes (Control; n = 12 eyes) in 6 dogs with normal eyes. *Significantly different in the PBA-injected eyes from control eyes ($P \leq .05$)

TABLE 4 Number of eyes with adverse events potentially associated with unilateral retrobulbar (RBA; 2 mL) or peribulbar (PBA; 5 mL) injection of bupivacaine 0.5% and iopamidol (4:1) in 6 dogs with normal eyes

Adverse event	RBA	PBA
Exophthalmos	3/6	6/6
Conjunctival edema (chemosis)	2/6	5/6
Conjunctival hemorrhage (ecchymosis)	1/6	2/6
Anterior uveitis	2/6 ^{a,b}	1/6 ^{a,b}
Corneal ulcer	1/6	1/6

^aOne dog developed anterior uveitis following both RBA and PBA.

^bAll dogs developing anterior uveitis were dogs that had successful injections based on CT.

anesthetic diffusion and distribution into the corpus adiposum of the orbit, including the intraconal space.^{2,19} In the present study, PBA was more reliable than RBA but still

had poor distribution around the optic nerve in 2 of 6 cases. Insufficient injectate volume can negatively affect distribution.^{2,20} A recent paper in dogs reported decreased corneal sensitivity in 15/15 dogs following a single-PBA injection in the ventrolateral orbit with or without the use of ultrasound guidance.¹¹ In that study, 0.3 mL/kg of ropivacaine 1% was used, whereas in the present study, a marginally lower volume (mean of 0.23; range 0.2-0.27 mL/kg) of bupivacaine at a lower concentration (0.4%) was used. The differences in the local anesthetic, its concentration, and the volume used could all play a role in the success.²¹⁻²³ Use of a single- vs a double-injection technique may also affect injectate distribution. In people, a single-injection technique was more reliable than a double-injection technique.^{2,24} It was noted in the present study that the second injection was made more difficult by exophthalmos produced following the first injection, which may have resulted in decreased distribution of the second half of the

injectate. Insertion of both needles prior to local anesthetic injection may reduce this concern, but was not assessed in the present study.

The duration of corneal sensory block following PBA in the present study persisted for 1–11 hours. Corneal sensory block in the study by Wagatsuma et al was similar, persisting for approximately 3–11 hours. However, duration in Wagatsuma's study was calculated as the interval from the first assessment until return of an aesthesiometric value to baseline,¹¹ whereas in the present study, the duration was calculated from injection to the time, at which corneal sensitivity was measured as ≤ 0.5 cm, and the duration of partial corneal anesthesia was longer. In the present study, distribution of local anesthetic into the eyelids following PBA, observed externally as chemosis, provided a significant decrease in periocular skin sensitivity for several hours, and may be beneficial in enucleation surgeries, as it would likely provide more complete regional anesthesia during dissection of the eyelids and periorbital fascia. The two successful RBA injections provided decreased skin sensitivity for shorter duration than PBA; therefore, coadministration of incisional line infiltration of the eyelids with RBA may provide better analgesia during enucleation, as recommended by some authors.¹

The IOP following PBA did not increase significantly, although, it tended to be higher than in RBA-injected or control eyes. Studies in people,^{3,24,25} and in cats¹⁶ revealed a brief but significant increase in IOP following PBA. In the present study, sedation resulted in ventral rotation of the globe, and IOP measurement took approximately 1–2 minutes longer than anticipated. Therefore, it is possible that the peak elevation in IOP occurred before IOP was measured. In dogs undergoing PBA with 0.3 mL/kg of 1% ropivacaine, the IOP was significantly increased following injection from a baseline IOP value of 18.8 ± 3.5 mm Hg to 23.3 ± 5.2 mm Hg in treated eyes. The IOP was also significantly different from the contralateral eyes treated using ultrasound guidance (18.6 ± 5.4 mm Hg). In that study, the measurement of IOP was not performed until the eyes became central, and the time for this to occur was not stated. The authors suggested that IOP was lower in the eyes injected with ultrasound guidance because the local anesthetic was deposited more accurately and balanced the IOP increase,¹¹ although, compression on the injected eye, as may occur with the use of an ultrasound probe, can decrease IOP.² Due to the potential risk of IOP elevation, PBA should be used with caution or avoided for procedures on viable globes. If, however, enucleation is planned, then IOP increase is less of a concern.

In the present study, HPD increased significantly and for several hours following injection of PBA and the two successful RBA injections. This is similar to data reported in dogs following RBA or PBA^{7,9,11} and in cats following

PBA and successful RBA.¹⁶ Mydriasis occurs following RBA and PBA due to anesthesia of the oculomotor nerve, cranial nerve III,²⁶ and is one of the benefits of using these regional anesthetic techniques for intraocular surgery.^{7,26} Surprisingly, HPD decreased for 2–3 hours in the treated eye of two dogs in the present study (one from each treatment group). To our knowledge, this has not been reported in cats or dogs, and we are unsure of the mechanism responsible. Because these two dogs developed anterior uveitis later, this paradoxical effect may have been the result of this inflammation. Alternatively, because in these two dogs, the paradoxical pupil size-resolved approximately coincident with waning of eyelid analgesia, it is possible that this resulted from differential block of the sympathetic fibers (carried in the long ciliary nerves) and parasympathetic fibers (carried in the short ciliary nerves). Regardless, direct and consensual PLR were absent or decreased for several hours. Reduced PLR was also reported in cats following PBA and RBA,¹⁶ and in dogs following PBA with ropivacaine 1%.¹¹ In the canine study, the PLR was absent or decreased for approximately 7 hours, which is similar to the mean duration of change in PLR in the present study (8 hours), even though different local anesthetics at different concentrations were used in these 2 studies.

Reversible adverse events, such as exophthalmos, chemosis, and ecchymosis occurred more frequently following PBA than RBA. This is likely attributable to the large volume of injectate used and the more anterior location of the injection relative to RBA. Similar adverse events have been reported in dogs,¹¹ cats,¹⁶ and people.^{24, 27} These usually resolve spontaneously several hours after injection, as was observed in the present study. Development of anterior uveitis, as observed in the present study, has not been reported, to our knowledge, following PBA or RBA in people or animals. However, punctate superficial ulcers were found in both eyes of 2 of 15 dogs following PBA injections.¹¹ In the present study, on those occasions where anterior uveitis was seen without corneal ulceration, this may have resulted from scleral contact by the hypertonic contrast agent included in the injectate. Interestingly, all three affected dogs had a successful injection based on CT. Therefore, it may be the proximity of contrast deposition in relation to globe structures. In those situations where corneal ulceration and anterior uveitis coexisted, it is possible that the corneal ulcer was primary and the anterior uveitis developed secondary to the ulcer. Certainly, corneal ulceration could develop as a result of exposure and desiccation secondary to exophthalmos or reduced lid closure or tear production following RBA or PBA.^{11,16} In the present study, corneal lubrication with isotonic solution was performed; although, it might not have been administered frequently enough. Serious adverse

events such as globe perforation, brainstem anesthesia, or optic nerve damage were not observed in the present study but can occur especially following intraconally administered RBA. Therefore, vital signs should be monitored closely during these injections.²⁷

The major limitations of the present study include the small sample size and use of young healthy animals of a similar size and skull conformation. It is difficult to know whether injectate distribution, anesthetic effects, and adverse events would be similar in animals with systemic or ocular disease, or dogs of different skull conformation or body weight/size. In addition, the need to use a contrast agent to assess injectate distribution may have altered outcomes in the present study including the possibility of direct irritation of the globe and periocular tissues potentially resulting in anterior uveitis. Addition of the contrast agent also diluted the local anesthetic to some extent and may have decreased the degree of local anesthesia produced.

In conclusion, the PBA technique resulted in intraconal distribution in 67% of eyes and produced clinically notable corneal and periocular anesthesia in 100% of eyes. The PBA technique was more reliable than the RBA technique in producing these effects; however, the PBA technique still requires further investigation and refinement to increase its success and duration of effect in dogs.

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