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RESEARCH PAPER

Retrobulbar and peribulbar regional techniques in cats: a preliminary study in cadavers

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Abstract

Objective To compare injectate distribution and potential complications of retrobulbar and peribulbar injections in cat cadavers.

Study design Prospective randomized masked study.

Animals Ten cat cadavers (20 eyes).

Methods A dorsomedial retrobulbar injection (RB) of 1 mL of 0.5% bupivacaine and iopamidol (1:1) was performed in seven eyes. A dorsomedial peribulbar injection (PB-1) of 4 mL of the same injectate was performed in seven eyes, and two peribulbar injections (PB-2) of the same injectate, divided equally between the dorsomedial and ventrolateral regions (2 mL each) were performed in six eyes. Intraocular pressure (IOP) was measured before, immediately and 15 minutes after injection. Cadavers underwent computed tomography before and following injections. A radiologist scored injectate distribution within the intraconal space (none, moderate, or large) and around the optic nerve (degrees). An injection was defined as likely to provide adequate regional anesthesia if the volume of distribution of intraconal injectate was 'large' and it contacted over 270° of the optic nerve circumference.

Results The success rate (95% confidence interval) of RB, PB-1, and PB-2 injections was 71% (29.0–96.3%), 86% (42.1–99.6%), and 67% (22.3–95.7%), respectively. With all three techniques, IOP increased significantly after injection, but returned to baseline by 15 minutes following RB injection. No intraocular, intravascular, intrathecal, or intraneural injectate was observed.

Conclusion and clinical relevance The single-peribulbar injection technique may be superior to retrobulbar or double-peribulbar injections, however, all techniques require further studies in live cats to determine safety and efficacy prior to clinical use.

Keywords cats, intraocular pressure, peribulbar anesthesia, regional anesthesia, retrobulbar anesthesia.

Introduction

Retrobulbar anesthesia (RBA) provides excellent extraocular muscle akinesia that is sometimes sufficient to replace use of neuromuscular blocking agents, and thus avoid the need for positive pressure ventilation (Accola et al. 2006; Hazra et al. 2008). Retrobulbar anesthesia has the added benefit of providing excellent analgesia that could reduce the need for perioperative systemic administration of analgesics (Accola et al. 2006; Myrna et al. 2010). This may be especially important in cats, which tend to be more susceptible to adverse effects from commonly used systemic analgesics, such as opioids

and non-steroidal anti-inflammatory drugs (NSAIDs) (Papich 2000; Robertson & Taylor 2004; Taylor & Robertson 2004).

In humans, RBA has been the gold standard for regional anesthesia of ocular and periocular tissues and is achieved by injecting a small volume (2–5 mL) of local anesthetic agent intraconally (i.e. inside the extraocular muscle cone) (Nouvellon et al. 2010b; Alhassan et al. 2011). Retrobulbar anesthesia has also been described in dogs (Accola et al. 2006; Skarda & Tranquilli 2007a; Giuliano 2008; Hazra et al. 2008; Dugdale 2010; Myrna et al. 2010), horses (Raffe et al. 1986), goats (Ravan et al. 2008), and cattle (Pearce et al. 2003; Skarda & Tranquilli 2007b), but to the authors' knowledge has not been reported in cats. In dogs, the needle is inserted without visual guidance ('blindly') through the inferior eyelid just above the lower orbital rim and passed into the orbital cavity behind the globe for injection of local anesthetic agents close to the optic and other orbital nerves (Accola et al. 2006; Hazra et al. 2008). This technique has been widely used in people, where complications of needle placement are rare but potentially devastating (Rubin 1995; Moorthy et al. 2003; Luyet et al. 2008). Possible complications of RBA include retrobulbar hemorrhage, intravenous injection of anesthetic, globe perforation, optic and other neuropathies, extraocular muscle damage, and intrathecal injection, which can induce seizures or cardiorespiratory arrest (Rubin 1995; Moorthy et al. 2003; Accola et al. 2006; Skarda & Tranquilli 2007a; Alhassan et al. 2011; Kumar 2011). The prevalence of complications in animals is unknown.

Peribulbar anesthesia (PBA) is believed to be safer than RBA and is beginning to replace RBA for human cataract surgery (Ripart et al. 2001; Kumar & Dodds 2006; Nouvellon et al. 2010a,b). For PBA, the needle is introduced into the extraconal space (i.e. outside the extraocular muscle cone) thereby limiting risk of injury to intraconal structures, especially the optic nerve and major blood vessels supplying the globe. The injectate spreads throughout much of the orbit, including the intraconal space. The injection of a large volume (6–12 mL in humans) encourages anterior spread to the eyelids, providing more complete analgesia as well as akinesia of the orbicularis oculi muscle (Ripart et al. 2001; Nouvellon et al. 2010a,b). Classically, PBA involves two injections, one ventrolateral (VL; named inferotemporal in the human literature), and the second dorsomedial (DM; named superonasal in the human literature); however studies in humans have shown that the distribution of the local anesthetic is similar with one injection site or two, and one injection may be safer (Demirok et al. 1997; El Said & Kabeel 2010; Ghali & Hafez 2010; Nouvellon et al. 2010b). Recently, the PBA technique has been reported in dogs for eyelid surgery and (in combination with RBA) for enucleations; however the method described involves a four-site injection technique (dorsally, ventrally, laterally and medially) (Giuliano 2008).

To the authors' knowledge, information regarding retrobulbar or peribulbar anesthesia in cats has not been published. Therefore the goals of this study were to evaluate and compare injectate distribution and potential complications of a retrobulbar and two peribulbar injection techniques in cat cadavers.

Materials and methods

Preliminary work

To investigate effects of cat body position (ventral *versus* dorsal recumbency), injection site (VL *versus* DM), and injectate volume (1, 2, 3, or 4 mL) on anatomic drug distribution a preliminary study was performed in five adult cat cadavers from an unrelated terminal study. Distribution of the local anesthetic-contrast mixture (equal parts of 0.5% bupivacaine and iopamidol) was assessed by computed tomography (CT) imaging.

Dorsal recumbency appeared to facilitate better distribution of the injectate into the caudal orbit and so was used for future investigations of injection site. The VL injection site did not result in the expected distribution of the injectate regardless of whether a retrobulbar or peribulbar technique was employed. Following retrobulbar injection at the VL location, the needle tended to penetrate through the ventral orbit into tissues below the orbit or into the oropharynx. Following peribulbar injection at this location, the injectate accumulated ventral to the orbit, instead of diffusing behind the globe, even when the volume of injectate was increased to 4 mL. The DM injection location was associated with repeatable injectate distribution following retrobulbar or peribulbar injection techniques. Retrobulbar injection of 1 mL and peribulbar injection of 4 mL resulted in appropriate intraconal distribution. Based upon these results, the remainder of the study was designed to more fully investigate the safety and distribution of injectate following a retrobulbar or

one of two peribulbar injection techniques in cat cadavers positioned in dorsal recumbency.

Comparison of injection protocols

Ten cat cadavers (four females and six males; nine Maine Coon crosses and one domestic long haired) euthanized at a mean ± standard deviation (SD; range) time of 98 ± 49 (44–191) minutes earlier as part of an unrelated study were used in a randomized, masked design. Mean ± SD (range) age and body weight of cat cadavers were 10.0 ± 1.0 (8.9–12.1) years and 4.7 ± 0.9 (3.6–6.6) kg, respectively. No gross ocular, periocular, or orbital abnormalities were detected in any cat. For imaging and injections, all cadavers were positioned in dorsal recumbency with the nose directed to the ceiling. In all injection techniques the injectate was a 1:1 mixture of 0.5% bupivacaine hydrochloride (Bupivacaine HCl 0.5%; Hospira Inc., IL, USA) and iopamidol (Isovue 200; Bracco Diagnostics, NJ, USA). Three injection techniques were tested: a single 1 mL retrobulbar injection at a DM site in seven eyes (RB; Fig. 1), a single 4 mL peribulbar injection at a DM site in seven eyes (PB-1; Fig. 2), and a pair of peribulbar injections (2 mL at the DM site and 2 mL at the VL site; PB-2; Fig. 2) in the remaining six eyes. Randomization of treatments and the eye to be treated (right or left) was performed using a computer-generated random list. All injections were performed by a veterinary anesthesiologist experienced with these techniques in other species.

Retrobulbar injections were performed using guidelines modified from those described in dogs (Accola et al. 2006). Briefly, an approximately 20° angle was created by bending a 1.5-inch (38-mm), 22-gauge spinal needle (BD spinal needle; BD Medical, NJ, USA) at its midpoint. The needle was inserted through the upper eyelid at the junction of its medial (nasal) and middle thirds (DM site). The needle was advanced for approximately three quarters of its length towards the back of the globe in close proximity to the upper medial wall of the orbit and the total volume was injected (Fig. 1). Peribulbar injections were performed based upon guidelines from the human literature (Troll 1995; Nouvellon et al. 2010b). A 5/8-inch (15.8-mm), 25-gauge needle (Kendall Monoject; Covidien, MA, USA) was inserted through the upper eyelid at the junction of its medial (nasal) and middle thirds (DM site) or through the lower eyelid at the junction of its middle

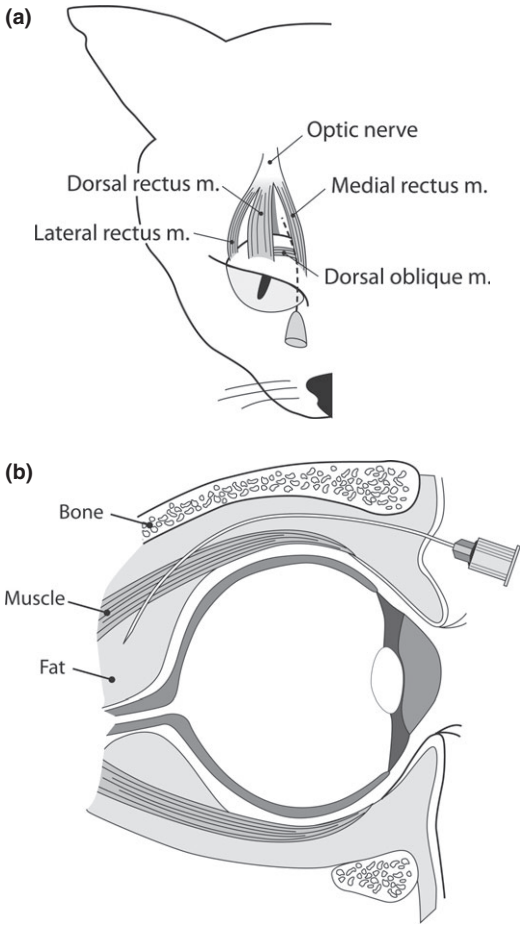

Figure 1 Dorsal (a) and parasagittal (b) views of the right eye of a cat showing a technique for retrobulbar injection at the dorsomedial site (m = muscle).

and lateral (temporal) thirds (VL site). At both sites the needle was advanced to its full length into the peribulbar space in close proximity to the wall of the orbit. Slight pressure was applied to the needle during injection to ensure that it stayed in the same location during injection (Fig. 2). All injections were performed with the bevel of the needle oriented towards the globe, and after assuring that no blood was aspirated during the application of negative pressure to the syringe plunger.

Before and 10 minutes after injections all cadavers underwent CT imaging (LightSpeed 16 slice helical CT scanner; General Electric Co., WI, USA) to establish the distribution of the combined anesthetic-contrast agent. All CT examinations consisted of contiguous, 0.6 mm collimated transverse images acquired using an edge-enhancing (bone) reconstruction algorithm.

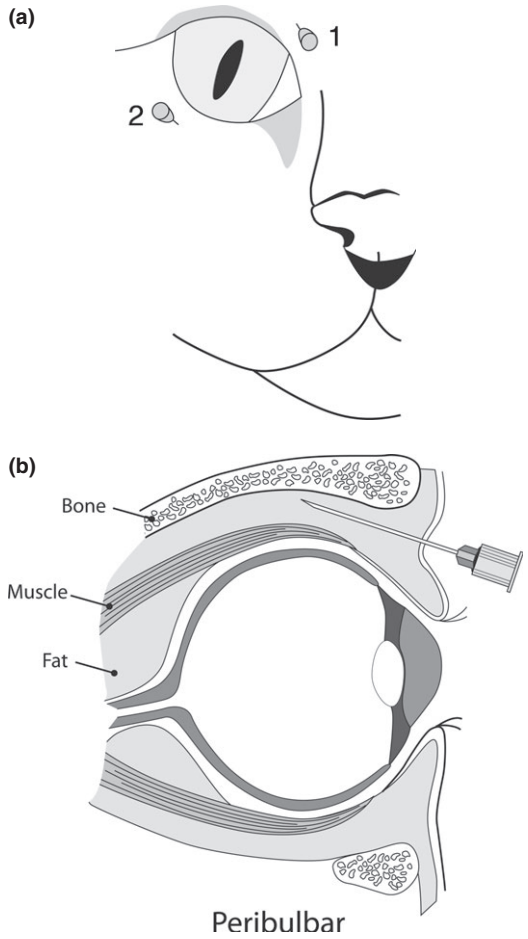

Figure 2 (a) Frontal view of the right eye of a cat showing techniques for peribulbar injections at the dorsomedial 1) and ventrolateral; 2) sites. (b) Parasagittal view of the eye and orbit showing technique for peribulbar injections at the dorsomedial site.

Digital images (DICOM: digital imaging and communication in medicine) were reviewed on a dedicated workstation using commercially available medical imaging software (eFilm 2.1; MERGE Healthcare, IL, USA). Image data sets were reformatted as necessary to view regions of interest in dorsal and oblique anatomic planes. A radiologist, masked as to injection technique, scored the images according to specific guidelines: extraconal and intraconal volume of distribution (none = 0; moderate = 1; large = 2), and the approximate contact area of the injectate around the optic nerve (0, 90, 180, 270, or 360°). An injection was defined as 'successful' (likely to provide adequate regional anesthesia) if the volume of distribution of intraconal injectate was 'large' (score = 2) and it contacted over 270° of the optic nerve circumference.

Intraocular pressure (IOP) was measured using applanation tonometry (Tono-Pen Vet; Reichert Technologies, NY, USA) prior to and immediately after injection, and at the end of the imaging procedures (approximately 15 minutes after injection). When eyes were too soft to measure, IOP was analyzed as a zero.

Statistical analysis

Exact Kruskal–Wallis analysis of variance was used to globally assess the distribution of the injectate scores among treatment groups. The exact Mann–Whitney U test was used for post-hoc comparisons between treatment groups when the global test was significant.

Intraocular pressure was compared among injection techniques with multi-level, mixed effects linear regression to evaluate effect of time, treatment, and their interaction. When a significant interaction was observed, post-hoc analyses were performed to compare treatments at each time point, and time points for each treatment.

The proportion of eyes with injectate distribution and volume sufficient to provide successful regional anesthesia (as defined in this study) is presented with exact 95% binomial confidence intervals (CI). For all analyses, $p < 0.05$ was considered significant.

Results

Based upon imaging data, the intraconal space was filled with injectate (Fig. 3) in 5/7 of the RB injections, and in all PB-1, or PB-2 injections. Extraconal volume of distribution was assessed as 'large' with all PB-1 and PB-2 injections (13/13), with two unsuccessful RB injections (injections were extraconal instead of intraconal), and was evident (moderate amount) in two of the five successful RB injections (i.e. the injectate was distributed from the cone to the extraconal area). Intraconal volume of distribution was assessed as 'large' with the majority of the injections (5/7 in RB, 7/7 in PB-1, and 4/6 in PB-2), i.e. the injectate was distributed from the extraconal area into the cone with the PB injections (Table 1A). Perineural distribution of >270° was achieved with the majority of the injections (5/7 in RB, 6/7 in PB-1, and 4/6 in PB-2; Table 1B). In all orbits in which perineural distribution was assessed as >270°, the intraconal volume of distribution was large, except in one PB-1 injection, where although the intrac-

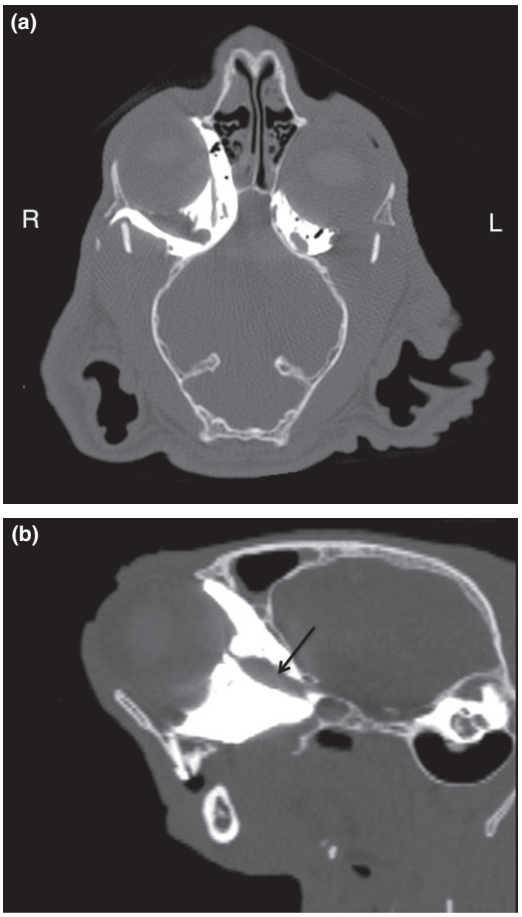

Figure 3 (a) Dorsal plane computed tomographic (CT) image of a cat cadaver head following injections of 1:1 mixture of bupivacaine 0.5% and contrast (iopamidol). The left orbit (L) received 1 mL of injectate via a retrobulbar injection (RB). The right orbit (R) received 4 mL of injectate via a single peribulbar injection (PB-1). Both injections were performed at the dorsomedial (DM) site. (b) Reformatted, oblique plane CT image through the left orbit of a cat injected with PB-1, including the optic nerve in long axis (arrow).

onal volume of distribution was large, perineural distribution was 180°.

Using 'large' intraconal volume and distribution of injectate of at least 270° around the optic nerve as defining factors, injections were deemed likely to provide successful regional anesthesia in five of seven eyes injected via the retrobulbar technique, six of seven eyes injected with a single peribulbar injection, and four of six eyes injected with double peribulbar injections. No significant difference in likely success rate was detected among injection techniques or between left and right eyes (Table 2).

Table 1 Number of eyes that each extraconal or intraconal score achieved (none = 0; moderate = 1; large = 2) (A), and number of eyes at each contact area (in degrees) around the optic nerve (B), as determined by computed tomography (CT), following injection of a 1:1 mixture of bupivacaine 0.5% and iopamidol into the retrobulbar (RB) or peribulbar (PB) region of 10 cat cadavers (20 eyes). Volumes injected and number of eyes treated were 1 mL in seven eyes (RB), 4 mL in seven eyes (PB-1), and 2 × 2 mL in six eyes (PB-2)

(A)

Region	Injection method	Score 0	1	2
Extraconal	RB	3	1	3
	PB-1			7
	PB-2			6
Intraconal	RB	2		5
	PB-1			7
	PB-2		2	4

(B)

Injection method	Contact area around the optic nerve				
	0°	90°	180°	270°	360°
RB	2				5
PB-1			1		6
PB-2		2			4

Baseline IOP was not significantly different among groups (Fig. 4). However, as expected for cadavers, most (70%) of the eyes were sufficiently hypotonic that an IOP reading could not be recorded by applanation tonometry and were assigned an IOP of zero for analysis. Immediately after injection, mean ± SD IOP increased significantly relative to baseline in all injection groups ($p < 0.001$), but was significantly lower in the RB treatment group (11 ± 5 mmHg) than the PB-1 (26 ± 5 mmHg) or PB-2 (29 ± 7 mmHg) treatment groups ($p < 0.001$). Approximately 15 minutes following injection, IOP returned to a value not significantly different from baseline in the RB injection group, but remained significantly higher than baseline (although within or below the reference interval) for the PB-1 ($p < 0.001$) and PB-2 ($p = 0.002$) injection groups.

Blood was never aspirated during the application of negative pressure prior to injection (although this

Table 2 Presumed successful anesthetic outcome following injection of a 1:1 mixture of bupivacaine 0.5% and iopamidol into the retrobulbar (RB) or peribulbar (PB) region of 10 cat cadavers (20 eyes). Volumes injected were 1 mL (RB), 4 mL (PB-1) or 2 × 2 mL (PB-2)

Eye	Injection method	'Success'*	95% CI
L and R	RB (n = 7)	5 (71%)	29.0–96.3
L and R	PB-1 (n = 7)	6 (86%)	42.1–99.6
L and R	PB-2 (n = 6)	4 (67%)	22.3–95.7
L	RB (n = 4)	2 (50%)	6.8–93.2
L	PB-1 (n = 3)	3 (100%)	29.2–100
L	PB-2 (n = 3)	2 (67%)	9.4–99.2
R	RB (n = 3)	3 (100%)	29.2–100
R	PB-1 (n = 4)	3 (75%)	19.4–99.4
R	PB-2 (n = 3)	2 (67%)	9.4–99.2

CI, confidence interval; L, left eye; R, right eye. *An injection was defined as 'successful' (likely to provide adequate regional anesthesia) if the intraconal injectate score was 'large' (score = 2) and it contacted over 270° of the optic nerve circumference.

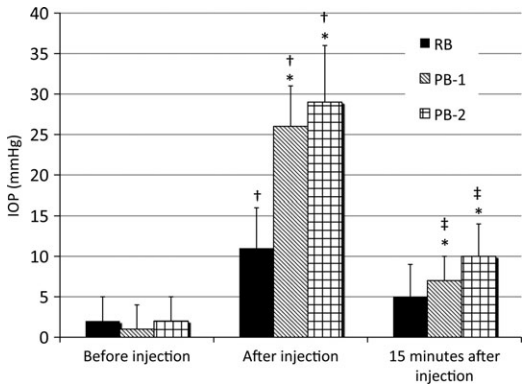

Figure 4 Mean ± SD intraocular pressure (IOP) before, immediately after, and approximately 15 minutes following injection of a 1:1 mixture of bupivacaine 0.5% and iopamidol into the retrobulbar (RB) or peribulbar (PB) region of 10 cat cadavers (20 eyes). Volumes injected were 1 mL (RB; seven eyes), 4 mL (PB-1; seven eyes) or 2 × 2 mL (PB-2; six eyes). The IOP in eyes that were too soft to measure was analyzed as zero. *Represents a significant difference among treatment groups at the same time point ($p \leq 0.002$). † / ‡ Represents a significant difference among time points within the same treatment group ($p \leq 0.01$).

cannot rule out an intravascular injection as there was no circulating blood present at the time of injection), and there was minimal resistance to injection in all eyes. Overt exophthalmos was noted immediately after peribulbar injections but never following retrobulbar injections. No intraocular, intravascular, intrathecal or intraneural injectate was observed in any CT image.

Discussion

In the present study the RB, PB-1, and PB-2 injection techniques introduced sufficient intraconal injectate that the injections were speculated to produce regional anesthesia in 71%, 86%, and 67% of the eyes, respectively. Minor differences in 'success' proportion between eyes (Table 2) are likely to be incidental, and a larger sample size is required to determine if there is a true influence of the injection site on 'success'. In our preliminary study, the VL injection location, which is the preferred location in humans for RBA or PBA (Ali-Melkkila et al. 1993; Bowman et al. 1996; Kallio & Rosenberg 2005; Kumar & Dodds 2006; Malik et al. 2010; Nouvellon et al. 2010a), and in dogs for RBA (Accola et al. 2006; Hazra et al. 2008; Myrna et al. 2010), did not result in appropriate injectate distribution. The unique anatomy of the cat's skull might be responsible for this observation. In comparison to humans, which have a complete skeletal orbit, cats and dogs have an incomplete orbit (missing the lateral aspect of the orbit, and the orbital floor) (Samuelson 2007; Dyce et al. 2010). Cats furthermore vary from dogs, and seem to have a smaller skeletal component of the inferior orbit (Dyce et al. 2010). This may explain why the anesthetic/contrast injectate diffused and accumulated below the orbit, and not behind the globe when a PB injection was performed at that location, and why the RB injection at the VL location sometimes penetrated into the oral cavity.

The DM injection location has been described for PBA in humans (Ali-Melkkila et al. 1993; Nouvellon et al. 2010a). However, at this site in humans, the distance between the orbital roof and the globe is reduced, theoretically increasing the risk of globe perforation (Troll 1995; Nouvellon et al. 2010a). Although we did not perform ocular examinations or dissections following injection, we did not observe any intraocular injectate on CT imaging. This suggests that globe perforation did not occur in any cat in the present study.

There is still some controversy regarding advantages and disadvantages of RBA *versus* PBA in humans. Although RBA is classically assumed to be more efficacious than PBA, it appears that, provided a sufficient volume of local anesthetic is injected, both techniques have similar efficacy (Ali-Melkkila

et al. 1993; Alhassan et al. 2011). This can be explained by the fact that there is no intermuscular membrane separating the extraconal and intraconal spaces, so that they form a contiguous space for spreading of local anesthetic (Ripart et al. 2001). If efficacy of the two techniques is similar, the primary basis on which to choose one technique over the other is safety. Theoretically, RBA carries a higher risk of complications because of intraconal introduction of the needle. However, to the authors' knowledge, the expected greater safety of PBA has never been confirmed. This may be because of the very low rate of complications and the subsequent lack of power of comparative studies including large series or meta-analyses (Nouvellon et al. 2010b; Alhassan et al. 2011). Although PBA is thought to be associated with fewer serious complications, a larger injection volume is required to perform PBA, and this is believed to explain the greater chemosis seen following PBA compared with RBA (Malik et al. 2010; Alhassan et al. 2011). Both approaches, however, may have potentially sight and life-threatening complications (Alhassan et al. 2011).

When considering the larger volumes required for PBA, systemic toxicity may be another disadvantage when applying this technique in cats, and may limit its use in this species. Relative to body weight, the feline orbit (24 mm wide × 26 mm high) and globe (approximately 20–21 mm diameter) are much larger than in humans (the globe is about 24 mm in diameter in the adult human) (Samuelson 2007). In addition, cats are susceptible to systemic adverse effects of local anesthetics (Duke 2000; Lemke 2007; Aprea et al. 2011). Taken together, these factors may increase the risk of systemic toxicity associated with PBA in cats. We used 4 mL of injectate because lower volumes in the preliminary study did not produce appropriate intraconal distribution in cadavers. The maximum recommended dose of bupivacaine for local and regional anesthesia in cats is 2 mg kg^{-1} (Lemke & Dawson 2000; Beckman 2002; Lamont 2002; Robertson & Taylor 2004; Lemke 2007; Webb & Pablo 2009; Dugdale 2010). Administration of 4 mL of bupivacaine 0.25% (10 mg) would exceed this recommendation in all cats weighing <5 kg. However, the authors are unaware of data regarding pharmacokinetics of bupivacaine following orbital or other perineural administration in cats. Studies assessing bupivacaine toxicity following intravenous infusion in cats revealed that arrhythmias, convulsions, hypotension, and cardiovascular collapse occurred at doses of 2.5, 3.8, 9.7, and 18.6 mg kg^{-1} respectively (Chadwick 1985; Kasaba et al. 1998). It would be helpful to know the pharmacokinetics of bupivacaine following PBA in cats, in order to find a dose range that will achieve adequate local infiltration without causing systemic toxicity. In the present study, there was a nonsignificant tendency for a single PBA injection to result in better distribution of injectate intraconally and around the optic nerve in comparison to the double PBA injection technique. In humans a single-injection technique is generally preferred because the success rate is typically similar to that achieved with the double-injection technique but with less anatomic distortion, and reduced risk of complications, such as subconjunctival hemorrhage, chemosis and ecchymosis that are associated with consecutive injections. This has led to the recommendation that a second injection is performed only when the first injection has failed to provide effective anesthesia (El Said & Kabeel 2010; Nouvellon et al. 2010a,b).

The increase in IOP seen in the present study following RBA and PBA is also seen commonly in humans (O'Donoghue et al. 1994; Morgan & Chandna 1995; Bowman et al. 1996; El Said & Kabeel 2010). In humans the average orbital volume is 30 mL, and an increase in intraorbital pressure and IOP is expected with injections into the orbit. The magnitude of the IOP increase varies among individuals, with the volume of anesthetic injected, and with the technique employed. As has been shown in previous studies in humans (O'Donoghue et al. 1994; Bowman et al. 1996) we noted a greater increase in IOP, which also lasted longer, in eyes after PB injection in comparison to eyes after RB injection. However, these effects may be different in cadavers and need to be assessed *in vivo* where physiologic mechanisms of IOP homeostasis are intact.

Limitations to the present study include the small sample size, limited experience with these techniques in cats, and concerns regarding extrapolation of these data from cadavers to live animals. The projected 'success' rate in the present study was based on distribution scoring that was defined arbitrarily, and analgesia and complications experienced in live animals may vary due to blood flow, temperature differences, disease status, and physiologic mechanisms.

In conclusion, retrobulbar, single-peribulbar or double-peribulbar injection techniques produced

intraconal and optic perineural distribution of injectate, estimated as likely to exert regional anesthetic effects in live cats, in 71%, 86%, or 67% of the eyes, respectively. Other than transient ocular hypertension, complications of injectate distribution were not noted. The single-peribulbar injection technique may be superior to retrobulbar or double-peribulbar injections, however, at this time, the authors cannot recommend the use of any of the techniques in clinical practice. Clinical use of these techniques requires further studies in live cats to determine safety and efficacy.

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