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A DISSERTATION
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

**Feasibility Study of Sub-Tenon's Anesthesia for
Phacoemulsification in Dogs**

개에서 백내장 수술 시
공막밖공간 마취의 유용성 연구

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Feasibility Study of Sub-Tenon's Anesthesia for Phacoemulsification in Dogs

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ABSTRACT

Cataract is one of the most common diseases that cause blindness in dogs and is conventionally treated with surgery such as phacoemulsification. During the surgery, exposure of surgical area (i.e. lens) by extraocular muscles akinesia and pupil

dilation is essential. Additionally, because the eyes are densely innervated structures, surgical stimuli may result in ocular pain and pain management during the surgery and postoperative period is important. The purpose of the present study was to evaluate the effects of sub-Tenon's anesthesia on extraocular muscles akinesia, pupil dilation and intraoperative and postoperative analgesia in dogs undergoing phacoemulsification.

In chapter 1, the feasibility of sub-Tenon's anesthesia was investigated in dogs with clinically normal eyes by injecting lidocaine into the sub-Tenon's space. A cross-over design was used with both eyes from five Beagle dogs randomly injected, under general anesthesia, with 1 ml of 2% lidocaine (1 ml-lidocaine group), 2 ml of 2% lidocaine (2 ml-lidocaine group) or 2 ml of normal saline (control group). Each eye was assigned to all treatments with a minimum 14 day interval between injections. Changes in eye position, pupil diameter, and intraocular pressure (IOP) were evaluated during the procedure. All eyes in the 2 ml-lidocaine group exhibited akinesia and mydriasis (pupil diameter >10 mm). The onset times of akinesia and mydriasis were 6.5 ± 4.9 and 4.2 ± 4.3 min, respectively. In the 1 ml-lidocaine group, akinesia was induced in 9 eyes and mydriasis occurred in 7 eyes with an onset time of 10.7 ± 5.8 and 5.4 ± 2.4 min, respectively. No changes in eye position or pupil diameter were observed in the control group. Akinesia was maintained for 44.3 ± 26.7 min in the 1 ml-lidocaine group and for 88.5 ± 17.2 min in the 2 ml-lidocaine group. Duration of mydriasis was 51.7 ± 28.9 min in the 1 ml-lidocaine

group and 82.9 ± 15.6 min in the 2 ml-lidocaine group. No significant change in IOP was observed between the mean pre- and post-injection values in all groups. These results suggest that a sub-Tenon's injection of 2 ml of 2% lidocaine provided effective extraocular muscle akinesia and mydriasis in dogs.

In chapter 2, the effect of sub-Tenon's lidocaine injections on akinesia and mydriasis was compared to those of systemic atracurium and retrobulbar lidocaine injections in dogs. Three treatments were performed on 10 beagle dogs with a minimum 7-day washout period: intravenous injection of atracurium (0.2 mg/kg, AT group); retrobulbar injection of 2% lidocaine (2.0 ml, RB group) in one eye; and sub-Tenon's injection of 2% lidocaine (2.0 ml, ST group) in the opposite eye. When the akinesia was not obtained within 10 min, an additional 1 ml of lidocaine was administered in the RB and the ST groups. Onset of akinesia in the AT (1.5 ± 0.9 min) and the ST (3.8 ± 5.8 min) groups was significantly shorter than that in the RB group (9.0 ± 6.5 min). Duration of akinesia in the ST group (116.2 ± 32.8 min) was longer compared to the AT (60.6 ± 23.6 min) and the RB (89.0 ± 52.8 min) groups, even though there was only a significant difference between the AT and the ST groups. Mydriasis was achieved in five eyes in the RB group and nine eyes in the ST group. There was no significant difference in onset (3.6 ± 3.1 and 2.9 ± 2.3 min, respectively) or duration (91.4 ± 31.9 and 102.1 ± 35.8 min, respectively) of mydriasis between the groups. Sub-Tenon's lidocaine injections provide excellent akinesia and mydriasis compared to systemic atracurium and retrobulbar lidocaine

injections. Therefore, sub-Tenon's anesthesia could be an alternative to the systemic administration of neuromuscular blockers and retrobulbar anesthesia for ophthalmic surgery in dogs.

Based on the results of chapter 1 and 2, the effect of sub-Tenon's anesthesia on akinesia, mydriasis, and intraoperative and postoperative analgesia were evaluated in dogs with normal eyes undergoing phacoemulsification in chapter 3. Dogs were anesthetized and assigned to 2 treatments: concurrent sub-Tenon's injection of 2% lidocaine hydrochloride solution (2 ml) and intravenous injection of saline (0.9% NaCl) solution (0.02 ml/kg; lidocaine group [n = 7]) or concurrent sub-Tenon's injection of saline solution (2 ml) and IV injection of 0.2 mg of atracurium/kg (0.02 ml/kg; control group [n=7]). Pupils were dilated by topical application of a combined tropicamide and phenylephrine ophthalmic solution. Ten min after the injections, pupil diameter was measured and phacoemulsification was performed. End-tidal isoflurane concentration was used to evaluate intraoperative pain. Subjective pain scores were recorded during the postoperative period. Akinesia was induced and maintained throughout the surgery in all eyes. Mean \pm SD pupil diameter was significantly greater in the lidocaine group (13.7 ± 0.7 mm) than in the control group (12.2 ± 0.8 mm). Isoflurane requirements were significantly lower in the lidocaine group than the control group. However, postoperative pain scores were not significantly different between the groups.

In the present studies, it was shown that sub-Tenon injection of 2 ml of 2%

lidocaine was an effective method for inducing akinesia of extraocular muscles, mydriasis, and intraoperative analgesia for phacoemulsification in dogs. Therefore, this could be another option for surgical field exposure and pain management during phacoemulsification in dogs.

Keywords: sub-Tenon's anesthesia, phacoemulsification, akinesia, mydriasis, dog

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GENERAL INTRODUCTION

Cataract surgery is one of the most common intraocular surgeries in dogs, which is performed under general anesthesia (Biros *et al.*, 2000). Because general anesthesia induces eyeball rotation in a medioventral direction (McMurphy *et al.*, 2004), systemic administration of neuromuscular-blocking agents have been commonly used for extraocular muscle akinesia in veterinary medicine (McMurphy *et al.*, 2004; Accola *et al.*, 2006). However, even though neuromuscular blocking agents induce akinesia effectively, they also cause paralysis of respiratory muscles. Therefore positive-pressure ventilation and close monitoring of respiratory function are essential (Accola *et al.*, 2006; Ahn *et al.*, 2013).

Regional anesthetic technique, such as sub-Tenon's anesthesia, could be an alternative to the systemic administration of neuromuscular blocking agents (Accola *et al.*, 2006; Hazra *et al.*, 2008). Moreover, regional anesthesia provides pupil dilation and analgesic effects that could not be obtained by systemic administration of neuromuscular blocking agents (Roman *et al.*, 1997; Lai *et al.*, 2005; Myrna *et al.*, 2010; Savino *et al.*, 2010). In veterinary medicine, however, studies demonstrating the effect of regional anesthesia are limited. Sub-Tenon's anesthesia, which is one of the widely used regional anesthetic technique for ophthalmic surgery in human, is obtained by injection of local anesthetics into sub-Tenon's space. Sensory and motor nerve located

in retrobulbar space and extraocular muscles are anesthetized by the procedure (Roman *et al.*, 1997; Canavan *et al.*, 2003). The aim of this study was to evaluate the effect of sub-Tenon's anesthesia on extraocular muscles akinesia, pupil dilation and analgesic effect in dogs undergoing phacoemulsification.

CHAPTER 1.

SUB-TENON'S ANESTHESIA TO INDUCE EXTRAOCULAR MUSCLE AKINESIA AND MYDRIASIS IN DOGS

ABSTRACT

The effect of local anesthetic on the extraocular muscles was investigated in dogs by injecting lidocaine into the space between Tenon's capsule and the sclera. A cross-over design was used with both eyes from five Beagle dogs randomly injected, under general anesthesia, with 1 ml of 2% lidocaine (1 ml-lidocaine group), 2 ml of 2% lidocaine (2 ml-lidocaine group) or 2 ml of normal saline (control group). Each eye was assigned to all treatments with a minimum 14 day interval between injections. Changes in eye position, pupil diameter, and intraocular pressure (IOP) were evaluated during the procedure. All eyes in the 2 ml-lidocaine group exhibited akinesia and mydriasis (pupil diameter >10mm) with an onset time of 6.5 ± 4.9 and 4.2 ± 4.3 min, respectively. In the 1 ml-lidocaine group, akinesia was induced in nine eyes and mydriasis occurred in seven eyes at 10.7 ± 5.8 and 5.4 ± 2.4 min after the injection, respectively. No changes in eye position or pupil diameter were observed in the control group. Akinesia was maintained for 44.3 ± 26.7 min in

the 1 ml-lidocaine group and for 88.5 ± 17.2 min in the 2 ml-lidocaine group. Duration of mydriasis was 51.7 ± 28.9 min in the 1 ml-lidocaine group and 82.9 ± 15.6 min in the 2 ml-lidocaine group. Marked chemosis and subconjunctival haemorrhage occurred in 16/30 and 15/30 eyes, respectively. No significant change in IOP was observed between the mean pre- and post-injection values in all groups. These results suggest that a sub-Tenon's injection of 2 ml of 2% lidocaine provided effective extraocular muscle akinesia and mydriasis in dogs.

INTRODUCTION

Veterinary ophthalmic surgery usually requires general anesthesia but this causes the eyeball to rotate in a medioventral direction, which impedes exposure of the cornea (McMurphy *et al.*, 2004; Hazra *et al.*, 2008). Access to the cornea is essential for intraocular and corneal surgery, so neuromuscular blockers (NMBs) are commonly used to facilitate exposure (McMurphy *et al.*, 2004; Accola *et al.*, 2006). Although effective, systemic administration of NMBs also causes respiratory muscle paralysis, which requires necessitates close monitoring of cardiopulmonary function and specialized specific equipment, including a positive-pressure ventilator and a train-of-four peripheral nerve stimulator (Accola *et al.*, 2006).

Retrobulbar and peribulbar anesthesia can used to centralize the eyeball without respiratory muscle paralysis (Friedman *et al.*, 2001; Accola *et al.*, 2006; Hazra *et al.*, 2008), but have been associated with rare but serious complications, such as globe perforations, optic nerve trauma and respiratory arrest caused by brainstem anesthesia (Roman *et al.*, 1997; Canavan *et al.*, 2003).

Sub-Tenon's anesthesia was first proposed in the early 1990s in human patients as a safer technique for analgesia and extraocular muscle akinesia (Raman *et al.*, 2008). Because a blunt cannula is inserted under the sub-Tenon's space, this technique reduces complications associated with the use of

a sharp needle (Roman *et al.*, 1997; Raman *et al.*, 2008). Sub-Tenon's anesthesia has become more popular in human medicine because of its safety and excellent analgesic effect (Canavan *et al.*, 2003).

The purpose of this study was to evaluate the feasibility of sub-Tenon's anesthesia using 2% lidocaine in dogs. The onset and duration of akinesia and mydriasis, changes in intraocular pressure (IOP), and complications were examined.

MATERIALS AND METHODS

1. Experimental animals

Both eyes of five beagle dogs (3 females, 2 males; mean age, 2.8 ± 1.1 years; mean bodyweight (BW), 11.3 ± 1.4 kg) were included. Prior to the start of the experiment, all dogs received a physical examination, complete blood counts, serum chemistry profiles, and complete ophthalmic examinations, including slit-lamp biomicroscopy (model SL-D7, Topcon), indirect ophthalmoscopy (Vantage plus®, Keeler), and applanation tonometry (Tonopen®, Mentor). Only systemically healthy dogs with normal eyes were enrolled in the study. All care and experimental procedures conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and the Guide for the Care and Use of Laboratory Animals of Seoul National University. This study was approved by the Institutional Animal Care and Use Committee of Seoul National University (SNU-101220-1).

2. Study design

Three treatments were defined for each eye: 1 ml of 2% lidocaine (1 ml-lidocaine group), 2 ml of 2% lidocaine (2 ml-lidocaine group) and 2 ml of normal saline (control group). Under general anesthesia, the agents were administered into the sub-Tenon's space and the change in eyeball position, pupil diameter, and IOP were measured. Each eye was assigned to all three treatments in random order with a minimum 14 day interval before treatment. A treatment was applied to only one eye during each session and dogs therefore had a minimum of 7 days between each general anesthetic. Eyes were evaluated for chemosis, conjunctival hyperemia, sub-conjunctival hemorrhage and healing of the conjunctival incision for 14 days post-operatively. All treated eyes were instilled with neomycin, polymyxin B and dexamethasone ophthalmic suspension (Maxitrol®, Alcon) twice daily during the experimental period.

3. Anesthesia and surgical procedures

General anesthesia was induced with propofol (Provive® 1%, Claris Lifesciences; 6 mg/kg, IV) without any pre-medication through a pre-installed intravenous catheter. Pre-medication was avoided since they can affect blood pressure and thereby intraocular pressure. After endotracheal intubation, anesthesia was maintained with isoflurane (Forane® solution, Choongwe) at 1.5 minimum alveolar concentration (MAC) during the evaluation of eye position. Physiological saline (10 ml/kg/h, IV) was infused during anesthesia. Electrocardiography, pulse oximetry, respiratory gas analysis, invasive mean arterial pressure (MAP) in the dorsal pedal artery, and rectal temperature were monitored using an anesthetic monitoring system (Datex-Ohmeda® S/5, GE Healthcare). While most intraocular procedures are performed in dorsal recumbency, animals were placed in sternal recumbency to facilitate obtaining digital photographs. The head was stabilized using a vacuum pillow. After installing an eyelid speculum with ruler attached (Fig. 1-1), the cornea was prepared aseptically using 0.2% povidone-iodine solution.

A small tent of the mediodorsal portion of the bulbar conjunctiva was raised approximately 5 mm from the limbus with Colibri forceps, and the tent was incised with ophthalmic scissors. The closed scissors were introduced via the conjunctival incision and Tenon's capsule was dissected bluntly from the underlying sclera in a tunnel fashion until the sub-Tenon's space was exposed

(i.e. approximately 5 mm from the conjunctival incision). A 19 G sub-Tenon's anesthesia cannula (Stevens Sub-Tenon's Anesthesia Cannula, Katena) was inserted along the contour of the globe with the syringe of the treatment solution attached until its tip reached to the posterior sub-Tenon's space (Fig. 1-2). The solution was injected slowly to minimize overflow and the cannula was held in the position without fanning as the anesthetic was injected. During the injection, ballooning of the conjunctiva was monitored to ensure that the solution is correctly injected into the posterior sub-Tenon's space. No digital massage was applied after the injection.

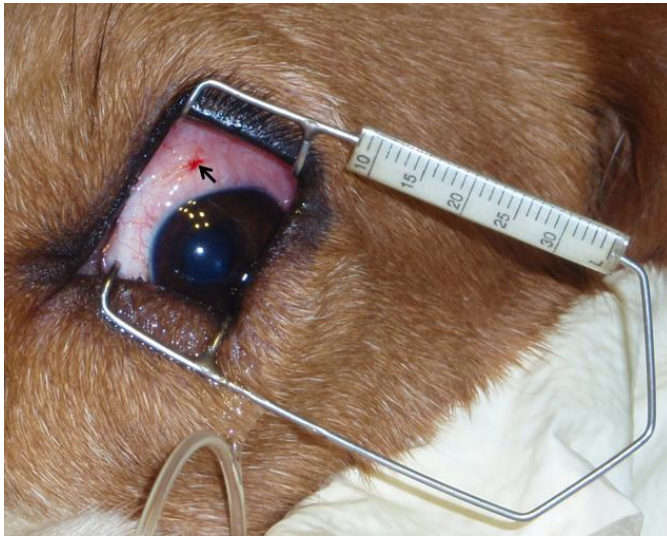


Figure 1-1. A mild sub-conjunctival hemorrhage (arrow) was induced during the conjunctival incision. The ruler strip was attached on the eyelid speculum to calibrate spatial measurements for image analysis of eye position and pupil diameter.

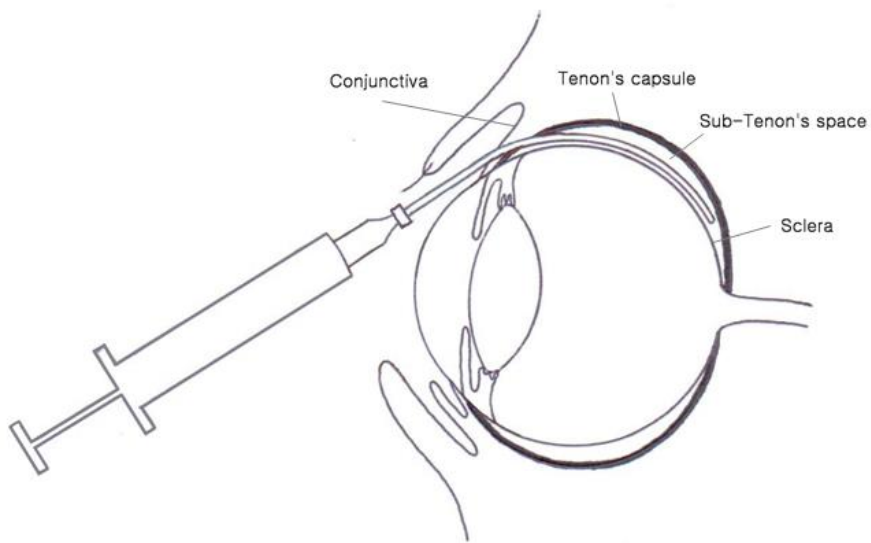


Figure 1-2. Schematic drawing of the proper placement of the Stevens sub-Tenon's anesthesia cannula. The cannula was inserted through a conjunctival incision into the sub-Tenon's space.

4. Evaluation of akinesia, mydriasis, and IOP

The observer could not be masked to the treatment group due to the different volume of solution injected. Digital photographs were taken immediately before injection, every minute for 10 min after injection, and then every 5 min until the eyeball rotated obviously. In case that the akinesia was not achieved within 30 min after the injection, the treatment was considered ineffective and measurement was suspended. Throughout the procedure, 0.1% sodium hyaluronate solution (Lacure®, Samil) was applied to prevent desiccation of the cornea. The camera was fixed firmly by mounting on a tripod and directed perpendicularly towards the ocular surface. After the procedure, the area of exposed cornea was measured with an image analysis program (ImageTool®, The University of Texas Health Science Centre) at each time point.

The ruler strip on the eyelid speculum was used to calibrate spatial measurements. Because the entire cornea was not exposed even when the cornea was maximally centralized (Fig. 1-3), two perpendicular diameters of cornea were measured using the image analysis program when the cornea was maximally exposed. The cornea was assumed to be an ellipse and the area of the entire cornea was calculated as follows:

$$\text{Multiplication of two perpendicular diameters} \times \pi/4$$

The degree of corneal exposure ($DCE = \text{area of exposed cornea} / \text{area of entire cornea}$) was calculated, and akinesia was defined as when $DCE > 80\%$. Pupil diameter was also measured using the image program in the same manner, and the mean horizontal and vertical diameter values were calculated. A pupil diameter > 10 mm was defined as mydriasis. Onset and duration of akinesia and mydriasis were calculated based on the data. IOP was measured immediately before the sub-Tenon's injection and 1 min after the injection.

5. Statistical analyses

Results are expressed as means \pm standard deviation (SD). All analyses were performed using statistical software (SPSS 12.0 for Windows). Student's t test was used out to compare onset and duration of akinesia and mydriasis between the 1 ml-lidocaine group and the 2 ml-lidocaine group. A two-way repeated-measure of analysis of variance was performed to evaluate the change in IOP. $P < 0.05$ was considered significant.

RESULTS

1. Evaluation of akinesia, pupil dilation, and IOP

All eyes rotated to ventral or medioventral directions prior to the sub-Tenon's injection (Fig. 1-3). No resistance to injection was found in any eye. In most cases, the pupil started to dilate during the lidocaine infusion. No eyes became exophthalmic during the injection. The mean onset and duration of akinesia and mydriasis in each group are presented in Table 1-1. Akinesia and mydriasis were achieved in all eyes in the 2 ml-lidocaine group, whereas they were not achieved in 1/10 and 3/10 eyes in the 1 ml-lidocaine group, respectively. No effect on akinesia or pupil dilation was observed in the control group (Fig. 1-3). The mean durations of akinesia ($P < 0.001$) and mydriasis ($P = 0.002$) in the 2 ml-lidocaine group were significantly longer than those in the 1 ml-lidocaine group.

Although no significant difference in onset time was observed between the two groups, akinesia ($P = 0.112$), and mydriasis ($P = 0.466$) were induced more rapidly in the 2 ml-lidocaine group. Duration of akinesia and mydriasis in the 2 ml-lidocaine group were >60 min in all eyes, whereas only 1/10 and 2/10 eyes in the 1 ml-lidocaine group presented akinesia and mydriasis > 60 min, respectively (Table 1-2). No significant difference in IOP ($P = 0.840$) was observed between pre- and post-injection periods in all groups (Table 1-3).

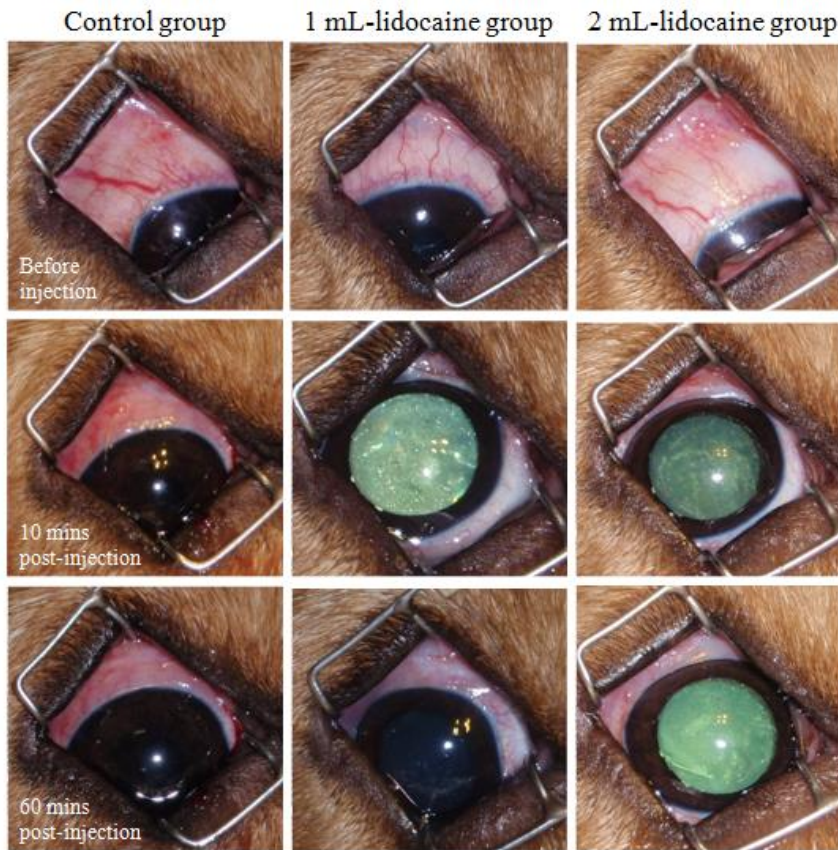


Figure 1-3. Corneal exposure and pupil size of the right eye according to the treatment agent in the same dog. The eyes in all groups rotated to the medioventral or ventral direction prior to the sub-Tenon's injection. Akinesia and mydriasis (pupil diameter >10 mm) were induced 10 min after the injection in the 1 ml and 2 ml-lidocaine groups in this eye. The cornea of the eye in the 1 ml-lidocaine group dropped in the ventral direction at 60 min post-injection, whereas the eye in the 2 ml-lidocaine group was still akinetic at the same time point. No effects on akinesia or pupil dilation were observed in the control group.

Table 1-1. Onset and duration (min) of akinesia and mydriasis after sub-Tenon's injection of agents

Groups	Akinesia		Mydriasis (pupil diameter >10 mm)	
	Onset	Duration	Onset	Duration
Control	-	0	-	0
1 ml lidocaine	10.7 ± 5.8 (3-20)	44.3 ± 26.7* (5-96)	5.4 ± 2.4 (2-8)	51.7 ± 28.9* (22-102)
2 ml lidocaine	6.5 ± 4.9 (1-15)	88.5 ± 17.2* (68-119)	4.2 ± 4.3 (1-15)	82.9 ± 15.6* (62-109)

Data are means ± SDs (range). *Statistically significant differences between the 1 ml and 2 ml lidocaine group.

Table 1-2. The number of eyes in which the duration of akinesia and mydriasis were greater than 60 and 90 min, respectively

Groups	Akinesia		Mydriasis (pupil diameter >10 mm)	
	> 60 min	> 90 min	> 60 min	> 90 min
Control	0	0	0	0
1 ml lidocaine	1	1	2	1
2 ml lidocaine	10	4	10	2

Table 1-3. Intraocular pressure (IOP, mmHg) between the pre- and post-injection periods

Groups	Pre-injection ¹	Post-injection ²
Control	8.9 ± 1.8	9.4 ± 2.1
1 ml -lidocaine	11.0 ± 1.9	10.8 ± 1.6
2 ml lidocaine	9.6 ± 2.9	9.8 ± 2.2

Data are means ± SDs.

¹ IOP immediately before the sub-Tenon's injection.

² 1 min after the sub-Tenon's injection. No significant changes in IOP were observed in any of the groups

2. Complications of sub-Tenon's injections

No marked fluid retention in the conjunctiva was observed during the sub-Tenon's injections. However, conjunctival swelling gradually developed after the injection in some cases; more than half the eyes (16/30) had marked chemosis at the end of anesthesia (Fig. 1-4, Table 1-4). No signs of discomfort associated with chemosis were observed postoperatively and this sign regressed within 3 days in all eyes. Sub-conjunctival hemorrhage occurred in 15/30 eyes while the conjunctiva was dissected down to the sclera (Fig. 1-1). Bleeding was limited and did not necessitate hemostasis in most eyes (29/30). However, marked hemorrhage was caused in one eye by severing the episcleral vein, which was controlled by cauterizing the vessel.

No signs of ocular pain associated with conjunctival wounds were observed in any of the groups during the monitoring period. The sub-conjunctival hemorrhage and conjunctival hyperemia caused by the conjunctival incision regressed completely without complications in all eyes within 2 weeks. No evidence of nerve damage, globe perforation, or retrobulbar hemorrhage was observed.

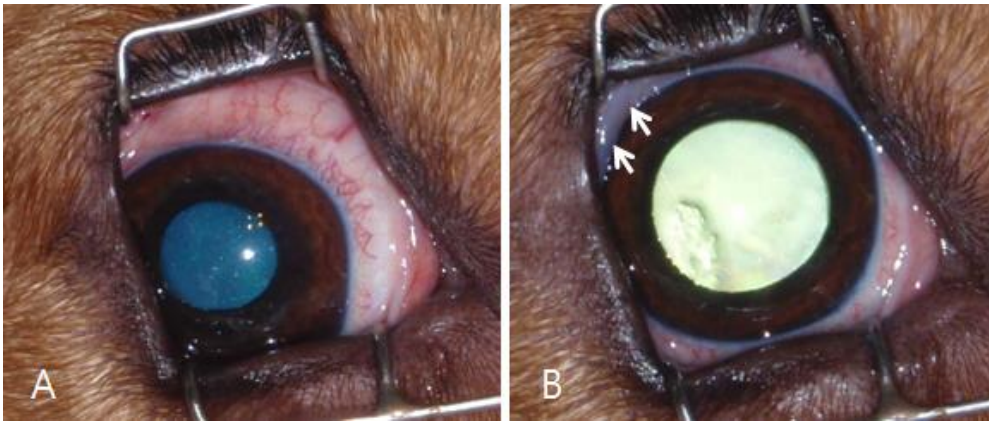


Figure 1-4. Development of chemosis in the right eye of a dog in the 2 ml-lidocaine group. (A) No chemosis was observed immediately after the injection and the pupil started to dilate; (B) Chemosis (arrows) developed markedly in the eye 60 min after the injection.

Table 1-4. The number of eyes showing chemosis at the end of anesthesia (0 = no chemosis; + = slight elevation of conjunctiva; ++ = marked elevation of conjunctiva without obscuring cornea; +++ = marked elevation of conjunctiva partially obscuring cornea).

Groups	0	+	++	+++
Control	1	6	2	1
1 ml lidocaine	3	2	2	3
2 ml lidocaine	1	1	3	5
Total	4	9	7	9

3. Evaluation of cardiopulmonary function

There was no evidence of complications associated with general anesthesia or systemic effects of the lidocaine, such as hypotension and electrocardiogram abnormalities. MAP, heart rate, respiratory rate, hemoglobin saturation, and concentration of end-tidal carbon dioxide were within normal ranges during anesthesia.

DISCUSSION

The results demonstrate that sub-Tenon's anesthesia provided satisfactory extraocular muscle akinesia and pupil dilation in dogs. Extraocular muscle akinesia and mydriasis were achieved for at least 60 min in all eyes after administering 2 ml of 2% lidocaine into the sub-Tenon's space. This technique could therefore be useful as an alternative to neuromuscular blockades for ocular surgery in dogs.

Extraocular muscle akinesia is essential during intraocular and corneal surgery to expose the surgical area and support manipulation of the eyes. Currently, non-depolarising NMBs are commonly used systemically in veterinary medicine because of their ease of administration and ability to induce effective extraocular muscle paralysis (Accola *et al.*, 2006). However, these agents inevitably induce respiratory muscle paralysis, which necessitates specific equipment to support respiration and monitor the effects of the NMBs (Accola *et al.*, 2006; Hazra *et al.*, 2008). Without close monitoring of patients' respiratory function, hypoventilation induces respiratory acidosis, which is a potential risk factor for cardiovascular, neurological, metabolic and ocular impairments (Wall, 2001; McMurphy *et al.*, 2004; Hazra *et al.*, 2008).

In humans, post-anesthetic residual neuromuscular blockade has been reported in 4–64% of patients (Murphy, 2006), which can lead to upper airway obstruction, decreased airway protective reflexes, and impaired hypoxic ventilator response

(Murphy, 2006; Yip *et al.*, 2010). These complications could be fatal in veterinary patients with impaired respiratory function. Moreover, general anesthesia should be maintained until recovery from the NMB, which means prolonged anesthesia and delayed discharge from the operating room. Otherwise, counteracting agents such as neostigmine should be used to reverse the effect of NMBs, which increases treatment costs (Flaherty *et al.*, 2007).

Local administration of anesthetic agents provides akinesia and additional analgesia without respiratory muscle paralysis (Roman *et al.*, 1997; Accola *et al.*, 2006; Hazra *et al.*, 2008). Retrobulbar anesthesia is achieved by an intraconal injection of anesthetic solution (Stevens *et al.*, 1993; Accola *et al.*, 2006). Because this technique involves insertion of a needle into the orbit, potentially severe complications can occur (Roman *et al.*, 1997; Accola *et al.*, 2006; Hazra *et al.*, 2008). Peribulbar anesthesia is safer than retrobulbar anesthesia, because the needle is inserted outside the extraocular muscle cone, not into the orbit (Grizzard *et al.*, 1991; Stevens *et al.*, 1993). However, diffusion of the agent is limited with this technique and it requires the infusion of a large volume of anesthetic agent (Stevens *et al.*, 1993; Ozdemir *et al.*, 2004). Sub-Tenon's anesthesia delivers anesthetic agent to the posterior sub-Tenon's space using a blunt cannula, and the agent diffuses back to the intraconal space (Roman *et al.*, 1997). This technique reduces the risks related to the use of a needle, requires a small anesthetic volume, and induces a minimal rise in IOP (Stevens *et al.*, 1993; Roman *et al.*, 1997).

In humans, extraocular muscle akinesia is assessed by the ocular movement score to estimate a patient's ability to move their eyes (Roman *et al.*, 1997). However, it is impossible to apply this system to veterinary patients because extraocular muscle akinesia is induced under general anesthesia. Thus, gross evaluation of eye position with naked eye has been used for animal patients as a subjective method (McMurphy *et al.*, 2004; Accola *et al.*, 2006). In this study, DCE was calculated using digital photography. Because a portion of the cornea was obscured by the eyelid even when the eye was positioned centrally, the cornea could not be exposed entirely in all eyes (Fig. 1-3). Therefore, a DCE >80% indicated that extraocular muscles were paralyzed enough to provide adequate conditions for operating on the eye. This method was more objective than a gross evaluation of eye position and was reasonable to estimate satisfactory exposure of the cornea when compared with a gross evaluation.

Studies in humans have reported that akinesia may be inconsistent (Canavan *et al.*, 2003), that 4–5 ml of anesthetic agent are required to achieve a sufficient motor block (Sohn *et al.*, 2008), and that maximal akinesia develops 5–15 min after sub-Tenon's anesthesia (Canavan *et al.*, 2003). In the current study, akinesia was achieved in all eyes with a mean onset time of 6.5 ± 4.9 min by sub-Tenon's injection of 2 ml of 2% lidocaine. It is possible that a smaller orbital volume in dogs (Cooper, 1985; Samuelson, 2007) provided a greater distribution of anesthetic agent from the posterior sub-Tenon's space to the intraconal space.

The mean duration of akinesia in the 2 ml-lidocaine group (88.5 ± 1.2 min) was shorter than that of retrobulbar anesthesia in a previous report (122.3 min, Accola *et al.*, 2006). This may have related to the difference in the injection technique, but could also be due to the smaller BW (mean 8.8 kg) and subsequent smaller orbital size of the experimental animals in this study and the difference in the evaluation method for akinesia (gross evaluation). The addition of long-acting anesthetic agents, such as bupivacaine, or supplemental injections through the tract already prepared can be carried out to extend the duration of akinesia (Canavan *et al.*, 2003). The convenience of an additional injection through the surgical field during the surgery is another advantage of the sub-Tenon's anesthesia over retrobulbar anesthesia (McMurphy *et al.*, 2004).

Previous reports have indicated that the diameter of the lens surface in dogs was 10.6–10.92 mm (Samuelson, 2007). A pupil diameter greater than 10 mm was considered sufficient exposure of the lens surface for surgery, such as phacoemulsification. However, there are only limited studies on the mydriatic effect of regional anesthesia, with one study showing that satisfactory mydriasis was not obtained in 25% of dogs after a retrobulbar injection of 2 ml of lidocaine and an additional 1 ml of 2% lidocaine (Accola *et al.*, 2006). In contrast, the current study achieved mydriasis for > 60 min in all eyes in the 2 ml lidocaine group, which may have resulted from the direct infusion of anesthetics into the posterior sub-Tenon's space where short ciliary nerves providing autonomic motor function to the iris

sphincter muscles traverse (Canavan *et al.*, 2003). Moreover, because NMBs have no effect on pupil dilation (Gray *et al.*, 1997), the excellent mydriatic property of sub-Tenon's anesthesia could be another advantage over systemic administration of NMBs in phacoemulsification.

Elevation of IOP immediately after a sub-Tenon's injection and subsequent reduction has been reported in some studies (Patton *et al.*, 2004; Sohn *et al.*, 2008). However, we found no increase in IOP after the sub-Tenon's injection in any groups.

No ballooning of the conjunctiva or excessive overflow of the injected solution during the sub-Tenon's injection indicated that the agent is correctly injected into the posterior sub-Tenon's space (Canavan *et al.*, 2003). However, marked chemosis gradually developed during the anesthesia in 16/30 eyes, which may have been caused by migration of the injected solution to the anterior compartment of the sub-Tenon's space from the posterior sub-Tenon's space (Canavan *et al.*, 2003), exacerbated by the patient's sterna recumbent position. Even though the chemosis does not usually impede the surgical field (Canavan *et al.*, 2003), it is recommended to reduce this migration and subsequent chemosis that the solution is injected while the patients is in dorsal recumbency and the patient's head is fixed in the surgical position to allow the injectant to remain in the posterior sub-Tenon's space by gravity.

The degree of sub-conjunctival hemorrhage was insignificant in all cases except

one eye. The use of cauterization before a conjunctival incision has been advocated to reduce the risk of hemorrhage (Stevens, 1992). However, careful incision of the conjunctiva so as not to sever the episcleral veins is sufficient if the conjunctiva is not severely hyperemic. In humans (Roman *et al.*, 1997; Canavan *et al.*, 2003), chemosis (39.4% of cases) and subconjunctival hemorrhage (32–56% of cases) was comparable with the current study in dogs. No signs of discomfort or complications were associated with chemosis or sub-conjunctival hemorrhage during the monitoring period. The conjunctival wounds healed up completely after topical administration of ophthalmic steroid-antibiotic suspension twice daily for 2 weeks.

The injection technique in the current study was slightly different from that used in human ophthalmic surgery. The inferonasal approach (Canavan *et al.*, 2003) is unsuitable for animal patients because the third eyelid obscures the area and the eyeball rotates medioventral under general anesthesia. Accordingly, the approach to the sub-Tenon's space was through the mediodorsal conjunctiva in the current study. Sub-Tenon's space was exposed without damaging the vortex vein or extraocular muscles with this approach.

CONCLUSIONS

The results of this study suggested that a sub-Tenon's injection of 2 ml of 2% lidocaine is a safe and effective method to achieve extraocular muscle akinesia and pupil dilation in dogs. Sub-Tenon's anesthesia could be an excellent alternative to NMBs for extraocular muscles akinesia and additionally provide a mydriatic effect during ocular surgery in dogs.

CHAPTER 2.

COMPARISON OF SYSTEMIC ATRACURIUM, RETROBULBAR LIDOCAINE, AND SUB-TENON'S LIDOCAINE INJECTIONS IN AKINESIA AND MYDRIASIS IN DOGS

ABSTRACT

The purpose of this study was to compare the effect of sub-Tenon's lidocaine injections (ST) on akinesia and mydriasis to those of systemic atracurium (AT) and retrobulbar lidocaine injections in dogs. Three treatments were performed on 10 beagle dogs with a minimum 7-day washout period: intravenous injection of AT (0.2 mg/kg, AT group); retrobulbar (RB) injection of 2% lidocaine (2.0 ml, RB group) in one eye; and sub-Tenon's injection of 2% lidocaine (2.0 ml, ST group) in the opposite eye. When the akinesia was not obtained within 10 min, an additional 1 ml of lidocaine was administered in the RB and the ST groups. Onset of akinesia in the AT (1.5 ± 0.9 min) and the ST (3.8 ± 5.8 min) groups was significantly shorter than that in the RB group (9.0 ± 6.5 min). Duration of akinesia in the ST group (116.2 ± 32.8 min) was longer compared to the AT (60.6 ± 23.6 min) and the RB (89.0 ± 52.8 min) groups, even though there was only a significant difference between the AT

and the ST groups. Mydriasis was achieved in five eyes in the RB group and nine eyes in the ST group. There was no significant difference in onset (3.6 ± 3.1 and 2.9 ± 2.3 min, respectively) or duration (91.4 ± 31.9 and 102.1 ± 35.8 min, respectively) of mydriasis between the groups. Sub-Tenon's lidocaine injections provide excellent akinesia and mydriasis compared to systemic AT and retrobulbar lidocaine injections. Therefore, sub-Tenon's anesthesia could be an alternative to the systemic administration of neuromuscular blockers and retrobulbar anesthesia for ophthalmic surgery in dogs.

INTRODUCTION

Intraocular and corneal surgeries require central fixation of the globe for appropriate exposure of the cornea (McMurphy *et al.*, 2004; Accola *et al.*, 2006). Because general anesthesia induces deviation of the eyeball in a medioventral direction (McMurphy *et al.*, 2004), neuromuscular-blocking agents (NMBs) have been commonly used for extraocular muscle akinesia in veterinary medicine (McMurphy *et al.*, 2004; Accola *et al.*, 2006). However, specific equipments, such as positive-pressure ventilators and train-of-4 peripheral nerve stimulators, are necessitated to support pulmonary functions and monitor the effect of NMBs, because the systemic administration of NMBs causes respiratory muscle paralysis (Accola *et al.*, 2006; Hazra *et al.*, 2008).

Regional anesthetic techniques could be an alternative to the systemic administration of NMBs for extraocular muscle akinesia (Accola *et al.*, 2006; Hazra *et al.*, 2008). Retrobulbar and sub-Tenon's anesthesia are widely used during ophthalmic surgery in humans (Canavan *et al.*, 2003; Lai *et al.*, 2005). In addition to extraocular muscle akinesia, these techniques could also provide mydriatic and analgesic effects (Roman *et al.*, 1997; Lai *et al.*, 2005; Myrna *et al.*, 2010; Savino *et al.*, 2010). However, the regional anesthetic techniques have generally been performed for intra- and postoperative analgesia for ophthalmic surgery such as enucleation in veterinary medicine (Herring, 2007; Myrna *et al.*, 2010). Moreover,

studies concerning the effects of sub-Tenon's anesthesia on extraocular muscle akinesia and mydriasis in animals are limited (Ahn *et al.*, 2013). The aim of this study was to compare the effect of sub-Tenon's anesthesia with lidocaine on akinesia and mydriasis (pupil dilation >10 mm) to those of the systemic administration of atracurium and retrobulbar anesthesia using lidocaine in dogs.

MATERIALS AND METHODS

1. Experimental animals

Both eyes of 10 healthy beagle dogs were included in this study. The mean age and weight were 3.1 ± 0.9 years (range, 2–4) and 7.8 ± 1.5 kg (range, 6.3–11.3), respectively. Prior to beginning the experiment, all dogs underwent complete ophthalmic examinations including slit-lamp biomicroscopy (Topcon®; Topcon corporation, Tokyo, Japan), indirect ophthalmoscopy (Vantage plus®; Keeler, Windsor, UK), and applanation tonometry (Tonopen®; Mentor, Norwell, MA, USA) to ensure the dogs had clinically normal eyes. All care and experimental procedures conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and the Guide for the Care and Use of Laboratory Animals of Seoul National University. This study was approved by the Institutional Animal Care and Use Committee of Seoul National University (SNU-111214-1).

2. Study design

Three treatments were established for each dog: intravenous administration of atracurium 0.2 mg/kg (AT group, n = 20); retrobulbar injection of 2 ml of 2% lidocaine in one eye retrobulbar (RB group, n = 10); and sub-Tenon's injection of 2 ml of 2% lidocaine in the opposite eye (ST group, n = 10). Under general anesthesia, only one treatment was performed at a time with a minimum 7-day washout period, and the order of treatments was randomly established. Following administration of the agents, changes in eyeball position, pupil diameter, and intraocular pressure (IOP) were recorded during the experiment. In the AT group, both eyes were simultaneously evaluated. When the akinesia was not obtained 10 min after the injection in the RB and ST groups, an additional 1 ml of lidocaine was administered.

3. Anesthesia and surgical procedures

General anesthesia was induced with propofol (6 mg/kg, IV) via a preplaced intravenous catheter. Following endotracheal intubation, anesthesia was maintained with isoflurane in oxygen at 1.5 minimum alveolar concentrations (MAC) using semi-closed rebreathing system. An intravenous infusion of physiological saline was administered at a rate of 10 ml/kg/h throughout the experiment. During the anesthesia, electrocardiography, respiratory gas analysis, pulse oximetry, invasive mean arterial pressure (MAP) in the dorsal pedal artery, and esophageal temperature were monitored using an anesthetic monitoring system (Datex-Ohmeda S/5®; GE Healthcare, Madison, WI, USA). General anesthesia was maintained until the centrally positioned eyeball was re-rotated ventrally. In the AT group, the anesthesia was discontinued when the response to the train-of-four stimulus was fully recovered.

Each dog was positioned in sternal recumbency with the head stabilized by a vacuum pillow, and an eyelid speculum was installed. In the AT group, mechanical ventilation was performed using a positive-pressure ventilator (Ventilator Ace-3000®; Acoma Co., Ltd., Tokyo, Japan) immediately after the administration of AT. The neuromuscular function was assessed by evaluating the twitch response of the distal limb to electrical stimulation of the ulnar nerve with a peripheral nerve stimulator (Peripheral nerve locator/stimulator®; Life-Tech Inc., Stafford, CA, USA)

at 2 Hz (four stimuli delivered over 2 s). Retrobulbar (Accola *et al.*, 2006) and sub-Tenon's injections (Canavan *et al.*, 2003) were performed as in previous studies with one difference: The approach to the sub-Tenon's space was performed through the mediodorsal portion of the bulbar conjunctiva. Briefly, retrobulbar anesthesia was performed using a 22-G spinal needle with a mechanically created 20-degree angle at the midpoint of the needle, which was inserted through the temporal thirds of the lower eyelid with a syringe. The needle was advanced toward the apex of the orbit, and lidocaine was infused. For sub-Tenon's anesthesia, the mediodorsal area of the bulbar conjunctiva was incised with ophthalmic scissors at 5 mm from the limbus, and the underlying Tenon's capsule was bluntly dissected until the sub-Tenon's space, or bare sclera, was exposed. The lidocaine was infused through the tunnel to the sub-Tenon's space using a 19-G sub-Tenon's anesthesia cannula (Stevens Sub-Tenon's Anesthesia Cannula; Katena, Denville, NJ, USA) with a syringe. After the administration of lidocaine in the RB and ST groups, digital ocular compression was applied for 1 min. The eyes in the ST group were instilled with neomycin, polymyxin B, and dexamethasone ophthalmic suspension (Maxitrol®; Alcon, Puurs, Belgium) twice a day for 2 weeks postoperatively.

4. Evaluation of akinesia, mydriasis, and IOP

Digital photography with a camera fixed by mounting on a tripod and an image analysis program (ImageTool®; The University of Texas Health Science Center, San Antonio, TX, USA) were applied to evaluate akinesia and mydriasis. To calibrate spatial measurements for the image analysis program, a ruler strip was attached to the eyelid speculum. The photographs were taken immediately before the injection of agents, every minute for 10 min after the injection, and then every 5 min until the eyeball became markedly rotated ventrally. During the procedure, 0.1% sodium hyaluronate solution (Lacure®; Samil Pharm Co., Ltd., Seoul, Korea) was applied to avoid desiccation of the cornea. To estimate akinesia, the degree of corneal exposure (DCE = area of exposed cornea/area of entire cornea) was calculated using the image analysis program, and akinesia was defined as the DCE >80%. The cornea was partially obscured by eyelids even when the eyeball was maximally centralized in all eyes. Therefore, on the assumption that the cornea was an ellipse, two perpendicular diameters of cornea were measured when the cornea was maximally exposed, and the area of the entire cornea was calculated as follows:

$$\text{Multiplication of two perpendicular diameters} \times \pi/4$$

The mean values of two perpendicular diameters were obtained using the image program, and mydriasis was deemed to have been achieved sufficiently when the pupil diameter was >10 mm (Park *et al.*, 2009). Based on the data, onset and

duration of akinesia and mydriasis were calculated.

Intraocular pressure (IOP) was measured using an applanation tonometer immediately before and 5 min after the administration of the agents.

5. Statistical analyses

The results were expressed as mean \pm standard deviation (SD). All analyses were performed using statistical software (SPSS 12.0K for windows; SPSS Inc., Illinois, IL, USA). To evaluate the differences in anesthetic values (heart rate, MAP, and concentration of end-tidal carbon dioxide) and onset and duration of akinesia between the three groups, a one-way ANOVA followed by Tukey's multiple comparison test was performed. Statistical analysis of onset and duration of mydriasis and the total volume of lidocaine injected to induce akinesia between the RB and ST groups was performed using the Student's t-test. Differences in pre- and postinjection values of IOP within the groups were compared with a paired t-test. A value of $P < 0.05$ was considered statistically significant.

RESULTS

The globe rotated medioventrally or ventrally prior to administration of the agents in all dogs (Fig. 2-1). Akinesia was obtained by a single injection of AT in all eyes in the AT group. However, 5/10 eyes in the RB group and 1/10 eye in the ST group required the administration of an additional 1 ml of lidocaine to achieve akinesia (Fig. 2-1). The mean volume of lidocaine administered in the RB group was significantly greater than that in the ST group ($P = 0.001$, Table 2-1). In the RB and ST groups, doses of lidocaine were 3.7–6.6 mg/kg in the single-dose group and 6.5–7.7 mg/kg in the double-dose group.

Mean \pm SD onset and duration times of akinesia and mydriasis are presented in Table 2-1. The onset of akinesia was significantly shorter in the AT and the ST groups compared to that in the RB group ($P = 0.000$). Except in the eyes that required additional administration in the ST and RB groups, akinesia was induced within 5 min. Moreover, 15/20 eyes in the AT group and 5/10 eyes in the ST group achieved akinesia within 1 min of the injection and immediately after the ocular compression, respectively, whereas only 2/10 eyes in the RB group achieved akinesia immediately after the ocular compression.

The duration of akinesia in the ST group was longer than that in the AT ($P = 0.001$) and the RB groups ($P = 0.104$). Moreover, all eyes in the ST group achieved akinesia for more than 60 min, whereas the duration of akinesia was longer than 60

min only in 6/10 eyes in the RB group and 9/20 eyes in the AT group (Table 2-2). No eyes in the AT group obtained an obvious mydriatic effect, while 5/10 eyes in the RB group and 9/10 eyes in the ST group achieved mydriasis. All the eyes presented with mydriasis within 10 min of the first injection of lidocaine (Fig. 2-1). Two eyes in the RB group that did not present with mydriasis received an additional injection of 1 ml of lidocaine to induce akinesia; however, there was no additional mydriatic effect of the injection. The onset and duration of mydriasis were not significantly different between the RB and ST groups (Table 2-1).



Figure 2-1. Eye position and pupil size according to the treatments in the same dog. The eyes in the atracurium (AT) group and sub-Tenon's lidocaine injection (ST) group achieved akinesia at 1 min after the injection, whereas the eyes in the retrobulbar (RB) group did not achieve akinesia 10 min after the injection, and an additional 1 ml of lidocaine was administered. Akinesia regressed at 60 min post-

injection in the AT group, whereas the eyes in the RB and ST groups maintained their position. Mydriasis (pupil diameter >10 mm) was achieved in the RB group within 10 min post-injection and in the ST group immediately after ocular compression. No change in pupil diameter was observed in the AT group during the experiment.

Table 2-1. Comparison of systemic atracurium, retrobulbar lidocaine, and sub-Tenon's lidocaine injections in akinesia and mydriasis in dogs.

Groups	AT	RB	ST	p-value
Agent (Dose)	Atracurium (0.2 mg/kg)	2% lidocaine (2.5 ± 0.5 ml, range 3.7 to 7.7 mg/kg)	2% lidocaine (2.1 ± 0.3 ml, range 3.7 to 7.5 mg/kg)	0.001*
Akinesia				
Number of eyes	20/20	10/10	10/10	
Onset	1.5 ± 0.9 ^a (1-4)	9.0 ± 6.5 ^b (1-15)	3.8 ± 5.8 ^a (1-20)	0.000
Duration	60.6 ± 23.6 ^a (29-109)	89.0 ± 52.8 ^{a,b} (11-164)	116.2 ± 32.8 ^b (63-164)	0.001
Mydriasis [#]				
Number of eyes	0/26	5/10	9/10	
Onset	No change	3.6 ± 3.1 (1-9)	2.9 ± 2.3 (1-6)	0.635*
Duration	0	91.4 ± 31.9 (36-118)	102.1 ± 35.8 (59-149)	0.589*

Data are means \pm SDs (range). AT = intravenous atracurium injection group; RB = retrobulbar lidocaine injection group; ST = sub-Tenon's lidocaine injection group. *Statistical analysis was performed between the RB and the ST groups. The same letters indicate non-significant differences between groups based on Tukey's multiple comparison test. #Mydriasis was defined as pupil diameter >10 mm.

Table 2-2. Number of eyes in which duration of akinesia was greater than 60 and 120 min, respectively

Groups	Duration of akinesia	
	> 60 min	> 120 min
AT	9/20	0/20
RB	6/10	4/10
ST	10/10	5/10

AT = intravenous atracurium injection group; RB = retrobulbar lidocaine injection group; ST = sub-Tenon's lidocaine injection group.

The mean postinjection IOP value significantly decreased compared to the pre-injection value in the AT group ($P = 0.000$, Table 3). There was no significant change in IOP in the RB and the ST groups.

At the end of the measurement, response to the train-of-4 stimulus and spontaneous respiration of the dogs were completely recovered in the AT group, and anesthesia was discontinued. There were no significant differences in heart rate, MAP, or concentration of end-tidal carbon dioxide at any time point between the three groups. There was no evidence of lidocaine toxicity (e.g., bradycardia, hypotension, nystagmus during the anesthesia) or retrobulbar infection (e.g., exophthalmos) in the RB and ST groups. In the ST group, the conjunctival wound regressed within 14 days postoperatively in all eyes.

Table 2-3. Intraocular pressure (IOP, mmHg) in the pre- and post-injection periods

Groups	Pre-injection*	Post-injection [#]	p-value
AT	13.0 ± 3.5	11.9 ± 3.8	0.000
RB	11.2 ± 2.6	11.7 ± 2.5	0.412
ST	9.7 ± 1.5	10.0 ± 1.7	0.584

AT = intravenous atracurium injection group; RB = retrobulbar lidocaine injection group; ST = sub-Tenon's lidocaine injection group. Data are means ± SDs.

*Immediately before the injection. [#]Five min after the injection. A significant decrease in IOP was observed in the AT group.

DISCUSSION

Sub-Tenon's anesthesia using 2% lidocaine provided a significantly longer duration of extraocular muscle akinesia and an additional mydriatic effect compared to the systemic administration of AT (0.2 mg/kg, IV). Moreover, sub-Tenon's anesthesia induced akinesia and mydriasis more efficiently with a significantly smaller volume of lidocaine than retrobulbar anesthesia. These results suggest that sub-Tenon's anesthesia could be a valuable alternative to the systemic administration of NMBs and retrobulbar anesthesia for ophthalmic surgery in dogs.

Central fixation of the globe for appropriate exposure of the cornea is essential for intraocular and corneal surgery. Several types of procedures have been proposed for extraocular muscle akinesia in veterinary medicine. The systemic administration of NMBs is commonly used, because they are easy to administer systemically and have the appropriate effect on akinesia (Accola *et al.*, 2006; Hazra *et al.*, 2008). However, with the administration of NMBs, respiratory muscles are also paralyzed, and positive-pressure ventilation is necessary to avoid apnea and subsequent respiratory acidosis or hypoxemia (Sullivan *et al.*, 1998; Accola *et al.*, 2006). Even though the use of low-dose NMBs to achieve akinesia sparing of spontaneous breathing was proposed, these produced mild to moderate respiratory depression (e.g., increases in the partial pressure of carbon dioxide in the arterial blood, which can indicate respiratory acidosis) and decreases in tidal volume (Lee *et al.*, 1998;

Auer *et al.*, 2007). Therefore, it is recommended that the respiratory functions of all patients receiving NMBs be closely monitored (Lee *et al.*, 1998).

Regional anesthesia is commonly used for a variety of ophthalmological procedures in human medicine (Canavan *et al.*, 2003; Ryu *et al.*, 2009). Retrobulbar anesthesia is achieved by direct injection of anesthetic solution into the intraconal space using a sharp needle (Stevens *et al.*, 1993). While it provides excellent akinesia and sensory block, this technique is associated with rare but serious complications, such as brainstem anesthesia, globe perforation, and retrobulbar hemorrhage (Rubin *et al.*, 1995; Friedman *et al.*, 2001). On the other hand, sub-Tenon's anesthesia is performed by delivering the anesthetic solution with a blunt cannula into the sub-Tenon's space, which diffuses into the retrobulbar muscle cone across the Tenon's capsule (Roman *et al.*, 1997; Canavan *et al.*, 2003). Because a sharp needle is not inserted into the orbital cavity, sub-Tenon's anesthesia is perceived to have a more acceptable safety level compared to retrobulbar anesthesia (Roman *et al.*, 1997; Canavan *et al.*, 2003; Khan *et al.*, 2009).

According to previous reports, the most commonly used anesthetic volumes for sub-Tenon's anesthesia in humans were 3–7 ml, and the onset times of akinesia were 4.0 ± 3.1 to 8.7 ± 3.2 min depending on the anesthetic volumes (Sohn *et al.*, 2008). However, the results of our study demonstrated that a sub-Tenon's injection of 2 ml of lidocaine could provide akinesia in most eyes (9/10) for approximately 2 h. Even though not all the intraocular and corneal surgeries necessitate prolonged

duration of akinesia, uniformity of duration of sub-Tenon's anesthesia was another advantage over retrobulbar anesthesia in this study. Moreover, 5/10 eyes achieved akinesia immediately after ocular compression. It is possible that the smaller orbital volume in the dogs, compared to that in humans (Cooper *et al.*, 1985; Samuelson *et al.*, 2007), and ocular compression promoted the distribution of the anesthetic agent to the intraconal space. Because beagle dogs (mean weight, 7.8 ± 1.5 kg) were used in this experiment, the administration of a smaller volume of anesthetic agent should be considered in dogs with smaller body weights, considering the possibility of lidocaine toxicity. Further studies would be necessary to assess the efficacy of smaller dose of lidocaine in smaller breed dogs. Although ocular compression could shorten the induction of akinesia, it is not an essential portion of sub-Tenon's anesthesia. A previous study demonstrated that sub-Tenon's injection of 2 ml of 2% lidocaine without ocular compression induced akinesia 6.5 ± 4.9 min after the injections in all eyes, which was longer than that in this study (Ahn *et al.*, 2013). Therefore, there is no necessity for performing ocular compression in cases that have a fragile or damaged globe such as descemetocoele or corneal perforation.

The total volume of the lidocaine used to induce akinesia in the ST group was significantly smaller than that used in the RB group. Moreover, the duration of akinesia was more than 60 min in all eyes in the ST group, while only 6/10 eyes in the RB group achieved akinesia for more than 60 min (Table 2-2). A previous study also reported that retrobulbar anesthesia (3.6 ml) required a significantly greater

volume of anesthetic agent for cataract surgery than that used for sub-Tenon's anesthesia (3.2 ml) in humans (Stevens *et al.*, 1993). This is important for animals whose body weight is much smaller than that of humans to minimize the dose of lidocaine not to cause lidocaine toxicity.

The different abilities to induce akinesia of retrobulbar and sub-Tenon's injections may be associated with the anatomic structures of extraocular muscles and Tenon's capsule. Because the insertion of the extraocular muscles is surrounded by Tenon's capsule (Canavan *et al.*, 2003), an anesthetic agent injected into the sub-Tenon's space may directly contact the insertion of the extraocular muscles and thereafter diffuse back through the Tenon's capsule to the retrobulbar muscle cone. This diffusion could have enabled the more uniform and efficacious delivery of the anesthetic agent to the retrobulbar muscle cone than when the agent is injected using a bolus injection into the retrobulbar space. Because ocular compression was applied after each of the injections to promote the distribution of lidocaine, these results may not be due to the inadequate distribution of the anesthetic agent caused by technical problems when the retrobulbar injection was performed.

Mydriasis induced by retrobulbar (Accola *et al.*, 2006) and sub-Tenon's anesthesia (Ahn *et al.*, 2013) has been previously described in dogs. It might be related to a block of the short ciliary nerve and ciliary ganglion providing autonomic motor function to the iris (Canavan *et al.*, 2003; Savino *et al.*, 2010). The higher success rate and shorter onset of mydriasis in the ST group than those in the

RB group in our study would be due to the fact that the sub-Tenon's injection could directly deliver anesthetic to the posterior sub-Tenon's space where short ciliary nerves traverse (Canavan *et al.*, 2003). Because the additional administration of lidocaine did not achieve a supplemental effect on mydriasis in the RB group, topical mydriatic agents (e.g., tropicamide) should be applied for intraocular surgery when retrobulbar anesthesia is performed for akinesia. Further study to elucidate whether additional sub-Tenon's injections of lidocaine could induce supplemental mydriasis is indicated.

Decreases in IOP after the systemic administration of NMBs have been previously investigated in humans. This has been suggested as being the result of relaxation of the extraocular muscles (Colle *et al.*, 1931) and a decrease in central venous pressure (CVP) (Jantzen *et al.*, 1986) or systemic arterial pressure (Al-Abrak *et al.*, 1974). These findings are in agreement with our study. McMurphy *et al.* reported that AT did not affect CVP in isoflurane-anesthetized dogs (McMurphy *et al.*, 2004), and there was no significant change in MAP values during the measurement of IOP in our study. Therefore, the decrease in IOP may be induced by extraocular muscle relaxation. Immediate elevations of IOP after retrobulbar and sub-Tenon's administration have been observed (Stevens *et al.*, 1993; Sohn *et al.*, 2008). The elevations tend to be resolved over time (Patton N *et al.*, 2004). However, they could also be controlled by ocular compression depending on the degree of IOP elevation (Sohn *et al.*, 2008). Although IOP was measured after

applying ocular compression to promote the distribution of the anesthetic, there was no significant increase in IOP values after retrobulbar and sub-Tenon's injections in our study.

Our sub-Tenon's injection procedure differed from that of human reports in one way (Canavan *et al.*, 2003; Sohn *et al.*, 2008). Because the inferonasal approach was considered inappropriate for animal patients due to the eyeball rotation in the medioventral direction under general anesthesia obscuring the area by the third eyelid, sub-Tenon's injections were performed through the mediodorsal conjunctiva in this study. The sub-Tenon's space could be accessed without damaging the vortex vein or extraocular muscles in all eyes.

Because retrobulbar injections of local anesthetics can lead to massive degeneration of the extraocular muscles and cause temporary diplopia and blepharoptosis in primates (Carlson *et al.*, 1992), further studies are required to evaluate histopathologic changes after sub-Tenon's injection of local anesthetics.

CONCLUSIONS

This study suggests that sub-Tenon's anesthesia could provide akinesia and mydriasis more effectively than the systemic administration of NMBs and retrobulbar anesthesia. Therefore, sub-Tenon's anesthesia could be an excellent alternative to the systemic administration of NMBs and retrobulbar anesthesia for ophthalmic surgery in dogs.

CHAPTER 3.

SUB-TENON'S ANESTHESIA FOR EXTRAOCULAR MUSCLES AKINESIA, MYDRIASIS, AND ANALGESIC EFFECTS IN DOGS UNDERGOING PHACO-EMULSIFICATION

ABSTRACT

The purpose of this study was to evaluate the effects of sub-Tenon injection of lidocaine hydrochloride on akinesia of extraocular muscles, mydriasis, and intraoperative and postoperative analgesia in dogs undergoing phacoemulsification. A blinded randomized controlled trial was performed. Fourteen beagle dogs with ophthalmically normal eyes were anesthetized and assigned to 2 treatments: concurrent sub-Tenon injection of 2% lidocaine hydrochloride solution (2 ml) and IV injection of saline (0.9% NaCl) solution (0.02 mL/kg; lidocaine group [n = 7]) or concurrent sub-Tenon injection of saline solution (2 ml) and IV injection of 0.2 mg of atracurium/kg (0.02 ml/kg; control group [7]). Pupils were dilated by topical application of a combined tropicamide and phenylephrine ophthalmic solution. Ten minutes after the injections, pupil diameter was measured and phacoemulsification was performed. End-tidal isoflurane concentration was used to evaluate

intraoperative pain. Subjective pain scores were recorded during the postoperative period. Akinesia was induced and maintained throughout the surgery in all eyes. Mean \pm SD pupil diameter was significantly greater in the lidocaine group (13.7 ± 0.7 mm) than in the control group (12.2 ± 0.8 mm). Isoflurane requirements were significantly lower in the lidocaine group than the control group. However, postoperative pain scores were not significantly different between the groups.

The present study suggests that sub-Tenon injection of lidocaine was an effective method for inducing akinesia of extraocular muscles, mydriasis, and intraoperative analgesia for phacoemulsification in dogs. Therefore, this could be another option for surgical field exposure and pain management during phacoemulsification in dogs.

INTRODUCTION

Cataract removal is one of the most common intraocular surgeries in veterinary ophthalmology (Biros *et al.*, 2000). Because the eyes are densely innervated structures, cataract surgery may result in the priming of pain perception pathways and subsequent ocular pain during the postoperative period (Smith *et al.*, 2004). Pain management in companion animals is usually achieved with opioids and NSAIDs. However, systemic administration of opioids commonly causes undesirable adverse effects, such as respiratory depression, bradycardia, and vomiting (Thurmon *et al.*, 1996). Moreover, opioids can induce pupillary constriction, which cannot be reversed by topical application of mydriatic agents (Kaswan *et al.*, 1992), that obstructs the surgical field during cataract surgery. Even though there is no effect on pupil diameter, systemic administration of NSAIDs has been associated with gastrointestinal distress, a decrease in platelet activity, and damage to organs such as the kidneys and liver. These factors potentially limit the use of this class of drug (Smith *et al.*, 2004).

Central fixation of the eyes and pupil dilation are critical factors for exposure of the surgical area (ie, lens) during cataract surgery (McMurphy *et al.*, 2004; Wilkie *et al.*, 2004). Because general anesthesia causes medioventral rotation of the eyes, systemic administration of a neuromuscular blocking agent such as atracurium is widely used in veterinary medicine for akinesia of extraocular muscles (McMurphy

et al., 2004; Accola *et al.*, 2006). Even though neuromuscular blocking agents effectively induce akinesia, they also cause paralysis of respiratory muscles, which requires positive-pressure ventilation and close monitoring of respiratory function (Accola *et al.*, 2006; Ahn *et al.*, 2013). Mydriasis is usually achieved with topically applied anticholinergics or sympathomimetic agents (or both), such as tropicamide and phenylephrine (Nikeghbali *et al.*, 2008; Park *et al.*, 2009). However, their effects can sometimes be insufficient for maximal exposure of the lens, especially in patients with uveitis (Lundberg *et al.*, 2003; Wilkie *et al.*, 2007).

Peribulbar anesthesia (ie, sub-Tenon injection; injection of a local anesthetic beneath the bulbar sheath [vagina bulbi; commonly known as Tenon's capsule (Murphy *et al.*, 2013)]) is effective in humans for perioperative analgesia, akinesia, and pupil dilation (Roman *et al.*, 1997; Canavan *et al.*, 2003). Local anesthetic agents administered via sub-Tenon injection spread to the retrobulbar space, where sensory nerves and extraocular muscles and their motor nerves are located (Roman *et al.*, 1997; Canavan *et al.*, 2003). Because a blunt cannula is inserted into the orbital cavity, it eliminates risks (eg, globe perforation) related to the use of a sharp needle (Roman *et al.*, 1997; Canavan *et al.*, 2003). Therefore, sub-Tenon injection of a local anesthetic is becoming more popular in human medicine (Canavan *et al.*, 2003). The purpose of the study reported here was to evaluate efficacy of sub-Tenon injection of lidocaine on akinesia and mydriasis during phacoemulsification and intraoperative and postoperative analgesia in dogs.

MATERIALS AND METHODS

1. Experimental animals

Fourteen healthy adult female Beagles with no ocular abnormalities were enrolled in the study. Dogs had a mean \pm SD age of 6.1 ± 1.1 years and mean body weight of 9.6 ± 1.5 kg. The eyes were assessed as ophthalmically normal on the basis of complete ophthalmic examinations, including slit-lamp biomicroscopy (SL-D7, Topcon Corp, Tokyo, Japan), a rebound tonometry (Tonovet, Icare Finland Oy, Espoo, Finland), and indirect ophthalmoscopy (Keeler Vantage plus, Keeler, Windsor, Berkshire, England). All animal care and experimental procedures were in accordance with guidelines for the care and use of laboratory animals of Seoul National University and were approved by the Institutional Animal Care and Use Committee of Seoul National University (SNU-121205-3).

2. Study design

A blinded randomized controlled trial was performed. Dogs were assigned into 2 treatment groups by drawing lots (7 dogs/group). For each dog of the lidocaine group, 2 ml of a 2% solution of lidocaine hydrochloride (Dai Han Pharm Co Ltd, Seoul, Republic of Korea) was administered via sub-Tenon injection of the left eye and saline (0.9% NaCl) solution (0.02 ml/kg) was simultaneously injected IV. For each dog of the control group, 2 ml of saline solution was administered via sub-Tenon injection of the left eye and 0.2 mg of atracurium/kg (0.02 ml/kg) was simultaneously injected IV. Atracurium was selected to induce akinesia in the control group because it does not have analgesic or sedative effects (Accola *et al.*, 2006; Plumb *et al.*, 2008). The dose of lidocaine for sub-Tenon injection was determined on the basis of results of a previous study (Ahn *et al.*, 2013). Phacoemulsification was subsequently performed in the left eye of each dog.

3. Anesthesia and surgical procedures

One drop of ophthalmic solution (a combination of 0.5% tropicamide and 0.5% phenylephrine; Mydrin-P, Santen pharmaceutical Co Ltd, Osaka, Japan) was instilled into the left eye of each dog every 5 min for 20 min prior to anesthetic induction. The dogs were administered lactated Ringer's solution (10 ml/kg/h, IV) throughout the anesthetic period. Dogs were premedicated with cefazolin (30 mg/kg, IV) and acepromazine maleate (0.03 mg/kg, SC) 30 min prior to induction of anesthesia with propofol (6 mg/kg, IV). After endotracheal intubation, anesthesia was maintained with isoflurane in oxygen. During anesthesia, the dogs were mechanically ventilated with a ventilator to maintain the end-tidal carbon dioxide concentration between 35 and 45 mm Hg. Electrocardiography, pulse oximetry, respiratory gas analysis, invasive MAP measurement in the dorsal pedal artery, determination of MAC of isoflurane, and measurement of rectal temperature were performed with an anesthetic monitor system (Datex-Ohmeda S/5, GE Healthcare, Madison, Wis.) every 2 min throughout the anesthetic period.

Sub-Tenon injection of lidocaine and phacoemulsification were performed by the same investigator (JA) in all dogs; that author was unaware of the treatments administered to each dog. Each dog was placed in dorsal recumbency, and the head was stabilized with a vacuum pillow. The left eye was aseptically prepared with 0.5% povidone-iodine solution. The mediodorsal portion of the bulbar conjunctiva

(approx 5 mm from the limbus) was incised with tenotomy scissors, and the conjunctiva and sub-Tenon capsule were bluntly dissected from the underlying sclera. The appropriate IV solution was injected; simultaneously, the assigned solution (lidocaine or saline solution) was administered via sub-Tenon injection with a 19-gauge, curved, blunt irrigating cannula (Stevens sub-Tenon's anesthesia cannula, Katena, Denville, NJ) and syringe (Fig. 3-1). Gentle digital ocular massage on the closed eyelids was performed for 1 min to promote distribution of the injected solution. Ten min after the injections, horizontal pupil diameter was measured with a caliper, and routine one-handed phacoemulsification (Millenium CX5920, Bausch & Lomb, Rochester, NY) was performed. At the end of the surgery, the incision created in the bulbar conjunctiva to assist with sub-Tenon injection was apposed with 8-0 polyglactin 910 (Coated Vicryl, Ethicon, Bridgewater, NJ) in a simple continuous suture pattern. Then, 4 mg of triamcinolone acetonide (Udenolon, Kukje Pharm, Ansan, Republic of Korea) and 4 mg of gentamicin sulfate were injected subconjunctivally. A nerve stimulator (Peripheral nerve locator-stimulator, Life-Tech Inc, Stafford, Tex) was placed on the ulnar nerve, and anesthesia was discontinued when the train-of-four twitch response was fully recovered. Duration of anesthesia (from intubation to extubation) and surgery (from corneal incision to conjunctival suture), mean elapsed ultrasonographic time, and phacoemulsification power were recorded.

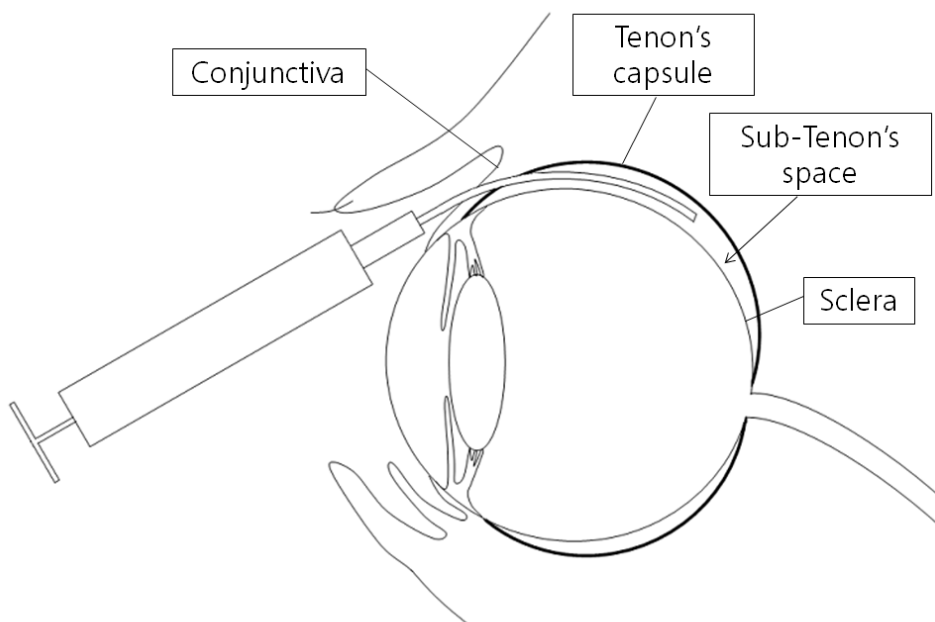


Figure 3-1. Schematic of the insertion of a cannula beneath the bulbar sheath (vagina bulbi; commonly known as Tenon's capsule). The cannula was inserted through a conjunctival incision in the left eye of each of 14 Beagles. None of the dogs had ophthalmic abnormalities, and all dogs subsequently underwent phacoemulsification.

4. Evaluation of intraoperative analgesia

Intraoperative analgesia was assessed by evaluating the end-tidal isoflurane concentration required for maintenance of heart rate and MAP within a baseline range. The baseline range was defined as the value obtained immediately before corneal incision $\pm 10\%$. End-tidal isoflurane concentration was maintained at 1.0% for at least 5 min before the beginning of surgery. After the start of the corneal incision, the inhaled isoflurane concentration was adjusted every 2 min on the basis of the heart rate and MAP in response to surgical stimuli: the inhaled isoflurane concentration was increased by 0.25% when heart rate or MAP increased by $> 10\%$ of the baseline value, and the inhaled isoflurane concentration was decreased by 0.25% when heart rate or MAP decreased by $> 10\%$ of the baseline value. The end-tidal isoflurane concentration was recorded every 2 min and at the time the following surgical procedures were started: making of the corneal incision, phacoemulsification, irrigation-aspiration, corneal suturing, and conjunctival suturing. End-tidal isoflurane concentration for each surgical procedure and mean end-tidal isoflurane concentration during the surgery were compared between the groups.

5. Evaluation of postoperative analgesia

A subjective pain score (Smith *et al.*, 2004; Park *et al.*, 2010) (6 categories; scale for each category, 0 to 3 or 0 to 4; total pain score scale, 0 to 21; Appendix) was determined by a trained observer (EL) immediately before each dog was premedicated; this score was used as a baseline value. At the end of surgery, dogs were transferred to a quiet room. The pain score was determined 0.25, 0.5, 1, 2, 4, 6, 8, and 24 hours after extubation by the same trained observer, who was not aware of the treatment group for each dog. Inadequate pain control was defined as a total pain score ≥ 9 or a score ≥ 3 for any category at any time point. Dogs with inadequate pain control received tramadol (4 mg/kg, IV) as a rescue analgesic; those dogs were excluded from further pain score evaluations and considered as treatment failures. The pain scores at each time point and time to treatment failure were compared between the 2 groups.

6. Statistical analyses

Results were expressed as mean \pm SD. All analyses were performed by use of statistical software (SPSS, version 12.0K for Windows, SPSS Inc, Chicago, Ill). Differences in intraoperative physiologic data (heart rate, MAP, end-tidal isoflurane concentration, and pupil diameter), duration of anesthesia and surgery, degree of surgical stimuli (mean ultrasonographic time and phacoemulsification power), and postoperative values (subjective pain score and time to treatment failure) were compared via the Mann-Whitney U test. Values of $P < 0.05$ were considered significant.

RESULTS

Before the sub-Tenon injections of the assigned solutions, the eyes of all dogs were positioned in a ventromedial or ventral direction. At the beginning of the surgery, all eyes in both groups were centrally positioned. Chemosis and mild subconjunctival hemorrhage were detected in 6 of 14 and 8 of 14 eyes, respectively. Swelling of the conjunctiva did not impede surgical procedures, including making the corneal incision and suturing. In all eyes, the degree of subconjunctival hemorrhage was limited and did not require hemostasis. Akinesia was maintained throughout the surgery (Fig. 3-2). Phacoemulsification was completed successfully without surgical or anesthetic complications in all eyes.

Heart rate, MAP at each point during the surgery, mean \pm SD duration of anesthesia (54.1 ± 3.6 min), and mean duration of surgery (14.4 ± 3.2 min) were not significantly different between the 2 groups. Mean ultrasonographic time and phacoemulsification power were 3.0 ± 1.3 min and $19.6 \pm 1.9\%$, respectively, for the control group and were 2.6 ± 0.8 min and $19.3 \pm 3.0\%$, respectively, for the lidocaine group. There was no significant difference in ultrasonographic time and phacoemulsification power between the groups. Mean pupil diameter immediately before corneal incision was significantly ($P = 0.007$) greater for the lidocaine group (13.7 ± 0.7 mm), compared with the value for the control group (12.2 ± 0.8 mm; Fig. 3-2).

Mean end-tidal isoflurane concentrations at each surgical stimulus were calculated (Fig. 3-3). Isoflurane requirements were significantly lower for the lidocaine group than for the control group at the start of irrigation and aspiration ($P = 0.007$), corneal suturing ($P = 0.001$), and conjunctival suturing ($P = 0.007$). Mean end-tidal isoflurane concentration during the surgical procedures was significantly ($P = 0.007$) lower for the lidocaine group (1.02%) than for the control group (1.18%). Moreover, anesthesia was maintained throughout the surgery with a MAC ≤ 1.0 for 5 of 7 dogs in the lidocaine group, whereas anesthesia was maintained with a MAC ≤ 1.0 for only 2 of 7 dogs in the control group.

The subjective pain score before dogs were premedicated and during the postoperative period were not significantly different between the groups at any time points (Fig. 3-4). Rescue analgesia was required by 2 dogs in the control group (mean \pm SD, 22.5 ± 10.6 min after extubation) and 1 dog in the lidocaine group (15 min after extubation); time to treatment failure did not differ significantly between the 2 groups.



Figure 3-2. Photographs of the eye position in a control dog that received 2 ml of saline (0.9% NaCl) solution administered via sub-Tenon injection into the left eye and simultaneous IV injection of 0.2 mg of atracurium/kg (0.02 ml/kg [A–C]) or a dog in the lidocaine group that received 2 ml of a 2% solution of lidocaine hydrochloride via sub-Tenon injection into the left eye and simultaneous IV injection of saline solution (0.02 ml/kg [D–F]). Photographs were obtained before the injections (A and D), 10 min after the injections (B and E), and at the end of phacoemulsification (C and F). In panels C and F, bubbles in the anterior chamber were created during filling of the anterior chamber with saline solution.

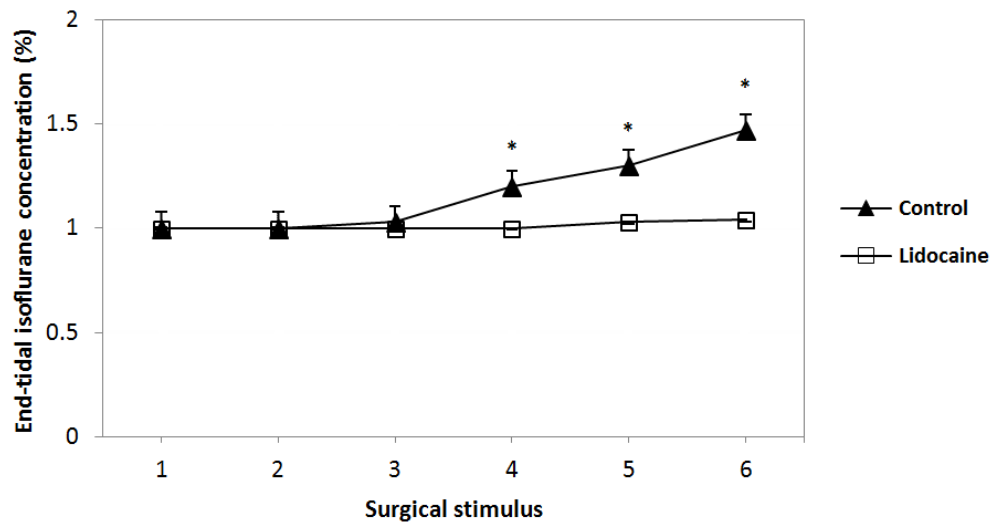


Figure 3-3. Mean \pm SD end-tidal isoflurane concentration immediately before corneal incision (1) and at the start of making the corneal incision (2), phacoemulsification (3), irrigation-aspiration (4), corneal suturing (5), and conjunctival suturing (6) for the 7 dogs of the control group and the 7 dogs of the lidocaine group. *Value is significantly ($P < 0.05$) different between the control and lidocaine groups.

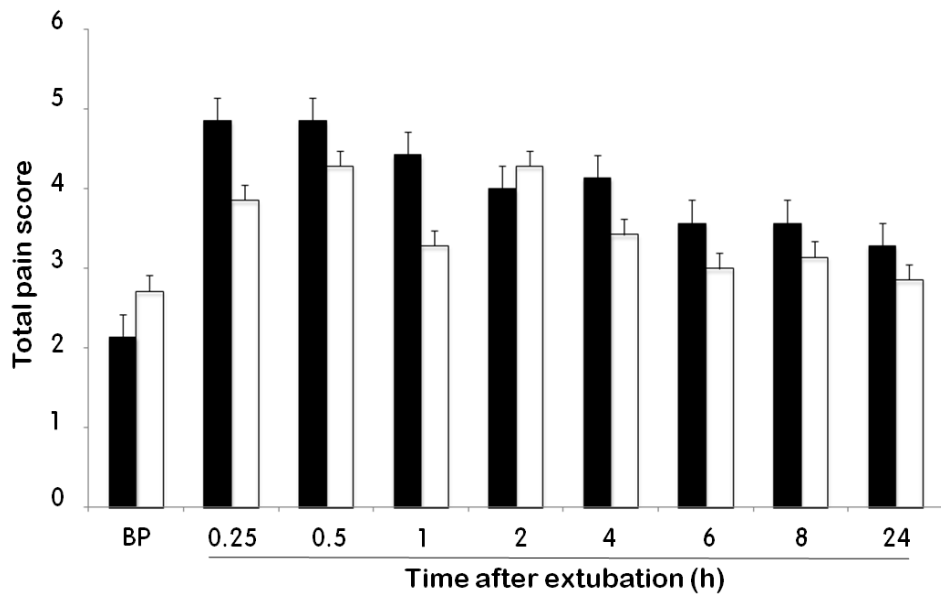


Figure 3-4. Mean \pm SD subjective pain score (total pain score scale, 0 to 21) for the 7 dogs of the control group (black bars) and 7 dogs of the lidocaine group (white bars) before premedication (BP) and at various time points after extubation. There was no significant difference in scores between the groups at any time point.

DISCUSSION

The study reported here was performed to evaluate the feasibility of administration of a local anesthetic via sub-Tenon injection to provide regional anesthesia and akinesia of extraocular muscles during phacoemulsification in dogs. Results of this study indicated that sub-Tenon injection of a local anesthetic could provide intraoperative analgesia, akinesia of extraocular muscles, and additional mydriasis during phacoemulsification. Although we hypothesized that the lidocaine group would have lower subjective pain scores during the post-operative period than the control group, there was no significant difference in the values between the 2 groups.

The space beneath Tenon's capsule is a potential cavity between Tenon's capsule and the sclera (Canavan *et al.*, 2003). The caudal portion of the space is not attached to the sclera, and the space can be approached by incising the conjunctiva and Tenon's capsule (Canavan *et al.*, 2003). Because extraocular muscles and sensory and autonomic nerve fibers in the retrobulbar space penetrate Tenon's capsule to infiltrate the sclera, anesthetic solution administered via sub-Tenon injection anesthetizes the insertion portion of the extraocular muscles and nerve fibers surrounded by Tenon's capsule. Then, the solution penetrates Tenon's capsule and spreads into the retrobulbar space, where extraocular muscle cone and sensory or motor nerves exist (Canavan *et al.*, 2003; Ahn *et al.*, 2013). This accounts for

development of sensory block, akinesia, and pupil dilation.

Administration of anesthetic via sub-Tenon injection is widely used in humans during intraocular surgery for intraoperative and postoperative analgesia (Roman *et al.*, 1997; Kwok *et al.*, 1999; Canavan *et al.*, 2003; Sohn *et al.*, 2008). In 1 study 15 in humans, 99.1% of patients undergoing various intraocular surgeries, including cataract removal, trabeculectomy, and vitrectomy, with anesthesia provided by administration of a local anesthetic via sub-Tenon injection, reported no pain during the surgery. The present study revealed that administration of a local anesthetic via sub-Tenon injection could provide excellent intraoperative analgesia during phacoemulsification in dogs because 5 of 7 dogs in the lidocaine group required a low isoflurane requirement ($MAC \leq 1.0$) during the surgery. Moreover, sub-Tenon injection of lidocaine reduced the mean end-tidal isoflurane concentration during surgery by 15.7%, compared with the concentration for the control group (1.02% vs 1.18%, respectively). These results suggested that phacoemulsification could be performed more safely in high-risk surgical patients (eg, geriatric animals) with sub-Tenon injection of a local anesthetic. Other general anesthetic regimens, such as ketamine combined with xylazine and diazepam (Hazra *et al.*, 2008) that cause less cardiovascular and respiratory suppression could also be combined with sub-Tenon injection of a local anesthetic for phacoemulsification in geriatric patients.

In a study (Kwok *et al.*, 1999) in humans, 90% of patients undergoing vitreoretinal surgery after sub-Tenon injection of a local anesthetic did not require

postoperative analgesia. However, we did not observe any differences in subjective pain scores between the 2 groups of dogs in the present study. According to studies (Smith *et al.*, 2004; Park *et al.*, 2010) of dogs undergoing phacoemulsification with anesthesia provided via systemic and intracameral injection of lidocaine, time to treatment failure was significantly longer in the lidocaine injection group than the control group. Moreover, the prevalence of treatment failure in the control group in that study ranged from 83.3% to 100%, which was markedly higher than the proportion of dogs with treatment failure in the present study (3/14). Although the pain score system used in the present study was appropriate for assessment of postoperative pain following phacoemulsification in another study (Park *et al.*, 2010), the system could not reflect the exact degree of pain in the present study because pain assessment in animals is highly subjective (smith *et al.*, 2004). Subjective pain scores did not differ significantly between the 2 groups at any time point, and atracurium does not have analgesic or sedative effects (Accola *et al.*, 2006; Plumb *et al.*, 2008). Therefore, the results did not appear to be attributable to the observer's underestimation of the pain score or to atracurium administration. Theoretically, a shorter surgical time could induce less surgical stimuli and pain perception, and it is possible that a shorter duration of the surgery time in the present study (mean \pm SD, 14.4 \pm 3.2 min), compared with that in other studies (mean \pm SD, 20.0 \pm 4.5 min; range, 55 to 75 min) (smith *et al.*, 2004; Park *et al.*, 2010), might have contributed to the results. Additionally, subconjunctival injection

of triamcinolone would reduce postoperative pain because anti-inflammatory properties of corticosteroids can contribute to relief of pain (Cole *et al.*, 2005).

Although the degree of akinesia is more variable than is the analgesic effect in humans (Roman *et al.*, 1997; Canavan *et al.* 2003), akinesia was achieved within 10 min after sub-Tenon injection of lidocaine and was maintained throughout the surgery in all eyes in the lidocaine group for the dogs of the present study. This result corresponds with results of a previous study (Ahn *et al.*, 2013) in dogs in which investigators found that akinesia was induced in a mean \pm SD of 6.5 ± 4.9 min and maintained for 88.5 ± 17.2 min after sub-Tenon injection of lidocaine. The difference in the ability to induce akinesia between humans and dogs is presumably attributable to a smaller orbital volume in dogs, compared with that in humans, that contributes to distribution of anesthetic agents (Ahn *et al.*, 2013). Moreover, in contrast to the procedures in humans, cataract surgery and sub-Tenon injection of a local anesthetic are performed in anesthetized dogs, which prevents conscious movement of the eye during the surgery. Therefore, sub-Tenon injection of a local anesthetic in domestic animals can be a useful alternative to systemic administration of neuromuscular blocking agents that cause respiratory muscle paralysis (Ahn *et al.*, 2013).

There are only a few reports (Wilkie *et al.*, 2007; Savino *et al.*, 2010; Ahn *et al.*, 2013) of studies in which the mydriatic effects of sub-Tenon injection of a local anesthetic in humans and other animals have been investigated because pupil

dilation for intraocular surgery is generally achieved by topical administration of anticholinergic agents such as tropicamide. However, the topical mydriatic agents have a slow onset of mydriatic effects, which delays the time until start of surgery, and these effects typically will disappear during the surgery. Moreover, mydriasis can be insufficient, especially in patients with preexisting uveitis, which is commonly accompanied by hypermature cataracts (Lundberg *et al.*, 2003; Wilkie *et al.*, 2007). Sub-Tenon injection of a local anesthetic can be used to overcome these disadvantages of topically applied mydriatic agents. Investigators of another study (Roman *et al.*, 1997) indicated that they favored sub-Tenon injection of a local anesthetic in cases of insufficient pupil dilation before cataract surgery. In another study (Ahn *et al.*, 2013) in dogs, investigators found that mydriasis was induced a mean \pm SD of 4.2 ± 4.3 min after the injection and was maintained for 82.9 ± 15.6 min. Mean pupil diameter 10 min after the sub-Tenon injection in the present study was significantly greater for the lidocaine group than for the control group, which indicated there was an additional mydriatic effect, even after mydriasis had been induced by topical administration of anticholinergic and sympathomimetic agents. Therefore, sub-Tenon injection of a local anesthetic can contribute to maximal dilation of the pupil and access to the lens during phacoemulsification.

Chemosis and subconjunctival hemorrhage are common complications after sub-Tenon injection of a local anesthetic (Roman *et al.*, 1997; Canavan *et al.* 2003; Ahn *et al.*, 2013). Chemosis is caused by rostral migration of solution administered via

sub-Tenon injection. The incidence of chemosis is 39.4% to 53.3%; however, it usually does not impede access to the surgical field (Canavan *et al.* 2003; Ahn *et al.*, 2013). In the present study, chemosis was evident in 6 of 14 eyes at the beginning of the surgery but did not impair surgical procedures in any of the effected eyes. Subconjunctival hemorrhage was detected in 32% to 56% of humans in a study (Canavan *et al.* 2003). Hemorrhage was limited and did not cause inconvenience during the surgical procedures in the dogs of the present study. Topical application of a vasoconstrictive agent (eg, phenylephrine) or cauterization of conjunctival vessels could reduce hemorrhage in hyperemic eyes (Canavan *et al.* 2003). Although blinking ability was not evaluated postoperatively in the present study, akinesia of the eyelids as a result of diffusion of anesthetic solution has been reported in humans (Rauz *et al.*, 1997). Therefore, close monitoring of eyelid function or topical application of ophthalmic lubricants should be considered after surgery to avoid the risk of corneal ulcers.

CONCLUSIONS

Analysis of the results of the present study indicated that sub-Tenon injection of a local anesthetic could be an effective method for providing intraoperative analgesia, akinesia of extraocular muscles, and pupil dilation for phacoemulsification in dogs. Sub-Tenon injection of a local anesthetic would enable cataract surgery without systemic administration of neuromuscular blocking agents, which cause respiratory muscle paralysis. In addition, sub-Tenon injection of a local anesthetic results in the need for only a low isoflurane concentration to maintain anesthesia during surgery, which could be an important factor in high-risk surgical patients. Furthermore, additional mydriatic effects could improve exposure of the surgical field and visibility of the lens during phacoemulsification.

GENERAL CONCLUSIONS

Sub-Tenon's anesthesia with 2 ml of 2% lidocaine provided excellent exposure of surgical area (i.e. cornea and lens) during phacoemulsification by inducing extraocular akinesia and mydriasis. Lower dose (1ml) of lidocaine was considered insufficient for phacoemulsification because akinesia and mydriasis were obtained in only 90% and 70%, respectively, whereas 2 ml of lidocaine in all eyes in chapter 1. Sub-Tenon's anesthesia required lesser dose of lidocaine for akinesia compared to retrobulbar anesthesia in chapter 2. Moreover, systemic administration of atracurium did not induce mydriasis which was obtained by retrobulbar anesthesia and sub-Tenon's anesthesia in 50% and 90%, respectively. Even though there was no significant postoperative analgesic effect, sub-Tenon's anesthesia provided excellent analgesia during phacoemulsification in chapter 3. Through these studies, it was shown that sub-Tenon injection of 2 ml of 2% lidocaine was an effective method for inducing akinesia of extraocular muscles, mydriasis, and intraoperative analgesia for phacoemulsification in dogs. Therefore, this could be another option for surgical field exposure and pain management during phacoemulsification in dogs.

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APPENDIX

Subjective pain scoring system for evaluation of postoperative analgesic effects after injection of a local anesthetic or saline (9% NaCl) solution beneath the bulbar sheath (vagina bulbi; commonly known as Tenon's capsule) of the left eye of 14 clinically normal Beagles undergoing phacoemulsification.

Characteristic	Score	Criteria
Comfort	0	Asleep or calm
	1	Awake and interested in surroundings
	2	Mild agitation or depressed and uninterested in surroundings
	3	Moderate agitation, restless, and uncomfortable
	4	Extremely agitated or thrashing
Movement	0	Quiet
	1	1 to 2 position changes/min
	2	3 to 6 position changes/min
	3	Continuous position changes
Appearance of treated eye	0	Normal
	1	Mild changes (affected eye partially closed)
	2	Moderate changes (blinking or third-eyelid protrusion of affected eye)
	3	Severe changes (affected eye continuously closed or pawing at eye)
Behavior (unprovoked)	0	Too sedate to evaluate
	1	Normal
	2	Minor changes
	3	Moderately abnormal (less mobile or alert than normal, unaware of surroundings, or restless)
	4	Markedly abnormal (very restless, vocalizing, self-mutilating, grunting, or facing back of cage)
Interactive behaviors	0	Too sedate to evaluate
	1	Normal
	2	Pulls away or blepharospasm when surgical site touched; mobile

	3	Vocalizes when wound touched and reluctant to move but will when coaxed
	4	Violent reaction to touching of surgical site, snapping, growling when approached, or failing to move when coaxed
Vocalization	0	Quiet
	1	Crying but responds to quiet voice and stroking
	2	Intermittent crying, with no response to quiet voice and stroking
	3	Constant crying (unusual for this particular dog), with no response to stroking or voice

(Adapted from Smith LJ, Bentley E, Shih A, et al. Systemic lidocaine infusion as an analgesic for intraocular surgery in dogs: a pilot study. *Vet Anaesth Analg* 2004;31:53–63. Reprinted with permission.)

국문 초록

개에서 백내장 수술 시 공막밖공간 마취의 유
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백내장은 개에서 실명을 유발하는 가장 흔한 질환 중 하나로, 수정체 유화 흡인술과 같은 수술적 방법을 통해 치료할 수 있다. 백내장 수술을 위해서는 외안구 근육의 마비 및 동공확장을 통한 술부의 노출이 필수적이다. 또한 안구는 신경 밀도가 높은 구조이기 때문에 수술적 자극은 통증을 유발할 수 있으며, 이에 따라 술 중 및 술 후 진통처치가 필요하다. 본 연구의 목적은 개에서 백내장수술 시 테논막하 마취를 적용했을 때 외안구 근육 마비와 동공확장, 술 중 및 술 후 진통효과를 유발할 수 있는지를 평가하는 것이다.

제 1장에서는 정상 눈을 가진 개에서 리도카인 주사제를 테논막하 공간에 주입하였을 때 외안구 근육 마비와 동공확장을 유발할 수 있는지에 대해 기술하였다. 전신마취 하에 5마리의 비글견의 양 쪽 눈을 대상으로 3단계 교차 실험을 실시하였다. 실험군으로 2% 리도카인 1 ml (1 ml 리도카인 군)와 2% 리도카인 2 ml (2 ml 리도카인 군)을, 대조군으로 생리식염수 2 ml를 최소 14일의 휴식기를 두고 테논막하 공간에 주입한 후 안구의 위치변화, 동공크기 및 안압의 변화를 평가하였다. 2 ml 리도카인 군에서는 모든 눈에서 외안구 근육 마비 및 동공확장(동공직경 > 10 mm)이 유발되었으며, 평균 유발 시간은 각각 6.5 ± 4.9 분 및 4.2 ± 4.3 분 이었다. 1 ml 리도카인 군에서 외안구 근육 마비는 9개의 눈에서, 동공확장은 7개의 눈에서 유발되었으며, 평균 유발 시간은 각각

10.7 \pm 5.8 분 및 5.4 \pm 2.4 분 이었다. 그러나 외안구 근육 마비 및 동공확장의 평균 유발 시간에 대한 두 실험군 간에 유의적 차이는 확인되지 않았다. 대조군에서 안구의 위치 및 동공 직경의 변화는 관찰되지 않았다. 외안구 근육 마비의 지속시간은 2 ml 리도카인 군의 경우 88.5 \pm 17.2 분이었으며, 이는 1 ml 리도카인 군에서의 44.3 \pm 26.7 분보다 유의적으로 길었다 ($p < 0.05$). 동공확장의 지속시간 또한 2 ml 리도카인 군의 경우 82.9 \pm 15.6 분으로, 1 ml 리도카인 군에서의 51.7 \pm 28.9 분보다 유의적으로 길었다. 모든 군에서 주사 전 후의 안압의 변화는 관찰되지 않았다.

제 2장에서는 테논막하 마취의 외안구근육 마비 및 동공확장 효과를 기존에 널리 쓰이고 있는 방법인 atracurium의 전신투여 및 안구후방마취와 비교하였다. 열 마리의 비글견에 최소 7일의 휴식기를 두고 다음의 세가지 처치를 하였다: atracurium (0.2 mg/kg, AT군)의 전신투여; 한쪽 눈에 2% 리도카인 (2.0 ml, RB군)의 안구 후방마취; 반대쪽 눈에 2% 리도카인 (2.0 ml, ST군)의 테논막하 마취. RB군과 ST군에서 리도카인의 투약 10분 후에도 외안구근육 마비가 유발되지 않을 경우, 1ml의 리도카인을 추가투여 하였다. 외안구근육 마비의 유발시간은 RB군 (9.0 \pm 6.5분)에 비해 AT군 (1.5 \pm 0.9분)과 ST군 (3.8 \pm 5.8분)에서 유의적으로 짧았다. 외안구근육 마비의 지속시간은 AT군 (60.6 \pm 23.6

분)과 RB군 (89.0 ± 52.8 분)에 비해 ST군 (116.2 ± 32.8 분)에서 길었으며, 통계적 유의성은 AT군과 ST군 사이에서만 확인되었다. 동공확장은 RB군의 5개의 눈에서, ST군에서는 9개의 눈에서 확인되었으며, 두 군 간에 유발시간 (각각 3.6 ± 3.1 분, 2.9 ± 2.3 분) 및 지속시간 (각각 91.4 ± 31.9 분, 102.1 ± 35.8 분)에는 유의적인 차이가 없었다. 이를 통해 테논막하 마취는 atracurium의 전신투여 및 안구후방 마취보다 외안구근육 마비와 동공확장을 효과적으로 유발할 수 있음을 확인하였다.

제 1장과 2장의 결과를 바탕으로, 제 3장에서는 정상 눈을 가진 개에 테논막하 마취 하에 수정체 유화 흡인술을 실시하는 동안 외안구 근육 마비 및 동공확장이 유지되는지의 여부와 술 중 및 술 후 진통효과를 평가하였다. 실험군 7마리에 2% 리도카인 2 ml를 테논막하 공간에 주사하였고, 생리식염수 (0.02 ml/kg)를 정맥주사 하였다. 대조군 7마리에는 생리식염수 2 ml를 테논막하 공간에 주사하였고, atracurium (0.02 ml/kg)을 정맥주사 하였다. 또한 수술 전에 tropicamide와 phenylephrine 합제 안약을 점안해 동공확장을 유발하였다. 해당약물의 주사 10분 후, 동공의 크기를 측정한 후 수정체 유화 흡인술을 실시하였다. 술 중 진통효과를 평가하기 위해 호흡중기 isoflurane 농도를 측정하였으며, 술 후 진통효과의 평가를 위해서는 통증평가표에 의거해 주관적

으로 통증의 정도를 평가하였다. 모든 개체에서 외안구근육 마비가 유발되었다. 동공 크기는 실험군에서 13.7 ± 0.7 mm로, 대조군 (12.2 ± 0.8 mm) 보다 유의적으로 큰 것을 확인하였다. 호흡중기 isoflurane 농도를 실험군에서 유의적으로 낮았다. 그러나 술 후 통증의 정도는 두 군간에 유의적인 차이가 없었다.

본 연구를 통해 2% 리도카인 2 ml를 이용한 테논막하 마취는 개에서 수정체 유화 흡인술 시 외안구 근육 마비와 동공확장 및 술 중 진통효과의 유발을 위해 효과적임을 확인하였다. 따라서 테논막하 마취는 수정체 유화 흡인술 시 술부의 노출 및 진통효과를 위한 효과적인 방법이 될 것으로 사료된다.

주요어: 개, 백내장수술, 테논막하 마취, 동공확장, 외안구근육 마비

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