Comparison of systemic atracurium, retrobulbar lidocaine, and sub-Tenon’s lidocaine injections in akinesia and mydriasis in dogs

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Abstract

Objective 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.

Animal studied Ten healthy beagle dogs without apparent ocular disease.

 Procedures 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.

Results 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.

Conclusions 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.

Key Words: atracurium, akinesia, mydriasis, retrobulbar anesthesia, sub-Tenon’s anesthesia

INTRODUCTION

Intraocular and corneal surgeries require central fixation of the globe for appropriate exposure of the cornea.1,2 Because general anesthesia induces deviation of the eyeball in a medioventral direction,2 neuromuscular-blocking agents (NMBs) have been commonly used for extraocular muscle akinesia in veterinary medicine.1,2 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.1,3

Regional anesthetic techniques could be an alternative to the systemic administration of NMBs for extraocular muscle akinesia.1,3 Retrobulbar and sub-Tenon’s anesthesia are widely used during ophthalmic surgery in humans.4,5 In addition to extraocular muscle akinesia, these techniques could also provide mydriatic and analgesic effects.6–8 However, the regional anesthetic techniques have generally been performed for intra- and postoperative analgesia for ophthalmic surgery such as enucleation in veterinary medicine.6,9 Moreover, studies concerning the effects of sub-Tenon’s anesthesia on extraocular muscle akinesia and mydriasis in animals are limited.10 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 (AT) and retrobulbar anesthesia using lidocaine in dogs.

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**MATERIALS AND METHODS**

*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).

*Study design*
Three treatments were established for each dog: intravenous administration of AT (Atra®; Hana pharm Co., Ltd., Seoul, Korea) 0.2 mg/kg (AT group, n = 20); retrobulbar injection of 2 mL of 2% lidocaine (Daehan Lidocaine HCl 2%; Daehan Co., Ltd., Seoul, Korea) 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.

*Anesthesia and surgical procedures*
General anesthesia was induced with propofol™ 1%, 6 mg/kg, IV; Claris Lifesciences, Vasana, India) via a preplaced intravenous catheter. Following endotracheal intubation, anesthesia was maintained with isoflurane (Forane soln.; Choongwae Pharm. Co., Seoul, Korea) 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 and sub-Tenon’s injections 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 third 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.

*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 after 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

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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.\(^1\) 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.

**Statistical analyses**

The results were expressed as mean ± 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. 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. 1). The mean volume of lidocaine administered in the RB group was significantly greater than that in the ST group \((P = 0.001, \text{Table 1})\). 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 ± SD onset and duration times of akinesia and mydriasis are presented in Table 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).

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. 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
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.

### 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.\(^1,3\) 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.\(^1,12\) 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.\(^13,14\) Therefore, it is recommended that the respiratory functions of all patients receiving NMBs be closely monitored.\(^13\)

Regional anesthesia is commonly used for a variety of ophthalmological procedures in human medicine.\(^4,15\)

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>AT</th>
<th>RB</th>
<th>ST</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agent (Dose)</td>
<td>Atracurium (0.2 mg/kg)</td>
<td>2% lidocaine (2.5 ± 0.5 mL, range 3.7–7.7 mg/kg)</td>
<td>2% lidocaine (2.1 ± 0.3 mL, range 3.7–7.5 mg/kg)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Akinesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of eyes</td>
<td>20/20</td>
<td>10/10</td>
<td>10/10</td>
<td></td>
</tr>
<tr>
<td>Onset</td>
<td>1.5 ± 0.9 (*–4)</td>
<td>9.0 ± 6.3 (1–15)</td>
<td>3.8 ± 5.8 (1–20)</td>
<td>0.000</td>
</tr>
<tr>
<td>Duration</td>
<td>60.6 ± 23.6 (29–109)</td>
<td>89.0 ± 52.8 (11–164)</td>
<td>116.2 ± 32.8 (63–164)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mydriasis†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of eyes</td>
<td>0/26</td>
<td>5/10</td>
<td>9/10</td>
<td></td>
</tr>
<tr>
<td>Onset</td>
<td>No change</td>
<td>3.6 ± 3.1 (1–9)</td>
<td>2.9 ± 2.3 (1–6)</td>
<td>0.635*</td>
</tr>
<tr>
<td>Duration</td>
<td>0</td>
<td>91.4 ± 31.9 (36–118)</td>
<td>102.1 ± 35.8 (59–149)</td>
<td>0.589*</td>
</tr>
</tbody>
</table>

Data are expressed as means ± 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 nonsignificant differences between groups based on Tukey’s multiple comparison test.

†Mydriasis was defined as pupil diameter >10 mm.

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**Table 2.** Number of eyes in which duration of akinesia was >60 and 120 min, respectively

<table>
<thead>
<tr>
<th>Groups</th>
<th>Duration of akinesia</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;60 min</td>
<td>&gt;120 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AT</td>
<td>9/20</td>
<td>0/20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RB</td>
<td>6/10</td>
<td>4/10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST</td>
<td>10/10</td>
<td>5/10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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**Table 3.** Intraocular pressure (IOP, mmHg) in the pre- and postinjection periods

<table>
<thead>
<tr>
<th>Groups</th>
<th>Pre-injection*</th>
<th>Postinjection†</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT</td>
<td>13.0 ± 3.5</td>
<td>11.9 ± 3.8</td>
<td>0.000</td>
</tr>
<tr>
<td>RB</td>
<td>11.2 ± 2.6</td>
<td>11.7 ± 2.5</td>
<td>0.412</td>
</tr>
<tr>
<td>ST</td>
<td>9.7 ± 1.5</td>
<td>10.0 ± 1.7</td>
<td>0.584</td>
</tr>
</tbody>
</table>

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.

†五分钟 after the injection. A significant decrease in IOP was observed in the AT group.
Retrobulbar anesthesia is achieved by direct injection of anesthetic solution into the intracanal space using a sharp needle. 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.

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. 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.

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. 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, 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. 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). 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. 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, 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 and sub-Tenon’s anesthesia 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. 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. 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 and a decrease in central venous pressure (CVP) or systemic arterial pressure. These findings are in agreement with our study. McMurphy et al. reported that AT did not affect CVP in isoflurane-anesthetized dogs, 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. The elevations tend to be resolved over time. However, they could also be controlled by ocular compression depending on the degree of IOP elevation. 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. 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, further studies are required to evaluate histopathological changes after sub-Tenon’s injection of local anesthetics.

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.

REFERENCES


