Evaluation of the mydriatic effect of intracameral lidocaine hydrochloride injection in eyes of clinically normal dogs

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Objective—To evaluate the mydriatic effect of intracameral injection of preservative-free 1% and 2% lidocaine hydrochloride solutions and determine the onset and duration of mydriasis according to the concentration and volume of lidocaine administered in healthy dogs.

Animals—5 healthy adult Beagles weighing 7 to 10 kg, with no apparent ocular disease.

Procedures—A double-blind randomized 9-session crossover trial was designed. Both eyes were assigned to 9 treatments with a minimum 7-day washout period between treatments: 0.1, 0.2, and 0.3 mL of 2% lidocaine solution; 0.1, 0.2, and 0.3 mL of 1% lidocaine solution; and 0.1, 0.2, and 0.3 mL of balanced salt solution. Dogs were anesthetized, and the allocated treatment was injected intracamerally after aspiration of the same volume of aqueous humor from the anterior chamber of each eye. Two perpendicular pupil diameters were measured. Intraocular pressure, heart rate, respiratory rate, ECG readings, and end-tidal partial pressure of CO₂ were monitored.

Results—Intracameral injection of 1% or 2% lidocaine solutions in volumes of 0.1 to 0.3 mL induced a significant degree of mydriasis, and the effect was maintained for 74 to 142 minutes. Lidocaine injection had no significant effect on intraocular pressure, heart rate, respiratory rate, ECG readings, or end-tidal partial pressure of CO₂.

Conclusions and Clinical Relevance—Intracameral lidocaine injection in healthy dogs induced mydriasis, the timing of which was affected by concentration and volume of lidocaine. This technique could serve as an alternative to topically administered mydriatics for intraocular surgery in dogs. (Am J Vet Res 2009;70:1521–1525)

Mydriasis plays an important role in most intraocular surgeries, including phacoemulsification, intraocular lens implantation, and vitreoretinal surgery to expose the lens and posterior segments. The effect is mainly achieved through topical administration of parasympatholytics such as atropine and tropicamide. Topically administered phenylephrine is also used sometimes as an adjunct medication to facilitate mydriasis. However, the mydriatic effects of topically administered mydriatics occasionally wear off during surgery, and the mydriatic effects of tropicamide are hindered or nonexistent when preoperative inflammation is present. Systemic cardiovascular adverse effects have been reported with the topical administration of sympathomimetics in human and dog eyes and of parasympathomimetics in human eyes.
tive-free 1% and 2% lidocaine hydrochloride solutions and determine the onset and duration of mydriasis according to the concentration and volume of lidocaine administered.

Materials and Methods

Animals—Both eyes of 5 healthy Beagles (2 females and 3 males), aged 2 to 4 years old and weighing 7 to 10 kg, were included in this study. Before the experiment began, complete opthalmic examinations were performed with a slit lamp, an indirect ophthalmoscope, and an applanation tonometer to verify the dogs had healthy eyes. All procedures adhered to the standards 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.

Study design—A double-blinded, randomized, 9-session crossover trial was performed, with a minimum 7-day washout period between treatments. Nine treatments were used: 0.1, 0.2, and 0.3 mL of 2% lidocaine hydrochloride solution; 0.1, 0.2, and 0.3 mL of 1% lidocaine hydrochloride solution; and 0.1, 0.2, and 0.3 mL of BSS. Lidocaine solutions used in this study were preservative-free, and the BSS was administered as a placebo. Ten eyes of the 5 dogs were assigned to receive all 9 treatments with a minimum 7-day interval between treatments. The order of treatments in each eye was randomly assigned. Only 1 eye/dog was treated in any given session, so each dog underwent a total of 18 treatment sessions.

Experimental procedure—Each dog was administered physiologic saline (0.9% NaCl) solution (10 mL/kg/h, IV) and anesthetized with acepromazine (0.05 mg/kg, IV), propofol (6 mg/kg, IV), and isoflurane (1.0% to 1.5% in oxygen). After endotracheal intubation, dogs were monitored via ECG and respiratory gas analysis by use of an anesthesia monitor. Dogs were positioned in dorsal recumbency, with the head stabilized with a vacuum pillow as is routine for intraocular surgery. The eye chosen for treatment was aseptically prepared with 0.2% povodone iodine solution. After initial measurements were obtained (baseline), paracentesis of the anterior chamber of the eye was performed slightly to the right side of the 12 o’clock position of the limbus under an operating microscope, and a volume of aqueous humor equal to that of the treatment to be injected was aspirated with a 30-gauge needle and a 1-mL syringe. Immediately after aspiration, a second paracentesis was performed with the same size needle and syringe, slightly to the right of the position of the first paracentesis, and the test treatment was injected into the anterior chamber of the eye.

Evaluation of mydriasis—Two perpendicular pupil diameters were measured on the surface of the cornea using the operating microscope by means of a caliper, and the mean pupil diameter was calculated. Measurements were obtained before injection, then every minute for 10 minutes after injection, every 5 minutes from 15 to 30 minutes after injection, every 10 minutes from 40 to 60 minutes after injection, and every 30 minutes until the pupil diameter was 4 mm. Sufficient mydriasis was defined as a pupil diameter > 10 mm. When sufficient mydriasis did not take place, measurements were performed for only 30 minutes after injection. The interval to onset and duration of sufficient mydriasis were recorded once mydriasis was achieved. Anesthesia was maintained until all measurements were completed.

Intraocular pressure was measured with an applanation tonometer before injection, 5 minutes after injection, and every 30 minutes during each of the 9 treatment sessions. Heart rate, respiratory rate, ECG readings, and PETCO2 were recorded every 5 minutes throughout each session.

Statistical analysis—Results are expressed as mean ± SD. Statistical analysis was performed by construction of a linear mixed model, with the Scheffe method used as a multiple-comparison (post hoc) test, by use of a commercially available statistical software program. To evaluate differences in mean pupil diameter, IOP, heart rate, and respiratory rate at each time point, as well as differences in interval to onset and duration of sufficient mydriasis, linear mixed models were created for each of these outcome variables by including all potential experimental variables as follows:

\[ y_{ijk} = \beta_0 + \alpha_{ij} + \beta_{j \text{treatment}} + \beta_{j \text{eye}} + \beta_{j \text{treatment} \times \text{eye}} + \epsilon_{ijk} \]

in which \( \alpha_{ij} \) represents a random-subject effect, \( \beta_0 \) is the intercept (representing the mean response in the absence of covariate effect), \( \beta_{j \text{treatment}} \) is the effect of each of the 9 treatments, \( \beta_{j \text{eye}} \) is the laterality (right vs left eye) effect, \( \beta_{j \text{treatment} \times \text{eye}} \) represents the interaction effect between treatment type and laterality, and \( \epsilon_{ijk} \) represents random error, which is identically and independently distributed.

To evaluate differences in IOP, heart rate, and respiratory rate over time for each treatment, the following linear mixed models were used:

\[ y_{ijk} = \beta_0 + \alpha_{ij} + \beta_{i \text{time}} + \beta_{j \text{eye}} + \beta_{i \text{time} \times \text{eye}} + \epsilon_{ijk} \]

in which \( \alpha_{ij} \) represents a random-subject effect, \( \beta_0 \) is the intercept, \( \beta_{i \text{time}} \) is the time effect, \( \beta_{j \text{eye}} \) is the laterality effect, \( \beta_{i \text{time} \times \text{eye}} \) represents the interaction effect between treatment type and laterality, and \( \epsilon_{ijk} \) is random error. A value of \( P < 0.05 \) was considered significant for all analyses.

Results

Pupil diameter—Changes in the mean pupil diameter before and after each treatment were summarized (Table 1). At baseline, there were no significant differences in pupil diameter among the treatments. The pupils of dogs after all lidocaine treatments dilated > 10 mm. A significant (\( P < 0.05 \)) treatment effect on pupil diameter was detected at each measurement point between 1 and 150 minutes after treatment. No significant effect of dog or laterality (right vs left eye) on pupil diameter was evident.

Multiple-comparison testing revealed the mean pupil diameters after all lidocaine treatments were significantly (\( P < 0.05 \)) greater than that after all BSS treatments at each measurement point between 1 and 30
The mean interval to onset was significantly (P < 0.05) greater than after 0.1 mL of 1% lidocaine solution was injected from 1 to 150 minutes after treatment, except at 30 minutes.

Onset and duration of sufficient mydriasis—The interval to onset and duration of sufficient mydriasis after each type of lidocaine treatment were summarized (Table 2). Sufficient mydriasis was achieved after all lidocaine treatments; however, BSS did not induce mydriasis, regardless of volume. The mean interval to onset of mydriasis was < 3 minutes after all lidocaine treatments, except for injection of 0.1 mL of 1% lidocaine solution. Injection of 0.3 mL of 2% lidocaine solution resulted in the fastest onset (1.4 ± 0.7 minutes) and longest duration (142.6 ± 23.0 minutes) of sufficient mydriasis. Choice of treatment was significantly (P < 0.001) associated with interval to onset and duration of mydriasis; a significant (P < 0.05) effect of dog on interval to onset was also detected. No significant relationship between laterality and interval to onset or duration of mydriasis was detected.

Multiple-comparison testing revealed that onset of sufficient mydriasis after 0.1 mL of 1% lidocaine solution was injected took place significantly (P < 0.05) later than it did after the other lidocaine treatments. The duration of sufficient mydriasis after 0.1 mL of 1% lidocaine solution was injected was significantly (P < 0.05) shorter than after 0.2 and 0.3 mL of 1% lidocaine solution and after 0.3 mL of 2% lidocaine solution were injected.

IOP and other variables—When IOP, heart rate, and respiratory rate were compared at each measurement point, no significant effect was evident with regard to treatment, dog, or laterality. Heart rate, IOP, or respiratory rate did not vary significantly with time after any treatment. There were no detectable differences in ECG readings or PetCO₂ before versus after injection.

Discussion

Intracameral injection of lidocaine hydrochloride is reportedly a rapid, effective, and safe means of induc-
The mydriatic effect of intracameral lidocaine injection was evaluated. Lidocaine was injected into the anterior chamber of the eye through a 3-mm corneal incision or a side-port incision. However, we injected lidocaine intracamerally with a 30-gauge needle to prevent leakage of lidocaine before it was distributed to the iris. We removed an equal volume of aqueous humor from the anterior chamber of the eye before intracameral injection was performed to eliminate the possibility of mechanical mydriasis caused by ocular hypertension (a potential confounding factor). There was no apparent drug leakage or ocular hypertension (as assessed via applanation tonometry) before or after drug injection in our study.

Topically applied mydriatics are absorbed systemically, and Atropine, with reported systemic absorption of 63%, has adverse effects similar to those of topically applied anticholinergics, including dry mouth, dry eyes, and disturbances in cardiac function. Cardiovascular adverse effects of topically applied phenylephrine are also reported for humans and dogs. Systemic adverse effects of lidocaine administration, such as cardiovascular and respiratory depression and CNS signs, are usually associated with a high plasma concentration of the drug. The systemic absorption rate of intracamerally injected drugs is limited by the rate of aqueous humor turnover, and the risk of systemic adverse effects is low. In a study in humans, intracameral injection of 0.5 mL of 1% lidocaine solution yielded no therapeutic systemic concentration and no detectable change in heart rate or ECG readings. The study reported here revealed no apparent changes in ECG readings and PetCO2, and no significant effect of lidocaine on heart rate or respiratory rate after intracameral injection of various concentrations and volumes of lidocaine in dogs.

Another concern related to intracameral injection of lidocaine is its effect on the corneal endothelium. Long-term and short-term clinical studies in humans have revealed no significant endothelial cell loss after intracameral injection of preservative-free 1% lidocaine solution, compared with endothelial cell loss in a control group. A study in dogs revealed that intracameral injection of preservative-free 1% or 2% lidocaine solution can yield adverse effects in the anterior aspect of the eye. Bupivacaine, another type of local anesthetic that has a theoretically longer duration than does lidocaine, has been compared with lidocaine with regard to efficacy and safety when injected intracamerally. In a study in humans, there were no significant differences in analgesic effect between intracameral injection of 1% lidocaine solution and intracameral injection of 0.5% bupivacaine, but the bupivacaine caused corneal endothelial damage attributable to its lipid solubility.

Reports exist of temporary loss of visual activity after intracameral injection or inadvertent intravitreal injection of lidocaine in humans. The electroretinographic b-wave amplitude reportedly decreases and b-wave implicit time increases after intracameral injection of lidocaine in humans, and these effects are no longer evident 24 hours after injection. Although results of other studies suggest the retinal toxic effects are transient, careful monitoring is needed when a patient has a clinical condition that allows diffusion of lidocaine to the posterior segment of the eye such as luxation of the lens and rupture of the posterior aspect of the lens capsule or when a patient undergoes surgery of the posterior segment of the eye.

In the present study, the mean interval to onset and duration of sufficient mydriasis were recorded after intracameral injection of 0.1, 0.2, and 0.3 mL of lidocaine at concentrations of 1% and 2%, which are reportedly safe in dogs. The interval to onset and duration of sufficient mydriasis appeared adequate for intraocular surgery for most volumes and concentrations of lidocaine, except for 0.1 mL of 1% lidocaine solution. The mean duration of action was 1 to 2 hours and varied with the concentration and volume of lidocaine administered. Therefore, in clinical settings, the concentration and volume of lidocaine used should be chosen on a case-by-case basis.

Some studies have been conducted to evaluate the analgesic effects of intracameral injected lidocaine in humans undergoing cataract surgery. Clinical trials in humans have revealed that patient cooperation increases when topical application of an analgesic to the eye is supplemented with intracameral injection of lidocaine prior to intraocular surgery. In the present study, we were primarily concerned with the mydriatic effect of intracameral injection of lidocaine on canine eyes, but it is likely such a treatment also has an analgesic effect in dogs undergoing intraocular surgery. Therefore, evaluation of the intraoperative and postoperative analgesic effect of intracameral injection of lidocaine in dogs will be necessary.

In the eyes of clinically normal dogs in the study reported here, intracameral injected lidocaine had no apparent changes in ECG readings and no significant effect of lidocaine on heart rate or cardiac function.
a significant mydriatic effect that began 1 to 10 minutes after injection and persisted for approximately 1 to 2 hours, depending on the volume and concentration used. This technique could serve as an alternative to topical administration of mydriatics for intraocular surgery in dogs and could be particularly beneficial in dogs that are at risk of the systemic adverse effects associated with administration of sympathomimetic and anticholinergic drugs. Furthermore, additional mydriatic effects may be achieved with use of intracameral injection of lidocaine when the mydriasis induced by topical applied drugs before intraocular surgery is not sufficient to permit commencement of surgery or when intraoperative miosis develops.

References