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Peribulbar (Extraconal) Injection of 0.67% Levobupivacaine - Investigation in Healthy Cats

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ABSTRACT

***Background*:** Peribulbar anesthesia is a technique for local anesthesia of the eyebulb and adjacent tissue, which comprises injection of the anesthetic solution outside of the muscular cone (extraconal anesthesia). In cats, peribulbar anesthesia has been performed both with 0.5% ropivacaine and 0.5% bupivacaine, but not with levobupivacaine. Therefore, the purpose of this study was to investigate the efficacy of levobupivacaine at 0.3 mL/kg for peribulbar (extraconal) anesthesia performed as a single inferior injection on healthy cats.

***Materials, Methods & Results*:** Eight cats deemed healthy according to physical examination, ophthalmologic evaluation, complete blood count and biochemical testing were anesthetized with intramuscular ketamine 10 mg/kg combined with xylazine 0.5 mg/kg. Peribulbar injections were performed according to 2 experimental treatment groups: levobupivacaine 2 mg/kg (diluted to 0.3 mL/kg, 0.67% - LT) and saline (CT, control) at equal volume on the contralateral eye. Eyes were randomly selected to receive one of each treatment and were assessed by a different anesthetist who was unaware of treatments. Following 20 min, motor blockade was assessed every 20 min through conjugate eye movement and sensory blockade through corneal touch threshold by use of a cotton swab moistened with saline. Statistical analysis comprised normality testing (Shapiro-Wilk) and a Kaplan-Meier survival analysis to compare return of variables to baseline. All analyses were performed under 5% significance. No differences were found between treated eyes for duration of motor ($P = 0.4817$) or sensory ($P = 0.0546$) block, thus demonstrating failure of blocks. A *post-hoc* sample size calculation demonstrated that 13 cats should have been used to avoid type II error. The Kaplan-Meier analysis for sensory blockade ($P = 0.0546$) showed a tendency towards significance.

***Discussion*:** This study used a technique, volume and approach previously described for dogs, which failed to result in successful blockade using 0.67% levobupivacaine in cats. Also, since this study was conducted without a previous sample size calculation and post-hoc calculation demonstrated that 8 cats were an insufficient number to avoid type II error, the correct number of subjects could have yielded different results. Although retrobulbar anesthesia has been widely described in cats, including with levobupivacaine, no studies had been found addressing the correct volume and concentration for its use in peribulbar anesthesia in cats. Another observation in this study was a very low volume. The maximum volume at 0.3 mL/kg was 1.1 mL and, in a few animals, it did not reach 1 mL, which might be insufficient to diffuse across tissues and reach the target nerves within the muscle cone. This might indicate that, in cats, the calculation should be different and a higher volume per kg should be used. Finally, diluting levobupivacaine from 0.75% to 0.67% could have impacted the success of the blockade. Therefore, more studies are needed using levobupivacaine for peribulbar anesthesia in cats. In conclusion, peribulbar injection of 0.67% levobupivacaine at 0.3 mL/kg does not result in desirable blockade in cats and requires more studies and adjustments on the sample size and the approach to achieve better efficacy and duration.

Keywords: local anesthesia, ophthalmic anesthesia, extraconal block, cats.

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INTRODUCTION

Ophthalmic anesthesia can involve neuromuscular blocking agents or locoregional techniques [1]. For years, retrobulbar anesthesia was the mainstay to provide akinesia and sensory blockade of the eye and surrounding tissues. However, intraconal injection can lead to damage to the optic nerve, hemorrhage and cardiac arrest [6,7,9-11]. Sharma *et al*. [9] have also reported palpebral and scleral necrosis in humans. In cats, retrobulbar anesthesia has been performed using 2% lidocaine and 0.5% levobupivacaine [15].

Peribulbar anesthesia, on the other hand, always deposits the anesthetic solution outside of the muscular cone (extraconal anesthesia) and can be a safer alternative to retrobulbar anesthesia [13]. In cats, 0.5% ropivacaine and 0.5% bupivacaine have been successfully used for peribulbar anesthesia [6,11].

Peribulbar blocks usually require a greater volume of solution to allow diffusion of the drug to the intraconal space [2,5] and levobupivacaine can be a good choice because of its long duration of action and short onset [15]. Studies using levobupivacaine for ophthalmic anesthesia report greater potency compared with bupivacaine [7]. In cats, no studies were found using levobupivacaine for peribulbar anesthesia, only for retrobulbar anesthesia using 0.2 mL/kg [15].

The technique and volume used for peribulbar block has been investigated in dogs and the results suggested that a single injection of 0.3 mL/kg at the lateral 3rd of the lower eyelid causes less complications [3].

The purpose of this study was to investigate the efficacy of levobupivacaine at 0.3 mL/kg for peribulbar (extraconal) anesthesia performed as a single inferior injection on healthy cats.

MATERIALS AND METHODS

Animals

The study was conducted at the Roque Quagliato Veterinary Hospital of the University Centre of Ourinhos. Eight healthy adult cats aged 2.7 ± 1.3 years and weighing 3.5 ± 0.5 kg were enrolled in the study. Cats belonged to the local community and were included after owner consent with the retribution of a complete clinical and ophthalmic checkup. Exclusion criteria comprised any clinical changes on complete blood count, thoracic auscultation or evidence of ocular problems such as corneal ulcers, discharge or periocular inflammation. In addition, only very docile cats were included, to facilitate handling and assessment of corneal touch threshold during the study.

Study design

Prior to the experiment, cats were fasted for 12 h, water was withheld for 1 h and animals were allowed to acclimate to the experimental room for 30 min. At baseline, the natural response of each subject to the corneal touch threshold test was assessed using a cotton swab moistened with sterile saline solution and the natural conjugate eye movement was assessed by slowly turning the heat to the sides and observing the adjustment of the eyes, as described elsewhere [3].

Anesthesia comprised a combination of ketamine[1] [Dopalen® - 10 mg/kg] and xylazine[2] [Calmiun® 2% - 0.5 mg/kg] given instramuscularly (IM). After 20 min to allow complete loss of conscience and muscle relaxation, animals were positioned in lateral recumbency and received a subcutaneous dose of meloxicam[3] [Elo-xicam® 0.2% - 0.1 mg/kg] as a preventive measure to minimize ocular inflammation that might occur after the study.

Peribulbar injections were then carried out on both eyes to comprise 2 treatment groups such as: LT (levobupivacaine treatment) = levobupivacaine[4] [Novabupi® 0.75% - 2 mg/kg]; diluted in 0.9% NaCl5 [Samtec® - final volume of 0.3 mL/kg and final concentration of 0.67%]; and CT (control treatment) = 0.9% NaCl5 [Samtec® - 0.3 mL/kg] to the contralateral eye. Sides were chosen randomly using an online randomizer and postanesthetic evaluations were performed by an anesthetist who was unaware of which side received each treatment and who had extensive previous training in peribulbar anesthesia of dogs and cats.

The technique used for peribulbar injection was the same described previously in dogs [3]. A 25 mm 22-gauge needle[6] [Solidor®] was introduced at the inferior conjunctival fornix of the lower eyelid at the lateral 3rd of the orbit and was advanced with the bevel angled towards the orbit. The cat was then turned to the other side and the same technique was performed on the contralateral eye. Twenty min following injection of both solutions, assessment of motor and sensory blockade were initiated and repeated at 20-min intervals until every criteria resumed its baseline presentation.

Motor blockade was assessed through the conjugate movement of the eyes. Sensory blockade was assessed using the same approach described for corneal touch threshold at baseline, with a sterile moist cotton swab touching and exerting slight pressure over the cornea. To both tests, a score was ascribed as: 0 - absent; 1 - diminished; and 2 - normal. After full recovery both from ocular anesthesia and dissociative anesthesia, animals were then discharged from the study and taken back to their owners.

Statistical analysis

Data were 1st tested for normality and log-normality using the Shapiro-Wilk test. Duration of blockades were compared using a paired *t*-test or Wilcoxon signed ranks test and were also analyzed using a Kaplan-Meier survival curve. Results are presented as median (range). All analyses were performed under 5% significance using a commercial software[7] [GraphPad Prism 6.01®]. A *post-hoc* sample size calculation was performed with the results of this study. The Cohen's d value was calculated 1st and then used for sample size calculation considering < of 0.05 and power of 0.9 using specific software[8] [G*Power].

RESULTS

All subjects completed the study successfully. Motor scores of 0 and 1 were seen for 60 (20-160) min in the CT and 60 (40-160) min in the LT. Sensory scores of 0 and 1 were seen for 60 (40-100) min in the CT and 100 (40-100) min in the LT. The Kaplan-Meier curve did not demonstrate a significant difference between the times for each treatment [$P = 0.0546$ for sensory assessment (Figure 1A), and $P = 0.4817$ for motor assessment (Figure 1B)].

The *post-hoc* calculation of Cohen's d number resulted in 0.9, which then rendered a sample size of 13 animals.

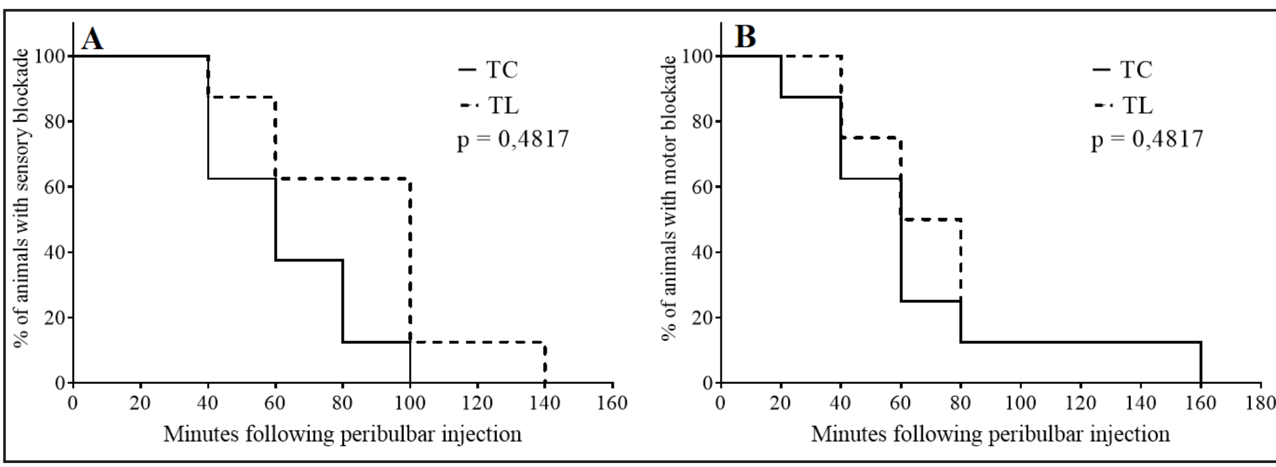

Figure 1. Kaplan-Meier survival analysis of the duration of sensory (A) and motor (B) blockade following peribulbar (extraconal) injection of saline (TC) or 0.67% levobupivacaine (TL) at 0.3 mL/kg to each eye bulb of healthy cats anesthetized with ketamine and xylazine.

DISCUSSION

This study has 2 important results. First, the use of a technique, volume and approach previously described for dogs [3] failed to result in successful blockade using 0.67% levobupivacaine in cats. Second, this study was conducted without a previous sample size calculation, and *post-hoc* calculation demonstrated that 8 cats were an insufficient number to avoid type II error. This can be interestingly observed in the Kaplan-Meier analysis for sensory blockade, which resulted in $P = 0.0546$, very close to significance. It is possible to suggest that the correct number of subjects could have yielded better results.

The eye bulb of cats is regarded as the largest among most carnivores. The periorbital space is small in proportion to the eye bulb and comprises a thin layer of connective tissue involving orbital structures [5,12,15]. Because of these particularities, the use of a technique described for dogs [3] proved insufficient to provide adequate blockade in cats.

Although retrobulbar anesthesia has been widely described in cats, including with levobupivacaine [15], the safety of peribulbar compared to retrobulbar anesthesia [6,7,9-11,12] determined the choice for extraconal injection in this study. For this approach, however, levobupivacaine had not been investigated and no studies were found addressing the correct volume and concentration for its use in cats. The safety of peribulbar injection of levobupivacaine was demonstrated in this study as no subjects showed any signs of complications such as hemorrhage or chemosis.

The choice for a single-point inferior approach was based on a study conducted in dogs by Ferreira [3], which demonstrated similar results for motor and sensory blockade comparing single- and double-point injection, but lesser complications (hemorrhage and chemosis) when using the inferior injection. The volume of 0.3 mL/kg for peribulbar anesthesia was also based on the same study previously cited [3], but since the results of our study failed to show a desirable blockade, perhaps the volume should also be adjusted in addition to other technical adjustments to peribulbar anesthesia in cats.

As much as a dog can be larger in size, the orbit does not necessarily grow proportionally larger with the dog's weight. One study [3] used dogs of around 9.0 kg and, therefore, volumes of around 3 mL. Another study [14] used the same volume in dogs weighing 6-40 kg, with volumes ranging from 2-12 mL. In our study, however, the maximum volume was 1.1 mL and, in a few animals, it did not reach 1 mL. This might indicate that, in cats, the calculation should be different and a higher volume per kg should be used.

Lower volumes, as low as 0.2 mL/kg, have been used for peribulbar anesthesia in cats. Mota *et al*. [13] demonstrated successful blockade of the eye with 0.2 mL/kg of 0.5% ropivacaine in cats. However, these authors used a bent needle approach (L-shaped needle), which could have benefited the deposition of the solution. In the study conducted by Wagatsuma *et al*. [14], the use of ultrasound determined the length of the bulb axis prior to peribulbar injections in dogs, which could be an important information to better position the needle also in cats.

Finally, the use of a fixed dose of levobupivacaine caused the solution to require dilution to achieve the final volume of 0.3 mL/kg. Since levobupivacaine has not been previously investigated for peribulbar anesthesia in the feline species, it is not possible to know how changing its concentration from 0.75% to 0.67% could negatively impact the success of the blockade. Therefore, more studies are also needed with regard to the preparation of the solution and final concentration of levobupivacaine that can provide adequate anesthesia of the eye in cats.

CONCLUSIONS

In conclusion, peribulbar injection of 0.67% levobupivacaine at 0.3 mL/kg does not result in desirable blockade in cats and requires more studies and adjustments on the sample size and approach to achieve better efficacy and duration. A different shape to the needle or perhaps a higher volume could be suggested in future studies using levobupivacaine in cats.

MANUFACTURERS

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***Ethical approval*.** The study was approved by the local Ethics Committee for Animal Usage (protocol No. 006/2019).

***Declaration of interest*.** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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