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A prospective, masked, randomized, controlled superiority study comparing the incidence of corneal injury following general anesthesia in dogs with two methods of corneal protection

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Abstract

Objective: To compare the incidence of corneal injury during general anesthesia (GA) and the immediate post-operative period in eyes protected with topical ocular lubricant alone with eyes protected with topical lubricant followed by complete eyelid closure using tape.

Animals Studied: One hundred client-owned dogs (200 eyes) undergoing GA for MRI scan.

Methods: Patients had ocular lubricant applied to both eyes upon induction of anesthesia. One eye was taped closed immediately after induction for the duration of anesthesia using Strappal® tape (BSN medical™; treatment group), and the other eye was not taped (control group). Eyes were randomly allocated to a treatment group. Ophthalmic examination was performed before and after anesthesia; the examiner was masked to eye treatment groups. Corneal injury was defined as corneal ulceration or corneal erosion. A McNemar's test was used to compare the incidence of corneal injury between groups. A paired-samples *t*-test was used to compare Schirmer-1 tear test (STT-1) readings between groups.

Results: Sixteen eyes (8%) developed corneal erosion. No corneal ulceration occurred. There was no significant difference between incidence of corneal erosion between groups ($p = .454$). There was a significant decrease in STT-1 readings following GA in both groups ($p < .001$), with no significant difference in STT-1 between groups ($p = .687$). No adverse effects of taping the eye closed were observed.

Conclusion: Taping the eyes closed during GA had no additional benefit to the lubrication protocol used in this study.

KEYWORDS

anesthesia, canine, cornea, corneal injury, corneal protection, dog

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1 | INTRODUCTION

Corneal epithelial injury following general anesthesia (GA) is a recognized complication in humans and animals. In human patients, the incidence of corneal injury is reported to be between 0.01% and 2.3% in protected eyes and up to 44% in unprotected eyes.^{1–3} In dogs, the incidence of corneal injury is reported to be 1.9%–18.6% in eyes protected with ocular lubricant.^{4,5,6} Corneal epithelial injury during GA arises from a combination of lagophthalmos due to relaxation of the orbicularis oculi muscle and reduced tear production secondary to drugs used for the GA.^{1,7} The combined effect leads to corneal exposure and drying. Corneal injury can also be a result of direct trauma or chemical injury.^{8–11} Risk factors for the development of corneal injury in human patients include prolonged duration of anesthesia, lateral or prone positioning, surgery on the head or neck and advanced age.^{2,7,12} A retrospective study in dogs identified that patients undergoing prolonged GA, brachycephalic dogs and patients undergoing neurosurgery were at increased risk of developing corneal injury.⁴ However, another prospective study did not identify these or any other risk factors for corneal injury in dogs undergoing GA.⁵ There is currently no gold standard protocol for intraoperative corneal protection in human patients.¹³ However, it is suggested that closure of the eyelids is the best preventative measure.^{1,13,14} The current recommendations in veterinary medicine are regular corneal lubrication intraoperatively and post-operatively.^{5,6,15} However, the frequency of lubrication or type of lubricant recommended is not standardized. There are currently no studies investigating closure of the eyelids during anesthesia in veterinary patients. To the authors' knowledge, this study is the first to evaluate taping the eyelids closed as a method of corneal protection during GA in dogs. It is also the first comparison between eyelid closure and the current recommendation of regular lubrication for corneal protection in dogs undergoing GA.

The aim of the current prospective study was to compare the incidence of corneal injury during GA and the immediate post-operative period when the eyes were protected with topical ocular lubricant followed by taping the eyelids closed or application of topical ocular lubricant alone. It was hypothesized that topical ocular lubricant followed by taping the eyelids closed would provide superior corneal protection compared to application of ocular lubricant alone.

2 | MATERIALS AND METHODS

The study was approved by the University of Bristol Animal Welfare and Ethics Review Board (UIN-20-004).

A power calculation based on the expected size of effect from similar research by Dawson and Sanchez⁵ suggested that 100 dogs (200 eyes) should be enrolled to test the hypothesis. One-hundred dogs (200 eyes) undergoing MRI scan were prospectively recruited into the study. Dogs undergoing MRI scan were chosen because they would be positioned in dorsal recumbency allowing easy access to both eyes and mitigating the potential effect of positioning on incidence of corneal injury, and because the GA would be a similar length of time (mostly under 2 h). Individuals with pre-existing corneal surface disease (including corneal erosion, ulceration, and keratoconjunctivitis sicca) and patients with facial nerve deficits were excluded.

Each patient had an ophthalmic examination before and after the GA performed by an ECVO diplomate or resident in training, including slit-lamp examination (SL-17, Kowa), Schirmer-1 tear test (STT-1) and fluorescein staining before and after GA for MRI scan. Patients were examined prior to the anesthetic and 1–3 h after extubation. The observer performing the ophthalmic examination was masked to the group of each eye.

Anesthetic agents were used in different combinations at the discretion of the anesthetist depending on patient requirements. Premedication agents included dexmedetomidine (Dexdomitor®, Vetoquinol UK Ltd), acepromazine (ACP®, Elanco), butorphanol (Dolorex®, MSD Animal Health), buprenorphine (Buprecare®, Animalcare), methadone (Methadyne®, Jurox), and fentanyl (Fentadon®, Dechra). Induction agent was either propofol (PropoFlo™ Plus; Abbott) or alfaxalone (Alfaxan™; Jurox); two patients had co-induction with propofol and midazolam (Hypnovel®, Cheplapharm Arzneimittel). Inhalational maintenance agent was either isoflurane (IsoFlo®; Abbott) or sevoflurane (SevoFlo®; Abbott).

Topical lubrication with a carbomer-based eye gel (Lubrital™ Eye Gel, Dechra) was applied to the ocular surface of both eyes immediately following induction of general anesthesia and tracheal intubation. Each patient then had one eye taped closed Strappal® tape (BSN medical™; treatment group), and the other was left open as a control (control group). The taping was carried out using 3 vertically placed pieces of tape, one central piece and two comparatively shorter pieces on either side of the first one, as shown in Figure 1. The central piece was placed first to ensure complete eyelid closure. The eyes were randomly allocated into one of the two groups using a random number generator. At the end of the GA, immediately prior to extubation, the tape was removed, allowing the eyelids to open, and both eyes received another application of topical ocular lubricant.

Corneal injury was described as corneal erosion or corneal ulceration. Corneal erosion was defined as superficial epithelial damage with no penetration into the basement



FIGURE 1 Method of application of Strappal® tape used to achieve eyelid closure

membrane of the epithelium that was seen as subtle, patchy uptake of fluorescein staining. Corneal ulceration was defined as loss of corneal epithelium exposing corneal stroma, with an obvious, strong uptake of fluorescein stain.¹⁶ When identified, corneal erosion was treated with frequent topical ocular lubrication.

Incidence of corneal injury between groups was analyzed using a McNemar's test, and Schirmer-1 tear test results were compared between groups using a paired-samples *t*-test. Statistical analysis utilized the statistical software SPSS version 27 (SPSS, IBM). A *p*-value <.05 was considered statistically significant.

3 | RESULTS

Two-hundred eyes from 100 dogs were included in statistical analysis, 56 were male (21 male entire and 35 male neutered) and 44 were female (11 female entire and 33 female neutered). There was a wide variety of breeds with cross-breed being the most commonly represented. Twenty-one dogs had a brachycephalic skull conformation. Incidental abnormalities found on ophthalmic examination included nuclear sclerosis ($n = 4$), incipient cataract ($n = 3$), distichiasis ($n = 2$), iris atrophy ($n = 1$), iridal cysts ($n = 1$), and anisocoria ($n = 1$). The mean duration of GA was 81 min (range 40–170 min). Fifty-eight (58/100) patients had cerebro-spinal fluid (CSF) sampling after the MRI scan; 49 were positioned in right lateral recumbency, and nine were positioned in left lateral recumbency for the duration of the CSF sampling (approximately 20 min). Positioning was dependant on the sampler's dominant hand.

One dog that was initially enrolled in the study was excluded from statistical analysis due to an episode of

regurgitation during the GA; the regurgitated liquid ran over the eye that was taped shut loosening the tape from the eye. This dog was replaced with another in a randomized and masked fashion, to ensure 100 dogs would be included in the statistical analysis. No other dogs were excluded.

The incidence of corneal erosion was 8% (95% confidence interval 4.2%–11.4%) (16 eyes; 16 dogs); no dogs developed corneal ulceration. Corneal erosion was seen in the eye that was taped closed in 6 dogs (6/100; 6%) and in the control eye in 10 dogs (10/100; 10%). The incidence of corneal erosion when compared between the two groups was not statistically significant ($p = .454$). Five (5/16) of the dogs that developed corneal erosion were brachycephalic breeds (31%). When compared with non-brachycephalic dogs, brachycephalic dogs were not more likely to develop corneal erosion ($p = .625$). Of the 16 dogs that developed corneal erosion, eight (8/16) had CSF sampling (50%). Of the eight patients with erosion that had CSF sampling, four dogs developed erosion in the dependant eye and four dogs developed erosion in the non-dependant eye. Patients that underwent CSF sampling were not more likely to develop corneal erosion than patients that did not ($p = 1.000$). Schirmer-1 tear test readings were normal (>15 mm/min) in all eyes prior to GA. There was a statistically significant decrease in tear production after general anesthesia in both groups ($p < .001$); the difference in tear production between groups was not statistically significant before or after general anesthesia ($p = .687$).

4 | DISCUSSION

The results of the present study demonstrated that there was no difference between lubricating the eyes and lubricating the eyes followed by taping the eyes closed in the setting chosen for the study. Overall, the incidence of corneal erosion in this study (8%) was lower than in previous studies (10%–18.6%).^{5,6}

Risk factors for corneal injury in association with GA in human patients include duration of anesthesia (odds ratio [OR] increased by 1.16 per hour of GA),⁷ lateral position (OR: 4.7⁷–7.1)² or prone position (OR 10.8),¹¹ head or neck surgery (OR: 4.4⁷–9.3)² and advanced age (OR: 1.17).⁷ A study by Park et al.⁴ found dogs that developed corneal ulcers following GA had longer duration of GA (175 ± 84.6 min) compared with dogs that did not develop corneal ulcers (104.7 ± 62.7 min), suggesting that increased anesthetic length increased the risk of corneal injury. However, Dawson and Sanchez⁵ did not find an increased incidence of corneal injury with increasing anesthetic time when comparing dogs undergoing GA duration less than 2 h with GA duration over 2 h. In the current study,

all patients underwent GA for MRI scan, as scans were expected to require a similar anesthetic time. Despite this, there was still a time variation between patients, as shown by the mean duration and range. However, none of the GA events were much longer than 2 h, which is a shorter time than some patients in the Dawson and Sanchez study.⁵ It is possible that this time difference might have resulted in a lower incidence of corneal injury in the present study. Previous studies in dogs failed to find an association between corneal injury and patient positioning.^{4,5} Lateral positioning is known to increase the risk of corneal injury of the down-facing eye in human patients,^{2,7} Patients undergoing MRI scanning were chosen for the present study to exclude the possible effect of lateral recumbency in the dependent eye. However, CSF sampling was performed in a percentage of these patients for part of the procedure. These patients were not excluded because the time they spent in lateral recumbency was only a fraction of the total amount of time spent under GA, the rest of which was spent in dorsal recumbency. Also, the data from those patients were used to look for a possible negative effect of having spent some time in lateral recumbency. This was found to be non-existent, which suggests that changing body position to lateral recumbency for a short period of time does not increase the incidence of corneal erosion in dogs under GA. However, this finding might have been limited by the relatively small number of patients included in that sub-group.

It is important to note that the globe position during GA differs between species. In human patients, the eye generally remains in a central position. Eccentric eye position occurs in less than 18% of patients and is most commonly seen as a dorsal elevation of the eye.^{17,18} Because of the central or elevated eye positioning, corneal injury is most commonly seen in the ventral cornea.^{1,19} The canine eye rotates ventromedially during GA,²⁰ this grants lower eyelid protection to part or all of the patient's cornea. One might expect this protective effect to result in corneal injury of the dorsal or dorsolateral cornea only. However, the lesions found in the present study were located in the axial cornea, which suggests that corneal injury in canine patients might occur during the immediate pre- or post-operative period when the eye is in a central position. Therefore, one might argue that corneal protection during the times immediately prior to induction of GA and during recovery from GA might be particularly important. The difference in eye position under GA between species might explain why taping of human patients' eyes has been shown to have a protective effect,^{1,13,14} while no difference was found in the present study between taping and not taping dogs' eyes.

The potential hazard of the adhesive tape rubbing on the cornea if the eyelid becomes partially opened was

something that was considered by the authors in the present study. Adverse effects caused by direct contact of the tape to the cornea, or effects of the adhesive on the eyelid skin, are not reported in the literature pertaining to human patients, except for patients that have allergies to the glue found on some forms of tape.^{13,21,22} It is possible that human eyelids are easily closed with tape due to the lack of hair in the eyelid skin. To account for the difficulty of closing haired eyelids, a strongly adhesive tape was chosen and applied in multiple, vertical strips (Figure 1). Furthermore, it would be advisable to periodically check that the tape was still in place and the eyelids were fully closed. One dog that was initially enrolled in the study was excluded from statistical analysis due to an episode of regurgitation during the GA; the regurgitated liquid ran over the eye that was taped shut. Although the regurgitate moistened the tape, which became loose, it protected the ocular surface from making contact with the regurgitate.

Eyelid closure interferes with observation of the eye and use of globe position and pupil size in the monitoring of the anesthesia, and depth of anesthesia must be monitored using other measurements such as non-invasive blood pressure, capnography, heart rate, and respiratory rate.^{23,24} Therefore, eyelid closure may not be applicable in all situations. The present study supports the idea that the eyes of a dogs undergoing a GA of a duration of up to the upper time limit recorded in this study do not require taping if a similar lubricant is used. The study of Dawson and Sanchez demonstrated that lubrication alone in longer anesthetics was effective in preventing injury in most cases.⁵ However, further studies would be necessary to investigate whether eyelid taping could lower the risk of corneal injury even further in anesthetic events of more than 2 h duration.

Many opioids and alpha-2 adrenergic agents commonly used in anesthetic protocols for sedation and analgesia have been shown to decrease tear production.²⁵⁻²⁹ Dexmedetomidine, medetomidine, butorphanol, pethidine, and fentanyl have all been shown to cause a significant decrease in tear production from baseline to below 15 mm/min 15–20 min after administration.²⁵⁻²⁸ A combination of methadone and ACP has been shown to significantly decrease tear production from baseline, with 30% dogs showing a decrease below 15 mm/min 30–45 min after administration.²⁹ Inhalant agents for anesthetic maintenance have also been shown to significantly decrease tear production in dogs.³⁰ Pre- and post-anesthetic medications varied between patients, with some but not all patients receiving opioids and/or alpha-2 adrenergic agonists. Some of the drugs given might have increased the risk of corneal injury due to their effects on tear production. However, the present study was not designed to assess the effects

of anesthetic drugs on corneal injury, and a variety of sedation and analgesia protocols were used depending on patients' needs. Further studies would be required to analyze whether different pre-anesthetic and anesthetic protocols, and post-operative medications have an influence on corneal injury under GA.

The control group in this controlled superiority study was based on the standard of care at the veterinary hospital where the research was carried out. A true placebo control group where eyes were not provided with any protection during the GA was considered ethically unacceptable. Topical lubricant is the standard of care for any veterinary patient undergoing GA. The ocular lubricant used in this study (LubriThal™ Eye Gel, Dechra) was different to that used by Dawson and Sanchez (Celluvisc® 1%, Allergan).⁵ This may be seen as a limitation of this study. However, studies in human patients comparing different ocular lubricants have not found one type of lubricant to be superior in preventing corneal abrasions.^{13,31} LubriThal™ Eye Gel was chosen in this particular study as it was the usual standard of care at the institution where the research was performed. Lubricant of similar composition has been shown to provide effective corneal protection in human patients.³²

The limitations of the study, as discussed, include lack of a true placebo control group, variable length of GA time, variation in pre-anesthetic and anesthetic drugs used and the use of a different lubricant than the study used for the basis of the power calculation.

5 | CONCLUSION

The findings of the present study demonstrated that closure of the eyelids with tape after lubrication did not reduce the incidence of corneal erosion compared to lubrication alone.

Further studies with patients undergoing GA of longer duration and positioning in different recumbency are required to establish whether taping the eyelids closed would offer superior protection to lubrication used on its own in these conditions.

CONFLICT OF INTEREST

None.

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