



A Comparative Evaluation of Sodium Hyaluronate- and Carbomer-based Ophthalmic Preparations on Tear Production in Cats under General Anesthesia

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ABSTRACT

Background: General anesthesia in cats causes a transient decrease in tear production, necessitating the use of topical lubricants to protect the cornea; however, comparative data on the rate at which different lubricants normalize tear production are limited. This study compared the effect of two different ophthalmic preparations based on sodium hyaluronate and carbomer on tear secretion in cats under general anesthesia.

Methods: The study was conducted using a contralateral eye model in 12 clinically healthy female cats scheduled for spay surgery under xylazine-ketamine-isoflurane anesthesia. Immediately after intubation and confirming the level of surgical anesthesia, one drop of a sodium hyaluronate-containing preparation was applied to the right eye (Group H) and a rice-sized amount of a carbomer-containing preparation was applied to the left eye (Group C). Tear production was measured quantitatively using the Schirmer Tear Test at specific time points before any sedation (T_0), during and after anesthesia ($T_{15-T_{60}}$ and $T_{+15-T_{+60}}$, respectively).

Result: Anesthesia caused a statistically significant decrease in Schirmer Tear Test values compared to baseline in both the groups ($p < 0.05$). At 30 minutes post-anesthesia (T_{+30}), the mean Schirmer Tear Test value in Group H (15.08 ± 2.71 mm/min) was significantly higher than that in Group C (11.00 ± 3.54 mm/min) ($p < 0.05$). At 60 minutes post-anesthesia (T_{+60}), STT values returned to baseline in Group H, while full recovery was not observed in Group C. In conclusion, this study demonstrated that both sodium hyaluronate/dexpanthenol eye drops and carbomer-based eye gel were effective in providing immediate protection to the ocular surface during anesthesia and accelerating recovery after anesthesia, but the sodium hyaluronate formulation provided a significantly faster recovery of tear production to baseline levels in the early post-anesthesia period.

Key words: Anesthesia, Carbomer, Cat, Dry eye, Ocular lubricant, Schirmer tear test, Sodium hyaluronate.

INTRODUCTION

The precorneal tear film is a critical, multilayered structure that moistens and lubricates the cornea and conjunctiva, removes foreign bodies and metabolic wastes, exhibits antimicrobial properties and transports nutrients essential for the corneal avascular structure (Gum and MacKay, 2014; Hartley, 2014). Keratoconjunctivitis sicca (KCS), characterized by insufficient production of the aqueous layer of the tear film, is a significant ophthalmological condition in cats (Hartley, 2014) and other species (Kokde *et al.*, 2025), that causes progressive inflammation of the cornea and conjunctiva. If left untreated, it can lead to serious complications such as conjunctival hyperemia, corneal vascularization, pigmentation, ulceration and even permanent vision loss (Kokde *et al.*, 2025; Mecvan *et al.*, 2024). While the etiology of KCS in cats is multifactorial, Feline Herpesvirus-1 (FHV-1) infections, immune-mediated disorders, trauma and the use of certain pharmacological agents are among the most frequently encountered causes (Hartley, 2014).

General anesthesia is a known risk factor for ocular surface health in veterinary practice (Dawson and Sanchez, 2016). During anesthesia, the palpebral reflex is suppressed and the eye muscle relaxes, leading to incomplete eyelid closure (lagophthalmos), which increases corneal exposure

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to ambient air. Furthermore, many anesthetic and analgesic drugs, particularly anticholinergic agents used for premedication or anesthesia, such as atropine, have been shown to directly reduce tear production by inhibiting the parasympathetic innervation of the lacrimal glands (Cullen *et al.*, 2005; Hartley, 2014; Kanay *et al.*, 2025). The combination of these two factors accelerates tear evaporation and reduces tear secretion in anesthetized cats, creating an iatrogenic (physician-induced) and transient KCS.

To prevent anesthesia-induced ocular surface dryness, the application of topical eye lubricants throughout the

procedure is a standard clinical protocol. Various artificial tear preparations with viscoelastic and mucoadhesive properties are available on the market, including sodium hyaluronate, carboxymethylcellulose, hydroxypropyl-guar and lipid-based products (Araújo and Galera, 2016). These products aim to prevent corneal dehydration and potential damage by creating a moist barrier on the ocular surface. However, comparative data on which type of ophthalmic product is superior in maintaining tear secretion and ocular surface health during anesthesia are limited.

This study aimed to quantitatively investigate the effects of two different types of ophthalmic preparations with different active ingredients on tear secretion in cats under general anesthesia using the Schirmer Tear Test (STT). The study results are intended to provide veterinarians with scientific evidence to guide the selection of the most effective prophylactic agent for the prevention of corneal complications during anesthesia.

MATERIALS AND METHODS

This study was conducted on 12 clinically healthy female cats, aged between 6 and 24 months, which were brought to the Balikesir University Faculty of Veterinary Medicine, Department of Surgery and a Veterinary Clinic (Pati Beurre Veterinary Clinic) for elective spaying. Approval for the study was obtained from the Balikesir University Animal Experimentation Local Ethics Committee (BAUN HADYK) (No: 2024/11-9). Informed consent forms were obtained from all cat owners regarding the inclusion of their animals in the study and the procedures to be performed. The clinical procedures for this study were carried out between December 2024 and February 2025.

The study was conducted using a contralateral eye model, the cats' right and left eyes were divided into two groups based on the topical preparations to be applied:

Group H (n=12 eyes)

Eye drops containing 0.15% sodium hyaluronate and 2% dexpanthenol (Bepanthol® Eye, Bayer, Istanbul, Turkey) were applied to the right eyes.

Group C (n=12 eyes)

Eye gel containing 2.0 mg/g carbomer (Viscotears®, Bausch and Lomb, Istanbul, Turkey) was applied to the left eyes.

Before surgery, detailed medical history information was obtained from the owners of all cats. A systemic physical examination was performed and vital signs; body temperature, heart and respiratory rates, mucosal color, capillary refill time and lymph node status were recorded. Ophthalmoscopic examination was performed on both eyes to exclude the presence of ocular pathology. Before any anaesthesia, the STT was performed on both eyes to determine baseline tear production. In cases, where a condition that could contraindicate surgery was suspected, routine hemogram and serum biochemistry analyses were performed and only healthy animals without anesthesia risk were included in the study.

All cats were fasted for 12 hours before surgery but continued to have free access to water. For premedication, all cats received an intramuscular (IM) injection of 2 mg/kg xylazine hydrochloride (Rompun® 2%, Elanco, Istanbul, Turkey), followed by 6 mg/kg ketamine hydrochloride (Ketasol® 10%, Richter Pharma, Ankara, Turkey) IM at 15 minutes as induction agent. After achieving adequate depth of anesthesia, the cats were intubated with an endotracheal tube and anesthesia was maintained with a mixture of 2% isoflurane (Isoflurane-USP®, Adeka, Samsun, Turkey) and oxygen. To ensure methodological standardization for comparing the recovery profiles of both groups, anesthesia was maintained for 60 minutes in all cats, regardless of the actual duration of the surgery. Anesthesia was terminated 60 minutes after intubation and the cats were extubated.

Immediately after intubation and confirming the level of surgical anesthesia, one drop of a sodium hyaluronate-containing preparation was applied to the right eye (Group H) and a rice-sized amount of a carbomer-containing preparation was applied to the left eye (Group C).

The Schirmer Tear Test (Fiona Vet Schirmer Tear Test Strip, Cat No: 1195) was performed by placing the notched end of a sterile test strip in the conjunctival fornix in the lateral third of the lower eyelid and holding it there for 60 seconds. The amount of wetting on the strip was recorded in millimeters (mm/min). Measurements were repeated for both eyes at the following time points:

Before anesthesia

Baseline (T_0) (measured before any sedative or anesthetic agents).

During anesthesia

At 15 (T_{15}), 30 (T_{30}), 45 (T_{45}) and 60 (T_{60}) minutes (measured after the application of ocular lubricants).

Post-anesthesia

At 15 (T_{+15}), 30 (T_{+30}) and 60 (T_{+60}) minutes following extubation.

During anesthesia, measurements were taken with the cats lying in a lateral position and their heads brought to the sternal position to eliminate the effects of gravity.

The data analysis was carried out using a software (SPSS ver. 30.0, IBM Corp., Armonk, USA). The Shapiro-Wilk test was used to check the data for normal distribution. The Friedman test was used to analyze time-dependent changes within groups. The Wilcoxon signed-rank test was used as a post-hoc analysis to determine the time points between which statistically significant differences occurred as a result of the Friedman test. The Mann-Whitney U test was used to compare the differences between two groups (Group H and Group C) at a specific time point. A p value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

This study compared the effects of two topical ophthalmic preparations with different compositions on tear production

in cats under general anesthesia using contralateral eye model. The findings highlight the importance of selecting lubricants in the management of anesthesia-induced transient keratoconjunctivitis sicca (TCS) and contribute to the existing literatura.

All 12 cats included in the study completed the procedures without any problems. In baseline measurements taken before anesthesia (T_0), the mean STT value was 18.58 ± 3.83 mm/min for Group H (right eye) and 17.50 ± 3.94 mm/min for Group C (left eye). No statistically significant difference was found between the baseline values of the groups ($p > 0.05$). Compared to the baseline values before anesthesia (T_0), a statistically significant decrease in STT values was observed at the first measurement point (T_{15}) during anesthesia in both group H (9.83 ± 3.58 mm/min) and Group C (11.08 ± 3.08 mm/min) ($p < 0.05$). This decrease in tear production during anesthesia reached its lowest levels toward the end of anesthesia in both groups (Table 1, Fig 1).

The baseline (T_0) STT values are in full agreement with the normal ranges reported in the literature for healthy cats (Cullen *et al.*, 2005; Davis and Townsend, 2011; Köstlin *et al.*, 2015). This confirmed that the study population had healthy lacrimal function and provided a reliable starting point for evaluating the effects of anesthesia and subsequent treatments. The statistically significant decrease in tear production observed when comparing the baseline before anesthesia (T_0) to the first measurement taken during anesthesia (T_{15}) is an expected finding and is supported by the literatura (Pietro *et al.*, 2016; Kanay *et al.*, 2025). The mechanism underlying this effect is multifactorial. Xylazine, used in premedication, as an alpha-2 adrenergic agonist, reduces tear secretion by directly suppressing the parasympathetic innervation of the lacrimal glands (Di Pietro *et al.*, 2021). Ghaffari *et al.* (2010) used xylazine at the same dose (2.0 mg/kg IM) as in the present study and showed that STT values decreased from ~ 13.9 mm/min to ~ 2.18 mm/min just 15 minutes after

sedation. Notably, this critical drop of ~ 2.18 mm/min STT remained significantly higher than the T_{15} findings in this study (Group H: 9.83 mm/min; Group C: 11.08 mm/min), demonstrating that lubricants actively reduce anesthesia-induced drying. Furthermore, isoflurane, used for maintenance of anesthesia, has been reported to reduce tear production even when used alone (Shepard *et al.*, 2011). This suggests that the T_{15} findings are a result of the strong pressor effect of anesthesia.

Group H (Sodium hyaluronate)

STT values decreased significantly during anesthesia, reaching their lowest levels at time points T_{45} (4.50 ± 0.80 mm/min) and T_{60} (4.58 ± 0.67 mm/min). Post-anesthesia, STT values began to rise rapidly and the value measured at time point T_{+60} (18.00 ± 3.86 mm/min) was not statistically different compared to baseline (T_0) ($p > 0.05$). This finding indicates that tear production returned to baseline levels

Table 1: Within-group changes in schirmer tear test values (Mean \pm SD).

Time point	Right eye (Group H) STT (mm/min)	Left eye (Group C) STT (mm/min)
T_0	18.58 ± 3.825^d	17.50 ± 3.943^c
T_{15}	9.83 ± 3.589^b	11.08 ± 3.088^b
T_{30}	6.00 ± 2.412^a	6.08 ± 2.021^a
T_{45}	4.50 ± 0.798^a	4.50 ± 0.905^a
T_{60}	4.58 ± 0.669^a	4.75 ± 0.754^a
T_{+15}	9.50 ± 4.167^b	8.08 ± 2.906^a
T_{+30}	15.08 ± 2.712^c	11.00 ± 3.542^{ab}
T_{+60}	18.00 ± 3.861^{cd}	16.25 ± 3.415^{bc}

T_0 : Baseline (pre-anesthesia).

$T_{15}, T_{30}, T_{45}, T_{60}$: 15, 30, 45 and 60 minutes during anesthesia.

$T_{+15}, T_{+30}, T_{+60}$: 15, 30 and 60 minutes post-anesthesia (recovery).

STT: Schirmer tear test.

Values in the same column with different superscript letters are statistically different ($p < 0.05$).

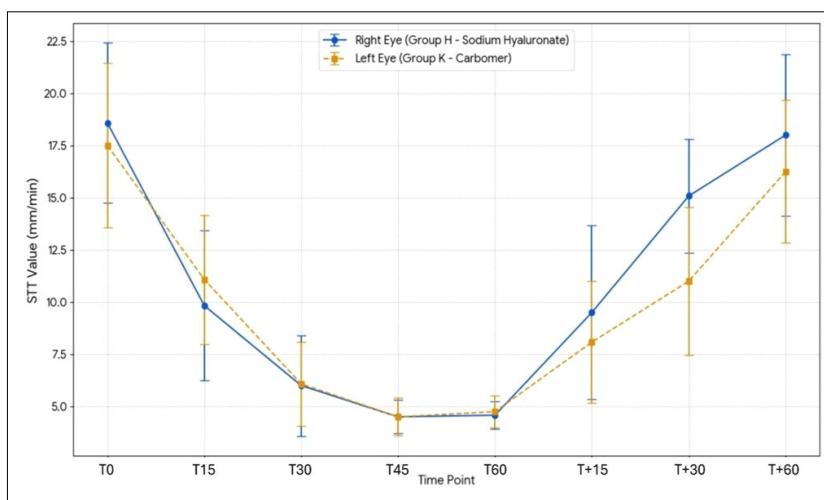


Fig 1: Within-group changes in STT values over time.

within 60 minutes of switching off the anaesthesia (Table 1, Fig 1).

Group C (Carbomer)

Similarly, STT values decreased significantly in Group C during anesthesia, reaching their lowest values at T_{45} (4.50 ± 0.91 mm/min) and T_{60} (4.75 ± 0.75 mm/min). Although an increase in STT values was observed during the post-anesthesia recovery period, this increase was slower than in Group H. The mean STT value at T_{+60} (16.25 ± 3.42 mm/min) was still statistically lower than the baseline T_0 value ($p < 0.05$). This suggests that tear production had not yet fully returned to baseline levels after the 60-minute follow-up period (Table 1, Fig 1).

When the STT values of the two treatment groups were compared at specific time points, no statistically significant difference was found between the groups at most time points ($p > 0.05$).

A statistically significant difference was found between the two groups at the 30th minute post-anesthesia (T_{+30}) ($p < 0.05$). At this time point, the mean STT value of Group H (15.08 ± 2.71 mm/min) administered sodium hyaluronate was significantly higher than the mean STT value of Group C (11.00 ± 3.54 mm/min) administered carbomer. This finding suggests that the recovery of tear production at T_{+30} was faster in Group H than in Group C. No statistically significant differences were found between the groups at all other time intervals.

Carbomer is an effective polymer that, thanks to its high viscosity, remains on the ocular surface for extended periods, providing a mechanical barrier and lubrication (Xiao *et al.*, 2008). However, this high viscosity may somewhat slow down the regeneration and spread of the natural tear film. In contrast, sodium hyaluronate is a natural glycosaminoglycan with biomimetic properties similar to the mucin layer of the tear film. The high water retention capacity and viscoelastic properties, provides lubrication during blinking and forms a stable film when the eye is open (Zheng *et al.*, 2014). Furthermore, dexpanthenol (provitamin B5), contained in the SH formulation in our study, is known for its properties that support epithelial cell regeneration and accelerate wound healing. Therefore, it can be assumed that the rapid recovery in the SH group is due not only to mechanical moisturizing but also to a biological effect that actively supports the physiological health of the corneal surface. These results have important implications for clinical practice. The difference in the rate at which tear production returns to normal after anesthesia directly impacts the duration of risk to the cornea. A difference in STT of a few millimeters or a 30-minute time advantage can play a critical role in preventing corneal dehydration, epithelial erosion and potentially painful ulcerations (Mecvan *et al.*, 2024). Our study demonstrates that lubricant selection should focus not only on the product's viscosity or persistence, but also on its biocompatibility and potential to promote physiological healing. Given that healing takes hours in studies without

any lubricant, as demonstrated in cats under xylazine sedation where recovery of tear production took 4-8 hours (Kanda *et al.*, 2019), it is clear that both groups in our study significantly shortened this time, but that the SH formulation accelerated this healing even further.

This study has some limitations. The protocol did not include a control group that received no topical lubricant during anesthesia (no-treatment). Previous studies have shown decreased tear production under anesthesia in this group and it was thought that depriving cats of protective eye lubrication for extended periods could pose a risk of iatrogenic corneal damage. The potential findings of such a group are largely predictable from relevant literature data. Ghaffari *et al.* (2010) already demonstrated decreased STT values in a study using xylazine. The duration of normal physiological recovery after anesthesia was also demonstrated by Kanda *et al.* (2019) in cats treated with xylazine and no lubricant. Therefore, this study focused on the comparative efficacy of two different active agents, using literature data as an indirect reference point, rather than a "no-treatment" group. The relatively small sample size and the study population limited to young, healthy female cats may limit the generalizability of the results. Results may vary in geriatric patients, those with systemic diseases, or those undergoing different anesthesia protocols. Additionally, this study used only a quantitative measure, STT. Future studies will incorporate qualitative tests such as fluorescein staining, tear break-up time and even tear osmolarity measurements to further assess corneal health, providing a more comprehensive picture of the effects of different agents.

CONCLUSION

In conclusion, this study demonstrated that both sodium hyaluronate/dexpanthenol eye drops and carbomer-based eye gel were effective in providing immediate protection to the ocular surface during anesthesia and accelerating recovery after anesthesia, but the sodium hyaluronate formulation provided a significantly faster recovery of tear production to baseline levels in the early post-anesthesia period.

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Disclaimers

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures for experiments were approved by the Committee of Experimental Animal care and handling Techniques were approved by the University of Animal Care Committee.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish, or preparation of the manuscript.

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