Original Article

Effects of morphine-alfaxalone-midazolam premedication, alfaxalone induction and sevoflurane maintenance on intraocular pressure and tear production in dogs

Mayordomo-Febrer A.*[a], Rubio M.[a], Martínez-Gassent M.[a], López-Murcia M.M.[a].

[a]*Departamento de Medicina y Cirugía Animal, Facultad de Veterinaria, Universidad CEU Cardenal Herrera, Alfara del Patriarca (46115), Valencia, España.*

*Corresponding author. Tel.: 0034660994014.
E-mail address: aloma.mayordomo@uchceu.es (Mayordomo-Febrer A.).

Abstract

Intraocular pressure (IOP) and tear production are ocular parameters commonly affected by general anaesthesia. A good control of both of them is necessary to guarantee a successful ophthalmic surgery. The purpose of this research was to analyse the effect of a common anaesthetic protocol based on morphine-alfaxalone-midazolam premedication, alfaxalone induction and sevoflurane maintenance on IOP and Schirmer tear test (STT-1) in healthy dogs. Twenty two adult mixed dogs scheduled for an ovariohysterectomy were used for this study. IOP and STT-1 were registered at baseline (T_0), 5 (T_1), 10 (T_2) and 15 (T_3) minutes after premedication with morphine-alfaxalone-midazolam combination; after induction (T_4) with alfaxalone and 15 (T_5) and 25 (T_6) minutes after maintenance with sevoflurane. A paired Student´s *t*-test and a Wilcoxon test were used to analyse the difference between IOP and STT-1 over time respectively.

This anaesthetic protocol produced a statistically significant increase in IOP ($P<0.05$) after premedication and induction, which was maintained after intubation. STT-1 showed a severe significant reduction during all the procedure ($P<0.001$). These conclusions should be taken into consideration, especially in dogs with damaged corneas, those predisposed to glaucoma and those who will be undergoing intraocular surgery. Ocular lubrication is necessary if this protocol is used.

Key words: Alfaxalone; Anaesthesia; Dogs; Intraocular pressure; Schirmer test.

Introduction

Selection of an anaesthetic protocol for ocular surgery should include consideration of the effects on ocular parameters, such intraocular pressure (IOP), pupil size or tear production. In fact, the success of an ophthalmic procedure may depend on their control before, during and after the surgery (Gross and Giuliano 2007; Hasiuk and others 2014).

It is well known that IOP is determined by aqueous humour (AH) dynamics, intraocular (choroidal) blood volume, central venous pressure and extraocular muscle tone (Gelatt and MacKay 1998). In veterinary medicine, several research groups have evaluated the effects of different anaesthetic agents on this parameter in the dog (Costa and others 2015; Gunderson and others 2013; Hasiuk and others 2014; Hofmeister and others 2008; Jang and others 2015; Kanda and others 2015). Most general anaesthetics seem to lower or maintain IOP within normal limits because of actions on the central nervous, respiratory, and circulatory systems (Jang and others 2015). In contrast, various anaesthetic drugs can increase IOP through a variety of mechanisms; generally altering extraocular muscle tone, inducing vasodilatation or changing the rate of AH outflow (Gelatt 2011).

General anaesthesia has been documented to decrease tear production in humans, dogs, cats and horses (Di Pietro and others 2016; Herring and others 2000; Komnenou and others 2013; Shepard and others 2011; Snow and others 1975). Ulcerative keratitis is a common complication associated with this decline due to corneal exposure and drying, mainly in brachycephalic dogs.

Morphine is widely used in veterinary medicine for its efficacy in treating intra and post-operative pain during moderate surgeries (Kongara and others 2012). Alfaxalone interacts with γ-aminobutyric acid receptors producing anaesthesia and muscle relaxation (Torres and others 2012). In veterinary medicine, it is commonly used in the dog to induce

and maintain general anaesthesia intravenously (Muir and others 2008, 2009). Midazolam, administered prior to anaesthetic induction, provide a good muscle relaxation reducing the alfaxalone related hyperkinesia (Miguel and others 2013). Regarding sevoflurane, due to its low blood:gas partition coefficient and rapid onset of action, allows easy control of anaesthetic depth (Kazama and Ikeda 1988).

The aim of this study was to investigate the effects of the combination of morphine, alfaxalone and midazolam as premedication, in association with the induction with alfaxalone and sevoflurane maintenance on the IOP and Schirmer tear test (STT-1) in healthy dogs. To our knowledge, the effect of the protocol previously described on these ocular parameters has not previously been investigated in the clinically normal dog.

Materials and methods

Case selection

Twenty two adult female dogs of mixed breed, scheduled for an ovariohysterectomy in the Veterinary Teaching Hospital of the CEU Cardenal Herrera University (Valencia, Spain) were enrolled for the study. The number of animals included was determined based on other research published earlier (Costa and others 2015; Ghaffari and others 2010; Gunderson and others 2013; Hasiuk and others 2014). A prospective clinical trial using client-owned dogs was designed and a signed consent was provided for the dog owners before the inclusion in the trial.

All animals were clinically normal on the pre-anaesthetic evaluation that included a physical examination, a complete blood count and serum biochemistry profile, thoracic radiographs and an electrocardiogram. Dogs were classified following the American

Society of Anaesthesiologists (ASA) classification. Only ASA I and ASA II patients were included in this study. Animals of higher risk were excluded. The surgery was performed using a right flank approach.

Ophthalmological examination

A complete ophthalmic exam was performed on both eyes of each dog, including STT-1 (Sno-Strips, Chauvin Pharmaceuticals Ltd), slit-lamp biomicroscopy (Kowa SL-15, Kowa Company Ltd), applanation tonometry (Tonopen XL, Reichert) and direct ophthalmoscopy (Panoptic ophthalmoscope, Welch Allyn). Only the patients with no ocular abnormalities were included.

Recording of data during the anaesthetic protocol

The IOP measurements were obtained, always by the same person, after application of topical anaesthetic (Tetracaine hydrochloride 0.5%, Colircusí anestésico doble, Alcon-Cusí Laboratorios). The IOP values were an average of 3 readings from each eye taken alternatively between eyes, using the values having less than 5% standard deviation (SD). All measurements were performed between 9.00-11.00 a.m. to minimize diurnal variation in IOP (Giannetto and others 2009). When necessary, a smooth clamping over the conjunctiva was made to rotate the eye and record the IOP.

The tear production was recorded, by the same investigator, by placing the commercial strip in the medial aspect of the inferior conjunctival fornix. Both eyes were assessed concurrently.

After ophthalmic exam, STT-1 and IOP measurements were registered at the following times: baseline (T_0), 5 (T_1), 10 (T_2) and 15 (T_3) minutes after anaesthetic

premedication with an intramuscular combination of alfaxalone (5 mg/Kg, Alfaxan 10 mg/ml, Vétoquinol especialidades veterinarias S.A.), morphine chloride (0,4 mg/Kg, Morfina Braun 2%, B Braun Medical S.A.), and midazolam (1 mg/Kg, Midazolam Normon 15 mg/3ml, Laboratorios Normon); after induction (T_4) with an intravenous injection of alfaxalone (3 mg/Kg, Alfaxan 10 mg/ml, Vétoquinol especialidades veterinarias S.A.) and 15 (T_5) and 25 (T_6) minutes after maintenance with sevoflurane (SevoFlo, Dr.Esteve).

When the animal was conscious, STT-1 values and IOP readings were recorded on sternal recumbence. After induction and during anaesthetic maintenance, for obviously reasons, data were recorded on right lateral recumbence.

Anaesthetic monitoring

Initially we recorded basal values of hearth rate (HR), respiratory rate (RR) and temperature (T). All this parameters were recorded 15 minutes after premedication.

During all the anaesthesia, every 5 minutes, we registered with the anaesthetic monitor (AS-3, Datex Ohmeda) various hemodynamic and respiratory variables: HR, RR, T, oxygen saturation, capnography, exhaled and inspired anaesthetic agent percentage, exhaled and inspired tidal volume and central venous pressure.

Statistical analysis

Normality was tested using the Shapiro-Wilk statistic. A paired Student´s t-test and a Wilcoxon test were utilized to analyse the difference between IOP and STT-1 over time respectively. To assess differences in IOP between both eyes, a one-way ANOVA was performed. All data were expressed as mean ± SD. Statistical tests were done using the

SPSS program (SPSS for Windows V.18.0.). A value of $P < 0.05$ was considered significant.

Results

The diagnostic as well the surgical procedures were performed successfully with the anaesthetic protocol previously mentioned.

The results (mean IOP and STT-1) for all the studied period are shown in Table 1. The mean ± SD baseline IOP for the right and left eye were 13.8 ± 3.0 and 14.2 ± 2.9 mm Hg respectively. For the SST-1, the mean ± SD baseline was 18.4 ± 4.4 and 17.8 ± 3.5 mm/min respectively.

The studied protocol produced a statistically significant increase in IOP ($P<0.05$) after premedication and induction, which was maintained after intubation (60 minutes). STT-1 showed a very marked significant reduction ($P<0.001$) during all the procedure (Fig. 1). We found no differences between both eyes over time either the SST-1 or the IOP (Fig. 2).

Discussion

In the present investigation, the effect on IOP and STT-1 following the administration of morphine-alfaxalone-midazolam as premedication, alfaxalone as induction and sevoflurane as maintenance has been studied, in order to evaluate the utility of a common anaesthetic protocol on ophthalmic surgeries. The regulation of these parameters, mainly the IOP, is important for successful ophthalmic surgery and can be

greatly affected by the anaesthetic procedure (Brunson 1980). Even the smallest increases in this parameter can reduce the axoplasmic flow causing damage on the retina.

The administration of preanaesthetic and anaesthetic agents typically cause decreases in IOP promoting relaxation of the extraocular muscles tone, depressing the central nervous system, increasing AH outflow and reducing arterial and venous blood pressure (Gross and Giuliano 2007). Some examples are medetomidine or dexmedetomidine (Artigas and others 2012; Kanda and others 2015). Studies performed with sevoflurane, desflurane and ketamine-midazolam combination did not alter this ocular parameter (Almeida and others 2004; Ghaffari and others 2010) and on the other hand alfaxalone and propofol showed a significant increase in the IOP (Costa and others 2015; Hasiuk and others 2014). The mechanism resulting in this increase remains unclear but is known that most anaesthetic agents depress the respiratory control centre resulting in elevations on the CO_2 levels. This respiratory acidosis induces a reflex vasodilation, also affecting the choroidal blood vessels, causing an increase in IOP (Gelatt 2011).

The baseline values of IOP observed in the dogs of our study were similar to those reported previously in normal dogs (Martin 2005a). In our research the IOP has significantly increased during anaesthetic premedication, induction and maintenance.

The premedication protocol selected included morphine chloride in combination with alfaxalone and midazolam. First one was selected to cover surgery analgesia and, although this drug decreases the basal IOP in humans (Drago and others 1985) in dogs, combined with acepromazine, had no significant effects in IOP values (Stephan and others 2003).

Alfaxalone generally produces a rapid and excitement free induction to anaesthesia and a good muscle relaxation, although it has been described a temporary period of head

shaking and hyperextension of the neck in some cases, that have not been find in our study (Miguel and others 2013; Muir and others 2008). The effect of a single injection of alfaxalone on IOP has been previously studied in the koala, sheep and dog. While in the koala the IOP showed no significant difference between conscious and anesthetized states, in the sheep and dog various researchers have demonstrated an initial and transient significant increase in this parameter (Costa and others 2015; Grundon and others 2011; Hasiuk and others 2014; Torres and others 2012).

Midazolam was included in the protocol to better control the alfaxalone side effects and to reduce the dose of the rest of the drugs. Gunderson et al. (2013) studied the effect of the anaesthetic induction with midazolam-etomidate and midazolam-propofol on ocular parameters and showed a clinically elevation of the IOP likely related to the propofol or etomidate rather than midazolam. Likewise midazolam-ketamine combination had no significant effect on IOP in clinically normal dogs (Ghaffari and others 2010).

Regarding to sevoflurane, Almeida et al. (2004) shown no significant clinical effects on IOP during 105 minutes of inhalant anaesthesia.

Therefore, we propose that the greater influence on IOP in our study was likely due to the alfaxalone action, rather than the effect of the other drugs. As we mentioned above, Costa et al. (2015) shown a transient increased on IOP followed by a significant decrease in their study performed with dogs. In contrast, we observed a significant and sustained increase in IOP during all the procedure. This could be related to the double injection of alfaxalone and his cumulative effect, which half-life is between 24.0 ± 1.9 and 37.4 ± 1.6 minutes depending on the dose (Ferre and others 2006). Further research is required to define more completely the mechanisms causing this increase but we relate them with its action on respiratory system. At the dose of 6 mg/kg, alfaxalone decreases respiratory rate,

minute volume and PaO_2 and increases the $PaCo_2$ (Ferre and others 2006; Muir and others 2008).

It is well known that IOP may vary according to sex, breed, age, animal behaviour, type of tonometer, expertise of the clinician, circadian rhythm or body position (Gelatt and MacKay 1998; Giannetto and others 2009; Martin-Suarez and others 2014; Piccione and others 2010). In our study, IOP readings were always done between 9.00-11.00 a.m. to minimize diurnal variation. Topic anaesthetic instillation was used to reduce discomfort or pain and all measurements were performed by the same person with wide experience in handling the applanation tonometer. Regarding body position, Broadwater et al. (2008) shown a significantly decreased in IOP in dogs that were dorsally recumbent or sitting. This parameter did not change significantly in sternal recumbent suggesting that this position may allow for the most consistent and repeatable IOP measurements. In our research, IOP was recorded avoiding pressure against globe, jugular veins or eyelids, first in sitting or sternal recumbent and after the induction in right lateral position. Although in human medicine has been found that the IOP can significantly increase on right and left lateral decubitus (Lee and others 2013; Malihi and Sit 2012; Seo and others 2015), there were no significant differences between right and left eye in any position probably due to anatomic dissimilarity (Fig. 2).

During general anaesthesia occurs a decrease of both basal and reflex tear production (Mouney and others 2011). It has been suggested that reduction of reflex tear formation during anaesthesia may be due to depression of autonomic pathways responsible for production of tears. These decrease is usually transient but may last for several days when combined with other postoperative complications (Martin 2005b).

In the present investigation the mean baseline STT-1 was similar to those described in normal dogs (Martin 2005a) and we found a progressive and dramatic decrease to values close to 0 mm/min at 35 and 60 minutes. As reported by other authors, morphine and sevoflurane do not reduce tear production (Mouney and others 2011). Costa et al. (2015) showed a significant diminution of the STT-1 followed by a single intravenous injection of alfaxalone that was recovered after 30 minutes. In our knowledge, the effect of midazolam on tear production is unknown so it is necessary to perform future studies to determine whether the reduction that we have detected on STT-1 is attributable to alfaxalone, to midazolam or combination of both of them.

We recognize, as a limitation of our study, that the evolution of IOP and tear production to recovering baseline values has not been analysed and it will be take into consideration in future research.

In conclusion, although the IOP values remained within the normal physiological canine range, the protocol used in this study induced a significant increase in this parameter and these findings should be taken into consideration, especially in dogs with fragile or ulcerated corneas, those predisposed to glaucoma as well as those who will be undergoing intraocular surgery. Furthermore, lubrication is necessary to prevent damage to ocular surface.

Acknowledgements

The authors gratefully acknowledge the excellence assistance and technical support provided by all Veterinary Teaching Hospital staff, specially our interns.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

ALMEIDA, D. E., REZENDE, M. L., NUNES, N. & LAUS, J. L. (2004) Evaluation of intraocular pressure in association with cardiovascular parameters in normocapnic dogs anesthetized with sevoflurane and desflurane. Vet Ophthalmol 7, 265-269

ARTIGAS, C., REDONDO, J. I. & LOPEZ-MURCIA, M. M. (2012) Effects of intravenous administration of dexmedetomidine on intraocular pressure and pupil size in clinically normal dogs. Vet Ophthalmol 15 Suppl 1, 79-82

BROADWATER, J. J., SCHORLING, J. J., HERRING, I. P. & ELVINGER, F. (2008) Effect of body position on intraocular pressure in dogs without glaucoma. Am J Vet Res 69, 527-530

BRUNSON, D. B. (1980) Anesthesia in ophthalmic surgery. Vet Clin North Am Small Anim Pract 10, 481-495

COSTA, D., LEIVA, M., MOLL, X., AGUILAR, A., PENA, T. & ANDALUZ, A. (2015) Alfaxalone versus propofol in dogs: a randomised trial to assess effects on peri-induction tear production, intraocular pressure and globe position. Vet Rec 176, 73

DI PIETRO, S., MACRI, F., BONARRIGO, T., GIUDICE, E., PALUMBO PICCIONELLO, A. & PUGLIESE, A. (2016) Effects of a medetomidine-ketamine combination on Schirmer tear test I results of clinically normal cats. Am J Vet Res 77, 310-314

DRAGO, F., PANISSIDI, G., BELLOMIO, F., DAL BELLO, A., AGUGLIA, E. & GORGONE, G. (1985) Effects of opiates and opioids on intraocular pressure of rabbits and humans. Clin Exp Pharmacol Physiol 12, 107-113

FERRE, P. J., PASLOSKE, K., WHITTEM, T., RANASINGHE, M. G., LI, Q. & LEFEBVRE, H. P. (2006) Plasma pharmacokinetics of alfaxalone in dogs after an intravenous bolus of Alfaxan-CD RTU. Vet Anaesth Analg 33, 229-236

GELATT, K. N. (2011) Anesthesia for ophthalmic surgery. In Veterinary Ophthalmic Surgery. Eds K. N. GELATT, J. P. GELATT. Edinburgh UK, Elsevier Saunders. pp 37–49

GELATT, K. N. & MACKAY, E. O. (1998) Distribution of intraocular pressure in dogs. Vet Ophthalmol 1, 109-114

GHAFFARI, M. S., REZAEI, M. A., MIRANI, A. H. & KHORAMI, N. (2010) The effects of ketamine-midazolam anesthesia on intraocular pressure in clinically normal dogs. Vet Ophthalmol 13, 91-93

GIANNETTO, C., PICCIONE, G. & GIUDICE, E. (2009) Daytime profile of the intraocular pressure and tear production in normal dog. Vet Ophthalmol 12, 302-305

GROSS, M. E. & GIULIANO, E. A. (2007) Ocular patients. In Lumb & Jones Veterinary Anesthesia and Analgesia. 4th edn. Eds W. J. TRANQUILLI, J. C. THURMON, K. A. GRIMM. Ames, Blackwell Publishing. pp 943–954

GRUNDON, R. A., ANDERSON, G. A., LYNCH, M., HARDMAN, C., O'REILLY, A. & STANLEY, R. G. (2011) Schirmer tear tests and intraocular pressures in conscious and anesthetized koalas (Phascolarctus cinereus). Vet Ophthalmol 14, 292-295

GUNDERSON, E. G., LUKASIK, V. M., ASHTON, M. M., MERIDETH, R. E. & MADSEN, R. (2013) Effects of anesthetic induction with midazolam-propofol and midazolam-etomidate on selected ocular and cardiorespiratory variables in clinically normal dogs. Am J Vet Res 74, 629-635

HASIUK, M. M., FORDE, N., COOKE, A., RAMEY, K. & PANG, D. S. (2014) A comparison of alfaxalone and propofol on intraocular pressure in healthy dogs. Vet Ophthalmol 17, 411-416

HERRING, I. P., PICKETT, J. P., CHAMPAGNE, E. S. & MARINI, M. (2000) Evaluation of aqueous tear production in dogs following general anesthesia. J Am Anim Hosp Assoc 36, 427-430

HOFMEISTER, E. H., WILLIAMS, C. O., BRAUN, C. & MOORE, P. A. (2008) Propofol versus thiopental: effects on peri-induction intraocular pressures in normal dogs. Vet Anaesth Analg 35, 275-281

JANG, M., PARK, S., SON, W. G., JO, S. M., HWANG, H., SEO, K. & LEE, I. (2015) Effect of tiletamine-zolazepam on the intraocular pressure of the dog. Vet Ophthalmol 18, 481-484

KANDA, T., IGUCHI, A., YOSHIOKA, C., NOMURA, H., HIGASHI, K., KAYA, M., YAMAMOTO, R., KURAMOTO, T. & FURUKAWA, T. (2015) Effects of medetomidine and xylazine on intraocular pressure and pupil size in healthy Beagle dogs. Vet Anaesth Analg

KAZAMA, T. & IKEDA, K. (1988) The comparative cardiovascular effects of sevoflurane with halothane and isoflurane. J Anesth 2, 63-68

KOMNENOU, A. T., KAZAKOS, G. M., SAVVAS, I. & THOMAS, A. L. (2013) Evaluation of aqueous tear production in dogs after general anaesthesia with medetomidine-propofol-carprofen-halothane. Vet Rec 173, 142

KONGARA, K., CHAMBERS, J. P. & JOHNSON, C. B. (2012) Effects of tramadol, morphine or their combination in dogs undergoing ovariohysterectomy on peri-operative electroencephalographic responses and post-operative pain. N Z Vet J 60, 129-135

LEE, T. E., YOO, C. & KIM, Y. Y. (2013) Effects of different sleeping postures on intraocular pressure and ocular perfusion pressure in healthy young subjects. Ophthalmology 120, 1565-1570

MALIHI, M. & SIT, A. J. (2012) Effect of head and body position on intraocular pressure. Ophthalmology 119, 987-991

MARTIN-SUAREZ, E., MOLLEDA, C., TARDON, R., GALAN, A., GALLARDO, J. & MOLLEDA, J. (2014) Diurnal variations of central corneal thickness and intraocular pressure in dogs from 8:00 am to 8:00 pm. Can Vet J 55, 361-365

MARTIN, C. L. (2005a) Anamnesis and the Ophthalmic Examination. In Ophthalmic Disease in Veterinary Medicine. Ed C. L. MARTIN. London, Manson Publishing. pp 11-40

MARTIN, C. L. (2005b) Lacrimal System. In Ophthalmic Disease in Veterinary Medicine. Ed C. L. MARTIN. London, Manson Publishing. pp 219-240

MIGUEL, L., PELÁEZ, P., ZORRILA, I., CARRILLO, J. M., SOPENA, J. J. & RUBIO, M. (2013) Clinical use of alfaxalone as anesthetic inductor in cats premedicated with alfaxaxalone-morphine for ovariohysterectomy. Revista Oficial de la Asociación de Veterinarios Españoles Especialistas en Pequeños Animales 33, 43-50

MOUNEY, M. C., ACCOLA, P. J., CREMER, J., SHEPARD, M. K., RODRIGUEZ GUARIN, C. & HOFMEISTER, E. H. (2011) Effects of acepromazine maleate or morphine on tear production before, during, and after sevoflurane anesthesia in dogs. Am J Vet Res 72, 1427-1430

MUIR, W., LERCHE, P., WIESE, A., NELSON, L., PASLOSKE, K. & WHITTEM, T. (2008) Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs. Vet Anaesth Analg 35, 451-462

MUIR, W., LERCHE, P., WIESE, A., NELSON, L., PASLOSKE, K. & WHITTEM, T. (2009) The cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in cats. Vet Anaesth Analg 36, 42-54

PICCIONE, G., GIANNETTO, C., FAZIO, F. & GIUDICE, E. (2010) Influence of different artificial lighting regimes on intraocular pressure circadian profile in the dog (Canis familiaris). Exp Anim 59, 215-223

SEO, H., YOO, C., LEE, T. E., LIN, S. & KIM, Y. Y. (2015) Head position and intraocular pressure in the lateral decubitus position. Optom Vis Sci 92, 95-101

SHEPARD, M. K., ACCOLA, P. J., LOPEZ, L. A., SHAUGHNESSY, M. R. & HOFMEISTER, E. H. (2011) Effect of duration and type of anesthetic on tear production in dogs. Am J Vet Res 72, 608-612

SNOW, J. C., PICKETT, J. P. & CHAMPAGNE, E. S. (1975) Evaluation of Aqueous Tear production in Dogs Following General Anesthesia J Am Anim Hosp Assoc 36, 427-430

STEPHAN, D. D., VESTRE, W. A., STILES, J. & KROHNE, S. (2003) Changes in intraocular pressure and pupil size following intramuscular administration of

hydromorphone hydrochloride and acepromazine in clinically normal dogs. Vet Ophthalmol 6, 73-76

TORRES, M. D., ANDALUZ, A., GARCIA, F., FRESNO, L. & MOLL, X. (2012) Effects of an intravenous bolus of alfaxalone versus propofol on intraocular pressure in sheep. Vet Rec 170, 226

Table 1

Mean IOP (mm Hg) and SST-1 (mm/min) values for the right and left eye. Data are presented as mean ± SD.

	IOP (mm Hg)[a]		STT-1 (mm/min)[b]	
Time	OD[c]	OS[d]	OD[c]	OS[d]
T_0[e]	13,8 ± 3,0	14,2 ± 2,9	18,4 ± 4,4	17,8 ± 3,5
T_1[f]	16,5 ± 4,2	17,4 ± 3,7	9 ± 4,3	9,2 ± 4,2
T_2[g]	15,9 ± 3,7	15,8 ± 3,4	4,8 ± 4,2	5,8 ± 4,5
T_3[h]	15,2 ± 3,4	16,1 ± 3,4	4,5 ± 4,8	4 ± 4,0
T_4[i]	16,6 ± 3,8	16,3 ± 3,1	2,7 ± 2,5	2,7 ± 2,2
T_5[j]	16,3 ± 4,3	16,4 ± 2,7	1,5 ± 1,8	1 ± 1,3
T_6[k]	16,6 ± 4,1	16,8 ± 3,2	0,9 ± 1,3	0,5 ± 0,9

[a] IOP (mm Hg), intraocular pressure; [b] STT-1, Schirmer tear test; [c] OD, right eye; [d] OS, left eye; [e]T_0, baseline (data before sedation); [f]T_1, [g]T_2 and [h]T_3, 5, 10 and 15 minutes after sedation with alfaxalone respectively; [i]T_4, 5 minutes after sevoflurane administration; [j]T_5 *and* [k]T_6, 15 and 25 minutes after sevoflurane administration.

Figure legends

Fig. 1: Mean IOP and SST-1 recorded at different time points during the procedure. Data are expressed as mean ± SD. $^{+}$ $p < 0.05$.

Fig. 2: Mean IOP values for the right and left eye along the experiment.