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Effects of Different Anaesthesia Procedures on Intraocular Pressure and Tear Quantity in Horses

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ABSTRACT

Background: Various tranquilizers and anesthetics are frequently used in horses for both ophthalmic and other examinations and many surgical procedures. Many tranquilizers and anesthetics increase intraocular pressure and tear volume. This study aimed to determine the effects of three different anesthetic protocols frequently preferred in horses on intraocular pressure and tear volume.

Methods: These horses were divided into 3 groups, each consisting of 6 horses. Group I (AXK) was administered 0.05 mg/kg Acepromazine, 1.1 mg/kg Xylazine HCl and 2.2 mg/kg Ketamine HCl, Group II (XK) was administered 1.1 mg/kg Xylazine HCl and 2.2 mg/kg Ketamine HCl, Group III (DK) was administered 0.03 mg/kg Dexmedetomidine HCl and 2.2 mg/kg Ketamine HCl intravenously. Tear volume, intraocular pressure, heart rate and respiratory rate and rectal body temperature were measured and recorded in all horses constituting the groups before premedication, at 5th and 20th minute and after recovery from anesthesia.

Result: From the study, it was determined that intraocular pressure decreased in all three groups during anesthesia, with slight increase in tear volume, but the data obtained were within the reference ranges. As a result, it is suggested that the three anesthesia procedures evaluated in this study can be used in ocular surgery in horses and in operative procedures of patients with high intraocular pressure.

Key words: Acepromazine, Anesthesia, Dexmedetomidine, Intraocular pressure, Xylazine.

INTRODUCTION

Intraocular pressure (IOP) is maintained by the balanced production and drainage of aqueous humor (Erol *et al.*, 2018; Erol *et al.*, 2020) and IOP measurement is an important examination procedure to determine eye health. IOP measurement or tonometry in horses is a part of routine eye examination (Komaromy *et al.*, 2006; Trbolova and Ghaffari, 2013). Accurate measurement of IOP is of critical importance in the evaluation of animals with ocular disorders such as glaucoma and uveitis (Trbolova and Ghaffari, 2013; Mrazova *et al.*, 2018). While high IOP indicates the presence of glaucoma, low IOP indicates the presence of uveitis. IOP values are reported to be between 15 and 30 mmHg in healthy horses. In general, it has been specifically stated that an IOP measurement higher than 35 mmHg is a diagnostic criterion for glaucoma (Komaromy *et al.*, 2006; Shivaraju *et al.*, 2022). Keeping IOP within physiological reference ranges is very important for the health of the retina and optic nerve, which are especially sensitive to the pathophysiological effects of glaucoma (Monk *et al.*, 2017).

IOP is affected by many factors such as intracranial pressure, cerebral perfusion pressure, episcleral venous pressure changes, bulbus oculi being under compression for various reasons, changes in blood volume to the uveal segment and keeping the head below the level of the heart (Monk *et al.*, 2017; Mrazova *et al.*, 2018; Baran *et al.*, 2015). It is also known that various anesthetic or sedative agents affect IOP in both humans and many animal species (Chae *et al.*, 2021; Mrazova *et al.*, 2018; Leonardi *et al.*, 2020; Schroder *et al.*, 2018). Sedation or anesthesia is required in horses when performing ocular procedures or other operative procedures or examinations. However, the effects of sedatives or anesthetics used during these procedures on IOP should be taken into account. In the presence of a deep ulcer or rupture, rapid changes in IOP can cause ocular complications such as corneal perforation (Holve, 2012). Acepromazine is a sedative, antiemetic, antiarrhythmic phenothiazine derivative agent (Rodrigues *et al.*, 2021). Previous studies have shown that the administration of sedatives such as xylazine and acepromazine leads to a decrease in IOP in horses (Aghababaei *et al.*, 2021; Trbolova and Ghaffari, 2013). Xylazine and detomidine are the most commonly used α_2 adrenoceptor agonists in horses and which have been reported to reduce intraocular pressure (Gökhan, 2008; Yanmaz *et al.*, 2021, Rabbani *et al.*, 2021).

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It is thought, that ketamine is widely used in horses for induction and may cause an increase in IOP by increasing extraocular muscle tone (Erol *et al.*, 2018; Ferreira *et al.*, 2013; Monk *et al.*, 2017; Shilo-Benjamini *et al.*, 2023; Topal *et al.*, 2023).

Tears play an important role in maintaining the health and normal function of the cornea and conjunctiva. Tears provide an important refractive surface in the eye, nutrients to the cornea, helps in removal of foreign matter and plays defense mechanism with immunoglobulins, lysozymes and other components contained in the tears Deficiency in tear production causes keratoconjunctivitis sicca (KCS) and inflammation of the cornea and conjunctiva. Visual function is adversely affected by the degree of damage to the cornea (Ofri *et al.*, 2002).

The aim of this study was to investigate the effects of different anesthetic procedures used in horses on IOP and tear volume.

MATERIALS AND METHODS

This study protocol was approved by the Dicle University health sciences application and research center animal experiments local ethics committee (25/09/2024-04-12).

The study was conducted on castrated male horses. Horses included in the study were of 9 purebred English and 9 purebred Arabian horses, aged 2-6 years and weighing around 330-450 kgs. All the horses included in the study underwent eye examinations by recording their heart rate (HR), respiratory rate (RR) and rectal body temperature (RT) before anesthesia. In the ophthalmological examination, tear strips (ERC Schirmer Test Strip, Turkey) were first applied to the fornix of the lower eyelid for 1 minute (in order to prevent tear volume from being affected by manual examination or any other procedure) and then measured tear volumes. Tear volumes measured in horses between 10-35 mm/min were considered normal and included in the study. This was followed by palpation of the orbits and palpebrae and examination of the conjunctiva, respectively. After examination of the cornea and sclera, ophthalmoscopic examination was performed. Horses with problems in any segment of the eye were excluded from the study. Intraocular pressure of all horses included in the study was measured with Tonovet (Icare Tonovet Plus, USA) before anesthesia. Horses with IOP values between 15-35 mmHg were included in the study. IOP values measured at 35 mmHg and higher were considered pathological and were not included in the study.

The horses selected were divided randomly into 3 groups of 6 horses each and subjected to different anesthetic protocols. Group I (AXK) received 0.05 mg/kg Acepromazine (Sedan 10 mg/ml, Bioveta, Ivanovice na Hane Crezh Republic), 1.1 mg/kg Xylazine HCl (Rompun 2%, Bayer, Turkey) and 2.2 mg/kg Ketamine HCl (Ketasol 10%, Richter Pharma, Turkey); Group II (XK) received 1.1 mg/kg Xylazine HCl (Rompun 2%, Bayer, Turkey) and 2.2 mg/kg Ketamine HCl (Ketasol 10%, Richter Pharma, Turkey); Group III (DK) received 0.03 mg/kg Dexmedetomidine HCl (Domosedan, Zoetis, Turkey) and 2.2 mg/kg Ketamine HCl (Ketasol 10%, Richter Pharma, Turkey) intravenously. The age, weight, time at which animal goes into sedation at which the animal goes into anaesthesia, surgerical time and recovery time from anesthesia were recorded for all horses in each group. The sedation time was determined according to the drooping of the ears, lower lip, eyelids and head and the penis protruding from the prepuce. Induction criteria included lying down on the ground, absence of palpebral reflex and weakening of the pulse, while criteria such as standing on all fours legs without support were considered for recovery from anesthesia. The amount of tears and intraocular pressure, respiratory rate (RR), heart rate (HR) and rectal body temperature of all horses included in the study were measured and recorded at 5, 20 and 30 days after anesthesia. In addition, fundus examination was performed with a fundus camera at the specified times and images were taken.

Data obtained before, during and after anesthesia were evaluated statistically. Statistical analysis of the data was performed using the Minitab-17 package program. After the data were subjected to the normality test, One-way ANOVA analysis was used for parametric values and Kruskal-Wallis test was used for non-parametric values. Differences were accepted as significant at $P<0.05$.

RESULTS AND DISCUSSION

The study revealed that the volume of tears in all of these horses generally increased very slightly (1-2 mm) after the first measurement and that the amount of tears was in the range of 13-22 mm/min in all horses. When the groups were compared within themselves in terms of tear volume before, during (5^{th} and 20^{th} minutes) and after anesthesia, there was no statistical significant difference, but when the groups were compared, it was observed that there was a statistical significant difference in the AXK group at the 5^{th} minute and during the postoperative measurements after anesthesia (Table 1).

Intraocular pressure was observed to decrease slightly after anesthesia in all horses included in the study, with a slight increase in postoperative measurements, approaching pre-anesthesia values. However, all measured IOP values were found to be within the normal reference range. When compared within and between groups, no statistical significant difference were observed.

The physiological parameters *viz*., respiration, heart rate, rectal body temperature of the horses included in the study decreased, which reverted back to normal values as that of before anaesthesia on recovery. Throughout the study, no statistical significant difference was found within and between the groups as far as physiological parameters.

The time taken to get sedated was shorter in the DK group and the time taken to get anaesthesized was shorter in the AXK group. However, these differences were not statistically significant between the groups. The surgical time were very similar in the groups, ranging between 20-25 minutes.

When the groups were evaluated in terms of the recovery time from anesthesia, it was observed that the horses in the AXK group recovered earlier and stood on all fours legs without support. This situation was found to be statistically significant when compared with the other two groups (Table 2).

The study was uneventful without any complications before, during and after anesthesia in all horses included in the study.

The tear film provides the cornea with an optical surface for light refraction, provides mechanical removal of debris and bacteria and lubricates the conjunctiva (Bhokre *et al.*, 2015; Abdelhakiem *et al.*, 2019; Leonardi *et al.*, 2020). Quantitative and qualitative assessments of the tear film are critical for ophthalmic examination (Leonardi *et al.*, 2020; Hendrix, 2005; Gilger and Stoppini 2011). If subtle changes in the superficial cornea, an opaque cornea, or

Table 1: Statistical comparison of tear volume, intraocular pressure, heart rate, respiratory rate and rectal body temperature before, during and after anesthesia.

Procedure performed	Eye	Group	Pre-anesthetic	Order of anesthesia		Postoperative
				5th min	20th min	
Schirmer test	R	AXK	16.00±2.09	18,16±2,13	17.66±1.75	19.00±2.28
		XK	20.00±3.03	20.16±2,13	20.16±2.78	21.33±2.80
		DK	20.00±2.42	20.66±2.33	20.16±2.78	21.16±2.63
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05
	L	AXK	14.50±1.22*	16.00±1.09*	16.50±1.22	16.50±1.87*
		XK	20.00±3.74	20.66±2.42	20.83±1.94	22.16±3.06
		DK	20.33±1.96	20.83±2.31	20.83±2.13	22.00±2.96
		p	p≤0.05	p≤0.05	p≤0.05	p≤0.05
IOP	R	AXK	28.33±4.03	24.66±3.50	23.16±4.07	24.83±3.86
		XK	26.33±5.24	23.83±3.65	23.50±3.61	25.50±4.76
		DK	29.33±2.42	25.00±2.09	20.83±2.48	27.16±2.85
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05
	L	AXK	29.16±4.21	25.66±3.01	22.26±3.00	26.16±3.12
		XK	27.16±3.86	24.83±3.18	22.52±2.18	26.16±4.07
		DK	29.66±2.06	25.33±1.63	20.20±1.17	27.66±2.25
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05
HR		AXK	42.66±5.00	36.33±7.65	33.50±5.64	42.50±6.12
		XK	41.66±2.42	33.00±4.51	30.50±3.72	40.50±3.32
		DK	41.33±2.06	31.83±4.21	29.50±2.73	40.66±3.07
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05
RR		AXK	21.16±8.15	17.66±7.50	16.83±7.41	21.50±8.26
		XK	18.50±3.01	15.16±2.13	13.83±1.94	17.66±2.42
		DK	18.33±2.80	14.66±2.42	13.66±1.86	17.33±2.63
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05
RT		AXK	37.26±0.29	36.73±0.22	36.58±0.21	36.95±0.23
		XK	37.36±0.43	36.95±0.56	36.90±0.58	37.28±0.43
		DK	37.41±0.46	36.86±0.51	36.81±0.59	37.30±0.38
		p	p≥0.05	p≥0.05	p≥0.05	p≥0.05

R: Right eye, L: Left eye, IOP: Intraocular pressure, HR: Heart rate, RR: Respiratory rate, RT: Rectal body temperature, AXK: Acepromazine, Xylazine, Ketamine group, XK: Xylazine, Ketamine group, DK: Detomidine, Ketamine group.

Table 2: Comparison of the groups in terms of age, weight, time to sedation, anaaesthetic time, surgical time and recovery time from anesthesia.

Group	Age	Weight (kg)	Sedation time (min)	Anesthestic time (min)	Surgical time (min)	Recovery time (min)
AXK	3.67±1.63	411.67±36.01	5.16±0.75	1.33±0.81	21.33±2.16	65.33±9.83*
XK	4.33±1.63	368.33±45.79	6.00±1.41	3.16±1.60	22.33±2.58	88.33±11.69
DK	3.50±1.04	381.67±38.17	4.50±1.04	2.83±1.16	22.16±1.60	88.33±8.16
p	p≥0.05	p≥0.05	p≥0.05	p≥0.05	p≥0.05	p≤0.05

*Indicates the difference between groups in each column at P≤0.05 AXK: Acepromazine, Xylazine, Ketamine group, XK: Xylazine, Ketamine group, DK: Detomidine, Ketamine group.

mild eye discharge are noted, inadequate tear production may be considered (Leonardi *et al.*, 2020; Crispin, 2000). Decreased tear production in horses is often associated with facial and trigeminal nerve dysfunction and associated eyelid problems (*e.g.*, incomplete blinking, lid margin malalignment, infection) (Crispin, 2000). Additionally, immune-mediated keratitis has been reported in horses (Leonardi *et al.*, 2020; Gilger *et al.*, 2005). It is important to distinguish dry eye from primary keratitis (Leonardi *et al.*, 2020; Knickelbein *et al.*, 2018). Definitive diagnosis of dry eye is made by evaluating clinical signs and Schirmer tear test I (Leonardi *et al.*, 2020). Schirmer tear test I (STT I) is a semi-quantitative method used without topical anesthesia to determine basal reflex secretion (Erol *et al.*, 2018; Alkan *et al.*, 2004). It is considered the gold standard compared to other methods in determining the qualitative volume of tears in veterinary medicine (Erol *et al.*, 2018; Ofri *et al.*, 2001; Swinger *et al.*, 2009). In horses, STT I value lower than 10 mm/min are pathological, whereas higher values are not pathological because horse tear production can be as high as 35 mm/min (Leonardi *et al.*, 2020; Hendrix, 2005). In our study, we used the STT I test to determine the qualitative tear volume. STT I was measured between 13-22 mm/min in the AXK group, 15-25 mm/min in the XK group and 18-25 mm/min in the DK group before and after anesthesia. The measured values are consistent with other reported studies. α_2-adrenoceptor agonists such as xylazine, detomidine, medetomidine and romifidine, which are commonly used for sedation in horses, may affect STT I value (Arican *et al.*, 2015; Leonardi *et al.*, 2020; Hendrix, 2005). In their study, Ghaffari *et al.* (2017) emphasized that detomidine reduces tear production but does not cause a change in head position, so it is frequently used for sedation in eye examinations. Another study (Muir 2009) reported that the sedative effect of detomidine peaked 15 minutes after intravenous administration and tear production decreased 15 minutes after sedation. Leonardi *et al.* (2020) reported in their study that the significant decrease in tear production was no longer present 30 minutes after sedation. Detomidine was not evaluated alone in this study. However, when the study data were examined, it was observed that there was no decrease in the volume of tears in either the DK group or the other groups, on the contrary, it increased them by small amounts. This may be due to the shortness of the surgery time, or the doses applied.

Many anesthetic and hypnotic agents, including volatile substances, α_2 adrenoceptor agonists, ketamine and benzodiazepines, have been reported to reduce IOP in humans and domestic animals (Erol *et al.*, 2018; Holve *et al.*, 2013). Trbolova *et al.* (2013) reported in their study that sedatives such as xylazine and acepromazine reduced IOP in horses. Similarly, Gökhan (2008) stated that adrenoceptor agonists such as xylazine and detomidine, which are frequently preferred for use in horses, reduced IOP. Okur *et al.*, (2022) emphasized that detomidine and medetomidine significantly reduced tear volume and IOP in a study they conducted in sheep. Karslı *et al.* (2023) reported that intraocular pressure decreased in cats sedated with dexmetodomid and mededomidine by intramuscular injection, but it was within reference ranges. In a study conducted on healthy dogs, it was reported that IOP decreased significantly at 35 and 60 minutes after intramuscular acepromazine injection and that acepromazine use was indicated in cases such as head trauma, corneal damage, glaucoma, *etc*. (Micieli *et al.*, 2018; Kovalcuka and Birgele, 2009; Imani Rastabi *et al.*, 2019; Gopinathan *et al.*, 2023). In this study conducted on ocularly healthy horses, xylazine, detomidine and acepromazine were used in combination with ketamine and not alone. However, it was determined that IOP decreased within the reference value ranges in all groups.

General anesthetics can cause changes in intraocular pressure (Mclver *et al.*, 2023; Kibar *et al.*, 2022). Ketamine is an anesthetic widely used in many animal species and has been reported to increase IOP when used alone in many animal species (cat, dog, rabbit) (Ghaffari and Moghaddasi, 2010; Hofmeister *et al.*, 2006; Kibar *et al.*, 2022). In a study conducted on rabbits, Ghaffari and Moghaddasi (2010) investigated the effects of Ketamine-Acepromazine and Ketamine-Diazepam anesthesia on IOP and emphasized that both anesthesia techniques increased IOP after the 5th minute after application. In another study conducted on healthy dogs, it was stated that intravenous ketamine administration at a dose of 5 mg/kg without premedication increased IOP significantly and clinically important (Hofmeister). Anesthetics and tranquilizers usually cause a decrease in IOP. However, ketamine may cause a temporary increase in intraocular pressure. This is thought to be due to spasm of the extraocular muscles (Ghaffari and Moghaddasi, 2010). Karabağlı *et al.* (2014) stated in a study they conducted on dogs that xylazine and ketamine anesthesia reduced intraocular pressure and could be used in eye surgery. Trim *et al.* (1985) reported in a study they conducted on horses that they applied xylazine and ketamine anesthesia that IOP decreased. Ferreira *et al.* (2013) reported in their study that there was no significant change in IOP after ketamine administration, that this could be due to high doses of xylazine and guaifenesin and that it could be due to the position of the head when the horses were in the sternal position. In this study, it was determined that although there was a decrease in IOP in all groups, the results obtained were within the reference ranges.

Head position has an effect on IOP. This effect occurs mostly through changes in episcleral venous pressure. Komaromy *et al.* (2006) reported in a study that IOP in horses with the head below the heart level was significantly increased compared to the head-up position. In our study, measurements were made before and after anesthesia with the horses standing and the head in a normal position (head-up position), while measurements were made during anesthesia with the horses in the supine position.

The measurements showed that IOP decreased but remained within the reference ranges.

In this study, 3 groups of horses were evaluated in terms of age, weight, sedation and anesthesitic and surgical time and the recovery time. According to the results obtained, there was no statistical difference between the groups in terms of age, weight, sedation and anesthetic and surgical time. However, there was a difference between the time of recovery from anesthesia which was shorter in the AXK group.

CONCLUSION

As a result, sedative and anesthetic preparations are frequently needed for both some examinations and various surgical procedures in horses. The effects on IOP should be considered in the selection of sedative and anesthetic agents. In this study, it was determined that all 3 anesthesia protocols evaluated reduced IOP and caused slight increases in tear volume, but the results obtained were within the reference ranges. Therefore, it is suggested that all three techniques can be used in eye surgery and operative procedures and when evaluated in terms of recovery time from anesthesia, the AXK anesthesia protocol is more preferred.

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Informed consent

This study protocol was approved by the Dicle University Health Sciences Application and Research Center Animal Experiments Local Ethics Committee (25/09/2024-04-12).

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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