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The effects of propofol-sevoflurane, midazolam-sevoflurane, and medetomidine-ketamine-sevoflurane anesthetic combinations on tear production measured by the schirmer tear test I (STT I) in healthy rabbits

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Abstract: The maintenance of corneal and normal eye function is necessary for the ocular health and integrity. Tear plays an important role in defense mechanism and nutrition of eye. The Schirmer tear tests (STT I, II) are widely used in ophthalmic examination to evaluate tear production as an aid to diagnose eye diseases. The aim of this study was to compare the different effect of anesthetic combinations and their action period on tear production in healthy rabbits. Forty healthy New Zealand female rabbits (mean weight 2.34 ± 0.67 kg), four months old, were used as materials. The animals were divided into four groups as propofol + sevoflurane (PS), midazolam + sevoflurane (MS), medetomidine + ketamine + sevoflurane (MKS), and control (C) groups, and each group contained 10 rabbits. The TP (tear production) was measured from left eyes before injectable anesthesia (0. min), during sevoflurane anesthesia at 5th, 10th, 15th, 20th, 25th and 30th min, and post anesthesia (after extubation) at 10th, 20th, 30th, 60th, 120th min and 24 h after in the study groups. In group C, at the same time intervals TP were also measured. In all groups statistical differences were recorded in different times of during and post anesthesia time periods. In post anesthetic time intervals the lowest TP values were detected in PS group. The new surgical techniques on eye surgery can require long general anesthesia periods. Extending of general anesthesia duration bring along risk factors such as perioperative dry eye syndrome. Perioperative dry eye syndrome (PDES) is the most common ophthalmologic complication of the general anesthesia. As a result of this study, PS anesthetic combination decreased the TP more than MS and MKS anesthetic combination during anesthesia. Although the present study put forward shows these results in rabbits, PS, MS and MKS anesthetic combinations may show different effects on TP.

Key words: Anesthesia, tear production, rabbit

1. Introduction

The maintenance of corneal and normal eye function is necessary for the ocular health and integrity. It depends on adequate supply of tear fluid covering the anterior segment of the ocular bulb and attached structures to it [1]. Tear play an important role in defense mechanism and nutrition of eye [2]. The cornea is under the risk in general anesthesia due to temporary disappearance of palpebral and corneal reflex. This risk conditions may cause corneal injury, dry eye disease, corneal abrasions and the other corneal diseases. Especially, alterations in tear production are the most common reason of the corneal injuries. Because of this, the measurement of the tear production during general anesthesia is very important for cornea health. The Schirmer tear tests (STT I, II) are widely used in ophthalmic examination to evaluate tear production as an aid to diagnose eye diseases. The filter paper is placed into the lower conjunctival fornix of eye, the amount of wetness is read after one or three minutes later. The specific diagnosis is made by comparing the recorded and normal values for the patients [3]. The STT I measures the basal and reflex tear production and it is most commonly used. The STT II measures the basal tear production after the topical application of an anesthetic, and, generally, it is used in animals with corneal ulceration [4].

Sedatives are commonly used to assist the ophthalmologists in routine clinical examination for to decrease stress factors effect and to enhance safety of both the patient and examiner. The knowledge of the effects of these drugs on the tear production is very important for ocular health [5]. In general, preanesthetic and anesthetic agents are known to decrease tear production [1,6].

The aim of this study was to compare the different effect of anesthetic combinations and their action period on tear production in healthy rabbits.

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2. Material and methods

Erciyes University Local Board of Ethics Committee for animal experiments has approved the study protocol of this research (EUHADYEK, decision no: 14/140). Forty healthy New Zealand female rabbits (Mean weight 2.34 ± 0.67 kg), four months old, were used as materials. Each of rabbits was kept in a separate cage, maintained on a 12 h light/dark cycle, 21 ± 1 ºC temperature in the Balıkesir University, Veterinary Faculty, Surgery Department, before the study. The rabbits were fed with normal pellet diet and given water *ad libitum*. The animals were divided into four groups; as propofol + sevoflurane (PS), midazolam + sevoflurane (MS), medetomidine + ketamine + sevoflurane (MKS) and control (C) groups, and each group contained 10 rabbits. Prior to anesthesia, the animals were transported to the examination table, and waited about 10 min to calm for accommodation to the environment conditions. The Schirmer tear test (STT I, Schirmer Tear Test Strip, ERC, Turkey) was placed into the lower conjunctival fornix of left eye of animals. At the end of three min, the test strip was taken, and the wetness values of the strips were recorded. During the measurements period the movement of animals and stripes were restricted.

2.1. Anesthesia protocol

In PS group; 7 mg/kg propofol (propofol 10 mg/mL, PROPOFOL ABBOTT, Abbott Laboratories, USA) was applied intravenously (IV) from right *vena auricularis*. In MS group 0.3 mg/kg midazolam (Demizolam, DEM, Turkey) and in MKS group 0.3 mg/kg medetomidine (Domitor, Zoetis, Turkey) were applied intramuscularly (IM). After 5 min, 30 mg/kg ketamine (Ketasol 10%, Interhas, Turkey) was applied IM in MKS group. Group C received no anesthetic.

For endotracheal intubation of the animals, the head and neck was held in atlantooccipital extension to displace the epiglottis to provide a straight passage for the endotracheal tube. The mouth was opened and local anesthetic 2% lidocaine HCL was sprayed into larynx. The neonatal intubation tube (2.5 mm diameter) was placed into trachea. After intubation the tube was connected to anesthetic machine (nonbreathing system, Magill circuit) and anesthesia was maintained 4% sevoflurane during 30 min in all study groups. At the end of anesthesia the anesthetic machine was shut down and the system was washed with oxygen, then oxygen support was carried out for 2 min. The animals were followed until chewing reflex returned, then extubated.

2.2. Tear production (TP) measurement

All animals were placed dorsoventrally on the operation table and fixed with hypoallergenic patch. The immobilization of animals was achieved by fixation, and the tightly fixing was avoided for the TP measurement. The TP was measured from left eyes before injectable anesthesia (0. min), during sevoflurane anesthesia at 5^{th}, 10^{th}, 15^{th}, 20^{th}, 25^{th} and 30^{th} min, and post anesthesia (after extubation) at 10^{th}, 20^{th}, 30^{th}, 60^{th}, 120^{th} min and 24 h after in the study groups. In group C, at the same time intervals TP were also measured.

2.3. Statistical analysis

The obtained data were statistically evaluated with IBM SPSS Statistics 21.0 (IBM Corp. Armonk, NY, USA) program. Shapiro–Wilk test was used for normality. One-way ANOVA was used to compare values between groups', Student–Newman–Keuls test was used for multiple comparisons. The differences between repeated measurements were analyzed by repeated measure variance analysis and Bonferroni test. $P < 0.05$ was accepted statistical significance, and the results are presented as Mean ± Standart eror (SE).

3. Results

In-group measurements and statistical evaluations of TP are presented in Table 1. In PS group the TP values started to decrease at 5^{th} min during anesthesia and the decrease continued up to post anesthetic 10^{th} min. Statistical differences were recorded between 10^{th}, 15^{th} 20^{th} min and 25^{th}, 30^{th} min during anesthesia, and between post anesthetic 10^{th}, 20^{th} min and 25^{th}, 30^{th} min during anesthesia ($p < 0.05$). In MS group TP started to decrease at 5^{th} min during anesthesia and continued up to 25^{th} min. The measured value at 15^{th} min during anesthesia was statically different from the other time periods in anesthesia time intervals ($p < 0.05$). In MKS group, the statistical differences were recorded between 15^{th}, 20^{th}, 30^{th} and 10^{th}, 25^{th} min during anesthesia ($p < 0.05$).

Between groups evaluation (Table 1) all study group's values were statistically different than obtained values from group C at 10^{th}, 15^{th} min during anesthesia ($p < 0.05$). The recorded values in PS and MS were statistically different than MKS and C groups at 20^{th} min during anesthesia. On the other hand, the measured values of TP in MS and MKS at 25^{th}, 30^{th} min were statistically different ($p < 0.05$) than PS and C groups. In post anesthetic time intervals, the lowest TP values were detected in PS group. The measured values of PS group at 10^{th}, 20^{th} and 30^{th} min were statistically different than other groups.

4. Discussion

In recent years rabbits have widely been used in ophthalmic researches, and their popularity increased as pet animals [7]. The important reason of the using rabbits in ophthalmologic research is they have different anatomic eye structures compared to other pets and give different clinical symptoms to the ophthalmic diseases [8]. Despite some researchers [9,10] have been focused on the report of

Table 1. Tear production levels of groups during and postanesthetic times (Mean ± SE).

Groups	0th min	DA 5th min	DA 10th min	DA 15th min	DA 20th min	DA 25th min	DA 30th min	PA 10th min	PA 20th min	PA 30th min	PA 60th min	PA 120th min	PA 24.h
PS	$11.40 \pm 2.50^{ab,A}$	$9.30 \pm 2.35^{ab,A}$	$6.90 \pm 2.13^{b,A}$	$5.20 \pm 1.87^{b,A}$	$5.40 \pm 1.95^{b,A}$	$3.90 \pm 1.72^{a,A}$	$3.0 \pm 1.63^{a,A}$	$6.80 \pm 2.14^{b,A}$	$7.40 \pm 3.13^{b,A}$	$7.80 \pm 2.52^{b,A}$	$9.30 \pm 2.21^{ab,A}$	$11.30 \pm 2.62^{ab,A}$	$11.60 \pm 2.91^{ab,A}$
MS	$10.70 \pm 1.88^{ab,A}$	$7.50 \pm 1.58^{b,A}$	$6.50 \pm 1.35^{b,A}$	$5.60 \pm 2.67^{a,A}$	$6.70 \pm 3.02^{b,A}$	$8.10 \pm 3.31^{b,B}$	$8.00 \pm 2.82^{b,B}$	$11.20 \pm 2.29^{ab,B}$	$11.40 \pm 3.20^{ab,B}$	$11.50 \pm 2.54^{ab,B}$	$11.30 \pm 3.77^{ab,A}$	$13.50 \pm 2.17^{ab,A}$	$12.50 \pm 2.01^{ab,A}$
MKS	$9.80 \pm 2.39^{ab,A}$	$8.30 \pm 5.07^{ab,A}$	$6.60 \pm 2.54^{b,A}$	$5.80 \pm 2.48^{a,A}$	$5.30 \pm 2.05^{a,AB}$	$6.70 \pm 3.09^{b,B}$	$5.80 \pm 1.68^{a,AB}$	$10.7 \pm 3.86^{ab,B}$	$9.30 \pm 4.62^{ab,B}$	$11.00 \pm 4.49^{ab,B}$	$11.60 \pm 3.02^{ab,A}$	$12.30 \pm 2.45^{ab,A}$	$11.80 \pm 3.42^{ab,A}$
C	11.50 ± 2.17^{A}	11.00 ± 2.86^{A}	12.10 ± 2.76^{B}	12.30 ± 2.90^{B}	10.70 ± 2.21^{AB}	11.20 ± 1.87^{C}	11.80 ± 2.20^{C}	11.60 ± 2.11^{B}	11.20 ± 2.61^{B}	11.00 ± 2.94^{B}	11.20 ± 1.87^{A}	11.70 ± 1.63^{A}	11.70 ± 2.00^{A}

DA: during anesthesia, PS: Propofol±Sevoflurane, MS: Midazolam± Sevoflurane, MKS: Medetomidine ± Ketamine ± Sevoflurane, C; control, PA: Post anesthesia, ^{a,b} in same line and ^{A,B,C} in same column are statistically significant during and post anesthetic time points ($p < 0.05$).

lacrimal parameters in different species (cats, dogs, equine) under anesthesia, the most suitable anesthetic procedure has not been found yet. Therefore, in the present study, we aimed to investigate the effects of different anesthetic combinations on TP in healthy rabbits. Tear secretion is controlled by the lacrimal function units which are cornea, conjunctiva, accessory lacrimal glands, meibomian glands, and the nervous system (Sensory afferents and autonomic efferent nerves) [11]. The sedatives and anesthetic agents are commonly used to calm the animals for eye examination and they are known to reduce the TP. Alweiller et al. [12] emphasized that rabbits tolerate the propofol despite high dose requirement compared to other domestics. On the other hand, propofol can produce respiratory arrest in surgical anesthesia, so maintaining of anesthesia should be carried on volatile agents. In the present study we maintained anesthesia with 4% sevoflurane in all study groups and no complication were detected in PS group. This condition supported the literature review.

Costa et al. [4] reported that TP decreases during general anesthesia, however in their study, they found no statistically significant changes following propofol administration in dogs with STT I measurement values. Some researchers [13,14] measured TP using STT I in rabbits, and they emphasized that STT I test values can show differences in normal rabbits. Koç et al. [15] determined that the mean value for STT I in clinically normal rabbits was 8.1 ± 3.4 mm/min. The mean values for STT I in New Zealand Angora and Mixed breed rabbits were of 7.9 ± 3.6, 7.2 ± 2.9 and 9.1 ± 3.3 mm/min, respectively. In our study, New Zealand female rabbits were used as material and the measured baseline values (0^{th} min) of groups were 11.40 ± 2.50 mm/min in PS group, 10.70 ± 1.88 mm/min in MS group, 9.80 ± 2.39 mm/min in MKS group, and 11.50 ± 2.17 mm/min in C group. Nevertheless, there were no statistical differences detected in TP values before anesthesia in all groups. Many researchers [16,17] stated that the age, sex, and weight could affect the TP values in animals. In our study, we connected the differences of 0^{th} min (before anesthesia) values in all groups to the animals' weight and age.

Propofol is an anesthetic agent and causes moderate degree muscle relaxation. Inhalation anesthetics decrease intraocular pressure dose dependently by suppressing diencephalon, which may reduce the production of humor aqueous, raise the outflow of humor aqueous, or relax the extraocular muscle. These effects of sevoflurane are more potent than other inhalation anesthetics due its low blood and tissue solubility [1,18]. In the present study we detected significant decreases in TP values in PS group during anesthesia and post anesthetic time intervals. When values obtained from groups compared; the lowest values were recorded during anesthesia (25^{th}, 30^{th} min) in PS group. These decreases showed that the relaxing effect of propofol on eye muscles is not moderate. Besides, we thought that the relaxing effect of PS anesthetic combination on eye muscle is more powerful than MS, MKS anesthetic combinations.

Benzodiazepines such as midazolam are widely used with ketamine in laboratory animals' anesthesia. It decreases systemic arterial blood pressure, cerebral blood flow, cerebral pressure and intraocular pressure [6]. In general, benzodiazepines cause relaxation on the extraocular muscles and increase outflow of humor aqueous [19]. Alkan et al. [20] investigated the effects of preanesthetic agents on baseline TP value in rabbits. They found that the TP value returned to baseline after 30 min in midazolam group. Erol et al. [7] investigated the systemic effect of midazolam, ketamine and isoflurane anesthetic agents on intraocular pressure and TP in rabbits. They found reduction in TP values, and reported that the reduction continued 30 min during anesthesia. They explained this reduction as the central depressive effects of anesthetic agents on the central nervous system. In the current study; the measured TP values of MS group were lower than 0^{th} min. The significant decreases were recorded during anesthesia. The TP values of MS group returned to baseline at 10^{th} min in postanesthesic time interval. The results of the present study supported the prior studies [6,20] about depressive effect of midazolam on the central nervous system and showed that midazolam+sevoflurane anesthetic combination effect on central nervous system could be longer on TP.

In veterinary anesthesia; ketamine hydrochloride and α-2 adrenoceptor agonists such as xylazine and medetomidine are commonly used especially in rodents. Ketamine induces an increase in cerebral blood flow, intracranial pressure, and intraocular pressure as a result of cerebral vasodilatation [19,21]. Medetomidine is a mixture of 2 optical enantiomers: dexmedetomidine and levomedetomidine. Levomedetomidine reduces the sedative and analgesic effect of dexmedetomidine and increases bradycardia. Many studies showed that medetomidine, xylazine and butorphanol and combination of these, reduce TP in animals [22,23,24]. Kanda et al. [24] investigated the effects of medetomidine and xylazine on TP in cats and they measured TP via STT I test. They reported that medetomidine and xylazine led to significant decrease STT I values in cats. Leonardi et al. [25] investigated the effects of dexmedetomidine and butorphanol on TP in dogs and they also found decrease in TP values. They emphasized that postsynaptic activation of α-2 adrenoceptor in central nervous system due to dexmedetomidine and changes in sympathetic activity due to butorphanol may have caused the decrease in the basal TP. In addition, they explained the reason of the decrease of STT I test values by the diminished nociceptive transmission of tear reflexes. In our study, TP values of MKS group decreased during anesthesia. We think that the decrease in TP values of MKS group could have taken

place due to the central effects of these drugs on autonomic regulation of TP.

The new surgical techniques on eye surgery can require long general anesthesia periods. Extending of general anesthesia duration bring along risk factors such as perioperative dry eye syndrome (PDES). PDES is the most common ophthalmologic complication of the general anesthesia [26]. The suppression of the parasympathetic innervation of the eye lacrimal glands in general anesthesia result in decrease of TP [27]. In the current study, we used healthy animals as material and detected reduction in TP in all study groups. These findings showed that anesthetic agents and duration of anesthesia are crucial for TP and ocular health.

As a result of this study, PS anesthetic combination decreased the TP more than MS and MKS anesthetic combination during anesthesia. Although the present study put forward shows these results in rabbits, PS, MS, and MKS anesthetic combinations may show different effects on TP in different species. Therefore, we concluded that different studies using different animal materials should be carried out not only on the TP, but also on biochemistry of TP to prevent PDES.

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References

1. De Sousa Pontes KC, Borges APB, Eleoterio RB, Ferreira PS, Duarte TS. A comparison of the effects of propofol and thiopental on tear production in dogs. Revista Ceres Viçosa 2010; 57 (6): 757-761. doi: 10.1590/S0034-737X2010000600009
2. Akgül MB, Şındak N, Gülaydın A, Özen D, Kahya S et al. Comparative evaluations of tear secretion in healthy and infectious keratoconjunctivitis Romanov sheep with schirmer tear test and phenol red thread tear test. Turkish Journal of Veterinary and Animal Sciences 2017; 41: 793-797. doi: 10.3906/vet-1702-31
3. Whittaker AL, Williams DL. Evaluation of lacrimal characteristics in clinically normal New Zealand White rabbits by using the schirmer tear test I. Journal of the American Association for Laboratory Animal Science 2015; 54 (6): 783-787.
4. Costa D, Leiva M, Moll X, Aguilar A, Pena T et al. Alfaxalone versus propofol in dogs: a randomized trial to assess effects on peri-induction tear production tear production, intraocular pressure and globe position. Veterinary Record 2015; 176 (3): 73. doi: 10.1136/vr.102621
5. Ghaffari MS, Rezaei MA, Mirani AH, Khorami N. The effect of ketamine-midazolam anesthesia on intraocular pressure in clinically normal dogs. Veterinary Ophthalmology 2010; 13 (2): 91-93. doi: 10.1111/j.1463-5224.2010.00762
6. Erol M, Erol H, Atalan G, Doğan Z, Yönez MK et al. Effects of systemic systemically used midazolam, ketamine and isoflurane anaesthetic agents on intraocular pressure and tear production in rabbits. Harran Universitesi Veteriner Fakültesi Dergisi 2018; 7 (1): 21-25, doi: 10.31196/huvfd.458783
7. Erol M, Erol H, Atalan G, Ceylan C, Yönez MK. The effects of propofol-sevoflurane, midazolam-sevoflurane and medetomidine-ketamine-sevoflurane anesthetic combinations on intraocular pressure in rabbits. Kafkas Üniversitesi Veteriner Fakültesi Dergisi 2020; 26 (4): 477-481. doi: 10.9775/kvfd.2019.23557
8. Oria AP, Gomes JDC, Arraes AE, Arraes EA, Estrela-Lima et al. Tear production, intraocular pressure and conjuctival microbiota, cytology and histology of New Zealand rabbits (Oryctolagus cuniculus). Pesquisa Veterinária Brasileira 2014; 34 (10): 1024-1029.
9. Kanda T, Shimizu Y, Hanazona C, Maki S, MaetaN et al. Effect of intramuscular administration of medetomidine and xylazine on tear flow measured by the schirmer tear test I in healthy cats. Journal of Feline Medicine and Surgery 2019; 21 (8): 788-792. 10.1177/1098612X18795723
10. Ibrahim A. Reference value of schirmer tear test I and II in clinically healthy adult donkeys (Equus asinus): effect of sex. Journal of Equine Veterinary Science 2018; 67: 23-26. doi:10.1016/j.jevs.2018.02.019
11. Williams DL. 2008. Immunopathogenesis of keratoconjunctivitis sicca in the dog. Veterinary Clinics North America Small Animimals Practice 2008; 38 (2): 251-268. doi:10.1016/j.cvsm.2007.12.002
12. Allweiler S, Leach MC, Flecknell PA. The use of propofol and sevoflurane for surgical anaesthesia in New Zealand White rabbits. Laboratory Animal 2010; 44: 113-117. doi: 10.1258/la.2009.009036
13. Abrams KL, Brooks DE, Funk RS, Theran P. Evaluation of the Schirmer tear test in clinically normal rabbits. American Journal of Veterinary Research 1990; 51: 1912-1913
14. Biricik HS, Oguz H, Sindak N, Gurkan T, Hayat A. Evaluation of the Schirmer and phenol red thread tests for measuring tear secretion in rabbits. Veterinary Record 2005; 156: 485-487.
15. Koç Y, Alkan F, Tepeli C. Schirmer tear test in different rabbit breeds. Hayvancılık Araştırma Dergisi 2005; 15: 1-5.
16. Mathers WD, Lane JA, Zimmerman MB. Tear film changes associated with normal aging. Cornea 1996; 15: 229-234.
17. Moss SE, Klein R, Klein BEK. Incidence of dry eye in an older population. Archives of Ophthalmology 2004; 122: 369-373.

18. Park JT, Lim HK, Jan KY, Um DJ. The effects of desflurane and sevoflurane on the intraocular pressure associated with endotracheal intubation in pediatric ophthalmic surgery. Korean Journal of Anesthesiology 2013; 64 (2): 117-121. doi:10.4097/kjae.2013.64.2.117

19. Hazra S, Palui H, Biswas B, Konar A. Anesthesia for Intraocular Surgery in Rabbits. Scandinavian Journal of Laboratory Animal Science 2011; 38 (2): 112-115. doi: 10.23675/sjlas.v38i2.230

20. Alkan F, Koç Y, Kamış Ü. Effects of preanaesthetics medications on basal tear production in rabbits. Indian Veterinary Journal 2005; 82: 1053-1055.

21. Kovaljuca L, Birgele E. The effects of some medication and general anesthesia drugs on intraocular pressure and pupil diameter in dog's eyes. Latvijas Lauksaimniecības Universitate Raksti 2011; 26: 77-83.

22. Dodam JR, Branson KR, Martin DD. Effects of intramuscular sedative and opioid combinations on tear production in dogs. Veterinary Ophthalmology 1998; 1: 57-59.

23. Sanchez RE, Mellor D, Mould J. Effects of medetomidine and medetomidine-butorphanol combination on schirmer tear test I readings in dogs. Veterinary Ophthalmol 2006; 9: 33-37.

24. Kanda T, Ishihara S, Oka M, Sako K, Sato Y et al. Temporal effects of intramuscular administration of medetomidine hydrochloride or xylazine hydrochloride to healthy dogs on tear flow measured by use of a Schirmer tear test I. American Journal of Veterinary Research 2016; 77: 346-350.

25. Leonardi F, Costa GL, Stagnoli A, Zubin E, Boschi P et al. The effect of intramuscular dexmedetomidine-butorphanol combination on tear production in dogs. Canadian Veterinary Journal 2019; 60: 55-59.

26. Zernii EY, Gancharova OS, Baksheeva VE, Golovastova MO, Kabanova EI et al. Mitochondria-targeted antioxidant skq1 prevents anesthesia-induced dry eye syndrome. Bulletin of Experimental Biology and Medicine 2018; 165 (2): 269-271. doi: 10.1007/s10517-018-4145-3

27. Zernii EY, Gancharova OS, Baksheeva VE, Golovastova MO, Kabanova EI et al. Alteration in tear biochemistry associated with postanesthetic chronic dry eye syndrome. Biochemistry (Moscow) 2016; 81 (12): 1549-1557. doi: 10.1134/S0006297916120166