HARRAN ÜNİVERSİTESİ VETERİNER FAKÜLTESİ DERGİSİ

Comparison Of The Effects Of Different Anesthesia Protocols On Intraocular Pressure In Rats

Muhammed Kaan YÖNEZ[1,a], Nevzat Emre ASLAN[2,b,*], Umut ALPMAN[1,c], Gültekin ATALAN[1,d]

[1] Erciyes University, Faculty of Veterinary Medicine, Department of Surgery, Kayseri, Turkey

[2] Yozgat Bozok University, Faculty of Veterinary Medicine, Department of Surgery, Yozgat, Turkey

[a] ORCID: 0000-0001-9160-6363

[b] ORCID: 0000-0001-8970-7763

[c] ORCID: 0000-0003-3533-7386

[d] ORCID: 0000-0002-2613-5638

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***Correspondence:** Nevzat Emre ASLAN

Deparment of Surgery, Faculty of Veterinary Medicine, University of Yozgat Bozok, Yozgat, Turkey.

e-mail: n.emre.aslan@bozok.edu.tr

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Abstract: Intraocular pressure (IOP) provides biomechanical support to the internal tissues as well as protecting the optical properties of the eye. Deviations from baseline values cause vision problems depending on the magnitude, direction, and duration of IOP changes. In the study, rats determined to be healthy were first randomly divided into 4 groups. In all groups, the right and left intraocular pressures of the rats were measured and recorded with a tonometer at 0 minutes. After the administration of the general anesthetic agent, the right and left intraocular pressures were measured and recorded at 20, 30, 60, 90, and 120 minutes. In the intra-group comparisons, it was observed that IOP values decreased over time in all anesthesia protocols applied. No significant difference was observed between the groups in the comparison of right and left eye IOP values of all groups between 0-30 min and 90-120 min ($p>0.05$). At 60 min, statistically significant differences were found between groups in both right and left eye IOP values ($p<0.05$). In conclusion, a decrease in IOP values in both the right and left eyes was observed in all anesthetic protocols applied. Based on the data obtained, it was concluded that the combination of xylazine-medetomidine-propofol-ketamine anesthesia can be used safely in rats without causing an adverse effect on IOP.

Keywords: *Anesthesia, Intraocular pressure, Ketamine, Medetomidine, Propofol, Xylazine*

Introduction

Ophthalmic surgery has the highest surgical case load worldwide, and perioperative changes in intraocular pressure affect clinical outcomes (Kelly DJ and Farrell SM, 2018; Qui et al., 2014). Intraocular pressure (IOP) provides biomechanical support to the internal tissues, as well as maintaining the optical properties of the eye. Deviations from reference values cause visual problems depending on the severity, direction, and period of IOP changes. Ocular hypotension may trigger retinal detachments. Ocular hypertension, on the contrary, may also result in glaucomatous degeneration of the retina and optic nerve. (Nicou et al., 2021). The baseline IOP value and the effect of deviations are not easily determined. Factors such as altitude, ambient temperature, anesthetics, body temperature, respiration, blood pressure, and cerebrospinal fluid pressure affect IOP values in both humans and animals over a time scale ranging from seconds to days (Ghaffari et al., 2010; Ficarrotta and Passaglia, 2020; Ikushima et al., 2025).

The xylazine-ketamine combination is widely used in both veterinary clinics and experimental studies due to its ease of administration and ability to provide stable anesthesia. In general, central nervous system depressants cause a decrease in IOP. Ketamine, a dissociative anesthetic, is contraindicated in ophthalmic surgeries because it causes an increase in IOP when administered alone. Xylazine is an α-2 agonist that lowers IOP by suppressing sympathetic neuronal function. The combination of xylazine and ketamine reduces and reverses the increase caused by ketamine (Chae et al., 2021; Murillo et al., 2021). Medetomidine, an α-2 adrenergic agonist, exhibits effects such as sedation, anxiolysis, and analgesia. Intravenous administration of medetomidine has been reported to decrease IOP and cause myosis (Gomez-Martinez et al., 2020).

Propofol is one of the most commonly used anesthetic agents to initiate and maintain anesthesia. In addition to its hypnotic effect on the central nervous system, it reduces intracranial pressure by decreasing cerebral blood flow and oxygen consumption. It has been reported that IOP values significantly increased in dogs where anesthesia was induced with propofol after premedication with dexmedetomidine-hydromorphone and acepromazine-hydromorphone (Kaleghi et al., 2024).

The present study aims to compare the effects of medetomidine-ketamine, medetomidine-propofol, xylazine-ketamine and xylazine-propofol anesthesia combinations on intraocular pressure and to determine the appropriate anesthesia combination for ophthalmic surgery.

Materials and Methods

Permission for this study was obtained from Erciyes University HADYEK under number 03.09.2025-25/175. Furthermore, the authors declare that they have complied with Research and Publication Ethics. The study material consisted of 40 healthy male Wistar-Albino rats weighing 200-250 g, provided by the Erciyes University Experimental Research Application and Research Center (DEKAM) for a period of 8-12 weeks. The animals used in the study were housed in the Erciyes University Laboratory Animals Unit throughout the study period under conditions of room temperature 21 ± 1 °C, 12 hours of light and 12 hours of darkness, with one rat per cage. Food and water were provided ad libitum.

Groups

In the study, rats determined to be healthy were first randomly divided into 4 groups.

Group I: Medetomidine-Ketamine (n=10)

Rats in this group received 0.3 mg/kg medetomidine (Tomidin, Provet, Istanbul, Türkiye) intraperitoneally (IP). Ten minutes later, 80 mg/kg ketamine HCl (Ketasol 10%, Vetviva Richter, Wels, Austria) was administered IP.

Group II: Xylazine-Ketamine (n=10)

Rats in this group received 8 mg/kg of xylazine HCl (Rompun 2%, Bayer, Istanbul, Türkiye) IP. Following xylazine administration, 80 mg/kg of ketamine HCl (Ketasol 10%, Vetviva Richter, Wels, Austria) was administered IP at the 10-minute mark.

Group III: Medetomidine-Propofol (n=10)

Rats in this group received 0.3 mg/kg medetomidine HCl (Tomidin, Provet, Istanbul, Turkey) IP. Ten minutes later, 20 mg/kg propofol (Propofol 1% Fresenius, Uppsala, Sweden) was administered IP.

Group IV: Xylazine-Propofol (n=10)

Rats in this group received 8 mg/kg xylazine HCl (Rompun 2%, Bayer, Istanbul, Turkey) IP. Ten minutes later, 20 mg/kg propofol (Propofol 1% Fresenius, Uppsala, Sweden) was administered IP.

Measurement of Intraocular Pressure

In all groups, intraocular pressure in the right and left eyes of the rats were measured and recorded at 0 minutes using a tonometer to ensure measurement consistency (Tonovet iCare Plus, Finland) (Figure 1). Premedication was administered to the rats in the groups. Ten minutes after premedication, the intraocular pressures of the right and left eyes were measured immediately before the administration of the general anesthetic agent. After the administration of the general anesthetic agent, the intraocular pressures of the right and left eyes were measured and recorded at 20, 30, 60, 90, and 120 minutes.

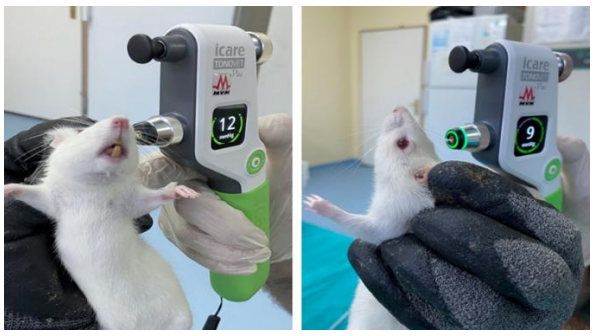

Figure 1. Measuring intraocular pressure with a tonometer.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 22.0. The results of our study are presented as Mean±SD, and p-values below 0.05 were considered statistically significant. The Shapiro-Wilk test was used to assess the normal distribution of the data. The t-test was used to assess the difference between right and left intraocular pressure measurements. Intergroup comparisons were evaluated using one-way analysis of variance (ANOVA). Statistical analysis was performed using the Student-Newman-Keuls test for multiple comparisons and the Kruskal-Wallis test for non-normally distributed data. Repeated measures analysis of variance and the Bonferroni test were used to determine differences between repeated measurements.

Results

No anesthesia-related complications were observed in any group during the study period. All rats in the post-anesthesia groups were observed to awaken from anesthesia in a healthy and normal manner. No adverse events were encountered during or after IOP measurements. IOP values for rats administered medetomidine-ketamine (Group I) are presented in Table 1. When measurements obtained at different time points in the right and left eyes were compared, a regular decrease in IOP values was observed over time in both eyes. However, no significant difference was found between the right and left eyes ($p>0.05$). In the intra-group evaluations, a statistically significant difference was found between measurements taken at different times ($p<0.001$). The IOP values of the right and left eyes of rats administered xylazine-ketamine (Group II) are presented in Table 2. When measurements obtained at different time points in the right and left eyes were compared, a regular decrease in IOP values was observed over time in both eyes. However, no significant difference was found between the right and left eyes ($p>0.05$). In the intra-group evaluations, a statistically significant difference was found between measurements taken at different times ($p<0.001$).

The IOP values of the right and left eyes of rats administered medetomidine-propofol (Group III) are presented in Table 3. When measurements obtained at different time points in the right and left eyes were compared, a regular decrease in IOP values was observed over time in both eyes. However, no significant difference was found between the right and left eyes ($p>0.05$). In the intra group evaluations, a statistically significant difference was found between measurements taken at different times ($p<0.001$).

The IOP values of the right and left eyes of rats administered xylazine-propofol (Group IV) are presented in Table 4. When measurements obtained at different time points in the right and left eyes were compared, a regular decrease in IOP values was observed over time in both eyes. However, no significant difference was found between the right and left eyes ($p>0.05$). In the intra-group evaluations, a statistically significant difference was found between measurements taken at different times ($p<0.001$).

No significant difference was observed between the 0-30 min and 90-120 min groups in the comparison of IOP values for the right and left eyes of all groups ($p>0.05$). At 60 minutes, however, a statistically significant difference was found between groups in both right and left eye IOP values ($p<0.05$).

Table 1. Comparison of intraocular pressures in the right and left eyes in the group administered medetomidine-ketamine.

Time (min)	Right (Mean±SD)	Left (Mean±SD)	p value
0	20.71±3.45	19.14±4.05	0.214
10	18.29±3.50	18.00±3.90	0.751
20	16.71±3.59	16.29±3.99	0.653
30	15.14±3.30	14.71±3.49	0.556
60	12.71±2.98	13.29±3.32	0.460
90	11.71±2.84	12.14±3.18	0.591
120	10.57±2.79	11.14±2.98	0.451
p value	p < 0.001	p < 0.001	

Table 2. Comparison of intraocular pressures in the right and left eyes in Group II (xylazine ketamine group).

Time (min)	Right (Mean±SD)	Left (Mean±SD)	p value
0	22.57±3.18	21.43±3.75	0.316
10	20.14±3.22	19.71±3.60	0.594
20	18.29±3.01	17.86±3.38	0.601
30	16.86±2.94	16.57±3.15	0.717
60	14.71±2.81	14.43±3.05	0.687
90	13.14±2.76	13.00±2.91	0.851
120	12.00±2.65	11.86±2.80	0.812
p value	p < 0.001	p < 0.001	

Table 3. Comparison of intraocular pressures in the right and left eyes in Group III (Medetomidine-Propofol group).

Time (min)	Right (Mean±SD)	Left (Mean±SD)	p value
0	21.14±3.12	20.71±3.40	0.541
10	18.71±3.08	18.29±3.31	0.578
20	16.86±2.98	16.43±3.15	0.601
30	15.57±2.92	15.14±3.09	0.562
60	13.43±2.85	13.14±2.99	0.680
90	12.29±2.80	12.00±2.94	0.725
120	11.14±2.75	10.86±2.88	0.772
p value	p < 0.001	p < 0.001	

Table 4. Comparison of intraocular pressures in the right and left eyes in Group IV (xylazine propofol group).

Time (min)	Right (Mean±SD)	Left (Mean±SD)	p value
0	23.00±3.20	22.57±3.45	0.529
10	20.71±3.14	20.43±3.33	0.709
20	18.71±3.05	18.57±3.22	0.842
30	17.14±2.96	17.00±3.12	0.861
60	15.14±2.90	15.00±3.06	0.880
90	13.57±2.84	13.43±2.98	0.890
120	12.29±2.79	12.14±2.92	0.889

Table 5. Comparison of right and left eyes between groups (Mean±SD)

Time (min)	Group I		Group II		Group III		Group IV		p value	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
0	20.71±3.45	19.14±4.05	22.57±3.18	21.43±3.75	21.14±3.12	20.71±3.40	23.00±3.20	22.57±3.45	0.12	0.11
10	18.29±3.50	18.00±3.90	20.14±3.22	19.71±3.60	18.71±3.08	18.29±3.31	20.71±3.14	20.43±3.33	0.08	0.09
20	16.71±3.59	16.29±3.99	18.29±3.01	17.86±3.38	16.86±2.98	16.43±3.15	18.71±3.05	18.57±3.22	0.15	0.18
30	15.14±3.30	14.71±3.49	16.86±2.94	16.57±3.15	15.57±2.92	15.14±3.09	17.14±2.96	17.00±3.12	0.10	0.14
60	12.71±2.98	13.29±3.32	14.71±2.81	14.43±3.05	13.43±2.85	13.14±2.99	15.14±2.90	15.00±3.06	0.04*	0.05*
90	11.71±2.84	12.14±3.18	13.14±2.76	13.00±2.91	12.29±2.80	12.00±2.94	13.57±2.84	13.43±2.98	0.06	0.07
120	10.57±2.79	11.14±2.98	12.00±2.65	11.86±2.80	11.14±2.75	10.86±2.88	12.29±2.79	12.14±2.92	0.07	0.10

Discussion and Conclusion

Success in ophthalmic surgery depends on controlling IOP before, during, and after the operation. Increased IOP can lead to corneal tearing, vision loss, disruption of ocular integrity, and increased surgical trauma. This situation is particularly important during intraocular surgical procedures and in deep corneal ulcers with a risk of rupture due to increased IOP (Pierce-Tomlin et al., 2020).

Erol et al. (2018) compared the effects of midazolam+ketamine and midazolam+ketamine+isoflurane anesthesia protocols on intraocular pressure in 20 New Zealand rabbits. They reported that there was no statistically significant difference in IOP values between the right and left eyes in either group. As a result, they emphasized that midazolam, ketamine, and isoflurane anesthetics reduced IOP in rabbits. The study presented found that the anesthesia protocols used lowered IOP but did not cause a statistically significant difference between the left and right eyes. In conclusion, the reduction in IOP values by the applied anesthesia protocols and the lack of statistical difference between the IOP values of the left and right eyes are consistent with the study by Erol et al. (2018).

Benjamini et al. (2023) compared intraocular pressures in 43 cats undergoing various anesthesia protocols. Cats premedicated with midazolam were anesthetized with propofol (n=15), alfaxalone (n=14), and ketamine (n=14). After anesthesia induction, they reported that IOP increased significantly in the propofol group compared to baseline values, while there was no increase in the alfaxalone and ketamine groups. They noted that midazolam administration caused a decrease in the alfaxalone group but did not cause any change in the propofol and ketamine groups. As a result, they emphasized that propofol should be used with caution in situations where an increase in intraocular pressure should be avoided. In the presented study, IOP values decreased compared to baseline values in all anesthesia protocols. Unlike Benjamini et al., (2023) premedication with xylazine and medetomidine was performed in the group receiving propofol. Our study found that anesthesia protocols using propofol reduced IOP values. It was concluded that the preanesthetic agents used have different effects on IOP values and that the choice of preanesthetic in general anesthesia affects IOP changes.

Joyner et al. (2021) applied four different intravenous sedation protocols to 12 healthy horses with a 48-hour withdrawal period in their study. They compared intraocular pressures measured using rebound tonometry at 5, 10, 15, 30, 45, and 60 minutes before and after sedation in horses receiving the xylazine-butorphanol, detomidine-butorphanol, detomidine, and xylazine protocols. They reported that IOP decreased compared to baseline values in

all protocols. In conclusion, they stated that the greatest decrease occurred in the detomidine-butorphanol protocol, while the smallest decrease occurred in the detomidine protocol.

Chae et al. (2021) compared the effects of isoflurane, xylazine-ketamine, and xylazine-ketamine-isoflurane anesthesia protocols on IOP values in New Zealand rabbits. They reported that the IOP value increased by approximately 12 mmHg in the group administered isoflurane, whereas it decreased by 5 mmHg in the xylazine-ketamine group. They noted that the IOP value decreased in the group administered isoflurane after premedication with xylazine-ketamine. In conclusion, they emphasized that the xylazine-ketamine combination could be used in glaucoma patients. In our study, a statistically significant difference was found between the values measured at 0 minutes and the measurements taken after anesthesia. In all anesthesia protocols, IOP values decreased compared to the 0-minute value. The greatest decrease was observed in Group I, while the smallest decrease was observed in Group IV. In terms of the decrease in IOP values during anesthesia compared to baseline values, our study is consistent with the studies conducted by Chae et al. (2021) and Joyner et al. (2021).

Yener et al. (2024), compared the effects of the preanesthetic agents xylazine, midazolam, and dexmedetomidine on IOP in their study. They reported measuring intraocular pressure at 0,5, 10, 15, 30, 45, 60, and 90 minutes. They noted that IOP values decreased from baseline in all groups. Lim and Seo (2025) applied three different anesthesia protocols with a 7-day washout period in their study involving 8 pigeons. They compared IOP values in the three anesthesia protocols using alfaxalone, medetomidine, and xylazine. They reported that IOP values decreased significantly in all protocols, but the greatest decrease was observed in the xylazine protocol. Alfaxalone reached maximum IOP reduction within 6 minutes, while medetomidine and xylazine reached maximum IOP reduction at 95 and 115 minutes, respectively. In conclusion, they stated that medetomidine and xylazine showed a longer duration of action and greater IOP reduction than alfaxalone. The presented study did not evaluate the effect of preanesthetics alone on IOP. When IOP values were evaluated only 10 minutes before the administration of the general anesthetic agent, a decrease was observed in all groups. This finding is consistent with the results reported by Lim and Seo (2025) and Yener et al., (2024). However, since the administered preanesthetics could not be monitored for a long period, it was not possible to determine which preanesthetic reduced IOP the most.

In conclusion, a decrease in IOP values in both the right and left eyes compared to baseline values was observed in all applied anesthetic protocols. However, in the intergroup comparison, it was determined that the applied anesthetic protocols did not create a significant difference in IOP values. Based on the data obtained, it was concluded that the combination of xylazine-medetomidine-propofol-ketamine can be used safely in rats without causing an adverse effect on IOP.

Conflict of interest

The authors declare that they have no actual, potential, or perceived conflict of interest regarding this article.

Ethical approval

Permission for this study was obtained from Erciyes University HADYEK 03.09.2025-25/175. The authors also declare compliance with Research and Publication Ethics.

Similarity Ratio

We declare that the similarity ratio of the article is 13%, as indicated in the report uploaded to the system.

Author Contributions

Concept/Idea: MKY, GA
Design: MKY
Supervision/Advising: GA
Data Collection and/or Processing: NEA, UA
Analysis and/or Interpretation: MKY
Literature Review: NEA, UA
Article Writing: MKY, NEA
Critical Review: GA

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