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Comparative evaluation of the effects of two anesthetic combinations and administration routes on lacrimal secretion in gerbils

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Summary

The present study aimed to evaluate the effects of two injectable anesthetic combinations administered via different routes on lacrimal secretion in gerbils (*Meriones unguiculatus*). Thirty-two healthy adult male gerbils were randomly assigned to four experimental groups (n = 8). Group 1 received ketamine-medetomidine-midazolam (KMM) via the subcutaneous (SC) route, Group 2 received the same combination intraperitoneally (IP), Group 3 received ketamine-dexmedetomidine-midazolam (KDM) subcutaneously, and Group 4 received the KDM combination intraperitoneally. Tear production was evaluated using the Endodontic Absorbent Paper Point Test (EAPPT) and the Phenol Red Thread Test (PRTT) before anesthesia (baseline), at 15, 30, 45, and 60 min after anesthetic administration, and 24 h later. Statistical analyses were performed by non-parametric methods, with significance set at $P < 0.05$. Both anesthetic combinations produced a temporary reduction in tear production during anesthesia. Significant temporal changes in EAPPT values were observed in Groups 1, 3, and 4, whereas Group 2 showed no significant variation. In contrast, PRTT measurements demonstrated significant reductions in tear production in all groups during the anesthetic period. Dexmedetomidine-containing protocols generally produced more pronounced and sustained decreases in lacrimal secretion than medetomidine-based protocols. Tear production progressively recovered following anesthesia and returned to baseline levels within 24 h in all groups. Intergroup differences were limited, with significant differences detected only at specific observation periods. In conclusion, both ketamine-medetomidine-midazolam and ketamine-dexmedetomidine-midazolam combinations induced transient suppression of lacrimal secretion in gerbils. PRTT appeared to be more sensitive than EAPPT in detecting anesthesia-associated changes in tear production. These findings may contribute to the refinement of anesthetic protocols and perioperative ocular care in gerbils used for experimental and clinical purposes.

Keywords: anesthesia, dexmedetomidine, gerbil, lacrimal secretion, *Meriones unguiculatus*, tear production

Gerbils (*Meriones unguiculatus*) are widely used in biomedical research and have gained increasing popularity as companion animals in recent years. Their physiological and anatomical characteristics make them valuable experimental models in various fields, including neurology, audiology, endocrinology, gastrointestinal research, and behavioral sciences. In addition to their importance in laboratory studies, gerbils are frequently presented to veterinary clinics for diagnostic and surgical procedures requiring sedation or general anesthesia. Consequently, the development of safe and effective anesthetic protocols for this species remains an important topic in both laboratory animal medicine and clinical veterinary practice (2, 3, 6, 7).

General anesthesia is routinely employed to facilitate surgical interventions, diagnostic procedures, and experimental manipulations while minimizing pain, stress, and movement. However, small rodents present unique anesthetic challenges because of their high metabolic rate, limited body reserves, rapid heat loss, and sensitivity to environmental stressors. These physiological characteristics may increase the risk of perioperative complications, including hypothermia, respiratory depression, cardiovascular instability, and delayed recovery. Therefore, optimization of anesthetic protocols is essential not only for animal welfare, but also for the reliability and reproducibility of experimental outcomes (4, 6-8, 15, 17, 27).

Ketamine-based anesthetic combinations are among the most commonly used injectable protocols in laboratory rodents. Ketamine alone provides dissociative anesthesia, but generally fails to produce sufficient muscle relaxation and analgesia for many procedures. For this reason, it is frequently combined with α2-adrenergic agonists, such as medetomidine or dexmedetomidine, as well as benzodiazepines including midazolam. These combinations enhance sedation, improve muscle relaxation, and provide superior analgesia while allowing the use of lower doses of individual agents. Dexmedetomidine, the active dextrorotatory isomer of medetomidine, possesses greater α2-adrenoceptor selectivity and has been reported to produce more profound sedative and analgesic effects than medetomidine in several animal species (1, 3, 10, 14, 16, 22, 25, 26).

Although the anesthetic efficacy and cardiopulmonary effects of ketamine-based combinations have been investigated extensively in rodents, less attention has been given to their influence on ocular physiology. Adequate tear production is essential for maintaining corneal integrity, ocular surface lubrication, and normal visual function. Reductions in lacrimal secretion during anesthesia may predispose animals to corneal drying, keratitis, epithelial injury, and postoperative ocular discomfort. Such complications are particularly relevant in laboratory animals undergoing prolonged anesthetic procedures, where ocular surface protection may be overlooked (8, 12).

Previous studies have demonstrated that several anesthetic and sedative agents significantly reduce tear production in animals (5, 12, 15, 18, 19, 21). Among injectable anesthetics, α_2-adrenoceptor agonists are consistently associated with suppression of lacrimal secretion (5, 12, 19). Medetomidine has been shown to produce a rapid and significant decrease in aqueous tear production in dogs, both when administered alone and in combination with other anesthetic agents, with tear secretion remaining below baseline values throughout the anesthetic period (19). Similar findings have also been reported in rats, indicating that this effect is not species-specific, but rather represents a common pharmacological consequence of α_2-adrenoceptor stimulation (9). Likewise, dexmedetomidine, the active dextrorotatory isomer of medetomidine, has been reported to significantly decrease tear production during sedation, and ocular lubrication has been recommended during and for several hours after anesthesia to prevent exposure keratopathy (5, 18, 21). Although the exact mechanism has not been fully elucidated, reduced parasympathetic stimulation of the lacrimal glands, altered autonomic regulation, decreased blink frequency, and changes in ocular blood flow have all been proposed to contribute to the reduction in tear secretion (20, 21). Furthermore, the magnitude of tear suppression appears to be influenced by the anesthetic protocol, drug dosage, duration of anesthesia, and species investigated. Despite these findings, information regarding the effects of medetomidine- and dexmedetomidine-based anesthetic combinations on tear production in gerbils remains extremely limited, particularly when different administration routes are compared (5, 9, 18, 19).

The route of anesthetic administration may also influence physiological responses. Intraperitoneal administration generally results in more rapid systemic absorption and a faster onset of action, whereas subcutaneous administration often produces a more gradual pharmacological effect. Differences in absorption kinetics may alter anesthetic depth, duration, cardiovascular responses, and potentially lacrimal gland function. However, information regarding the effects of different administration routes on tear production in gerbils remains limited (1, 14, 26, 27).

Assessment of lacrimal secretion can be performed using several diagnostic techniques. The Phenol Red Thread Test (PRTT) is widely used in small rodents because it requires only a short measurement period and can be performed with minimal restraint. Endodontic absorbent paper point techniques have also been proposed as practical alternatives for evaluating tear production in small animal species. Simultaneous use of these methods may provide a more comprehensive assessment of anesthetic-related changes in lacrimal secretion (9, 12, 19).

To the authors' knowledge, limited information is available regarding the comparative effects of ketamine-medetomidine-midazolam and ketamine-dexmedetomidine-midazolam combinations administered via different routes on lacrimal secretion in gerbils. Therefore, the aim of the present study was to compare the effects of these anesthetic protocols administered by subcutaneous and intraperitoneal routes on tear production using the Phenol Red Thread Test and Endodontic Absorbent Paper Point Test.

Material and methods

Ethical approval. The study was performed following approval from the Aydın Adnan Menderes University Animal Experiments Local Ethics Committee (ADÜ-HADYEK) (Approval No: 64583101/2026/093; Date: 04.06.2026). All experimental procedures were conducted in accordance with institutional guidelines for the care and use of laboratory animals and complied with internationally accepted animal welfare principles.

Animals. The study material consisted of 32 healthy adult male gerbils (*Meriones unguiculatus*), weighing 80-100 g and aged between 8 months and 1 year. Before initiation of the experiment, all animals underwent a 7-day acclimatization period and were subjected to a complete clinical examination. Only clinically healthy animals were included in the study.

The gerbils were obtained from the Experimental Animal Unit of Aydın Adnan Menderes University Faculty of Veterinary Medicine. Throughout the study period, animals were housed under standardized laboratory conditions with

an ambient temperature of 20-24°C, relative humidity of 40-60%, and a 12 h light/12 h dark photoperiod. Sterile wood shavings were used as bedding material, and cages were cleaned daily. Standard laboratory rodent chow and fresh water were provided *ad libitum*.

Experimental design and anesthetic protocols. Following acclimatization, the animals were randomly allocated into four experimental groups (n = 8).

Group 1 received ketamine (50 mg/kg; Ketalar®, Pfizer, Turkey), medetomidine (0.1 mg/kg; Domitor®, Orion Pharma, Finland), and midazolam (5 mg/kg; Dormicum®, Roche, Switzerland) via the subcutaneous (SC) route. Group 2 received the same ketamine-medetomidine-midazolam combination via the intraperitoneal (IP) route. Group 3 received ketamine (50 mg/kg), dexmedetomidine (0.25 mg/kg; Dexdomitor®, Orion Pharma, Finland), and midazolam (5 mg/kg) via the SC route. Group 4 received the same ketamine-dexmedetomidine-midazolam combination via the IP route. All anesthetic combinations were administered as a single injection through the designated route.

Evaluation of lacrimal secretion. Tear production was evaluated using the Phenol Red Thread Test (PRTT; Zone-Quick®, Menicon Co., Ltd., Nagoya, Japan) and the Endodontic Absorbent Paper Point Tear Test (EAPTT; Sure-Endo®, Sure Dent Corporation, Gyeonggi-do, South Korea). The methodology was adapted from previously published studies evaluating tear production in laboratory rodents (9). For both tests, the test material was gently placed into the lower conjunctival fornix of the right eye and maintained for 15 s. Following removal, the wetted length was measured in millimeters using a millimeter ruler and recorded. Measurements were performed before anesthetic administration (baseline) and at 15, 30, 45, 60 min and 24 h after anesthetic administration.

To minimize the effects of reflex tearing and handling stress, a minimum interval of 30 min was maintained between PRTT and EAPTT measurements. All tear production measurements were performed by the same investigator throughout the study.

Statistical analysis. Statistical analyses were performed using SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). Data distribution was evaluated using the Kolmogorov-Smirnov test.

Changes in tear production and physiological parameters over time and differences between groups were analyzed using two-way repeated-measures analysis of variance (ANOVA). When significant differences were detected, Tukey's post hoc test was applied for pairwise comparisons.

Data not meeting the assumptions of normality were analyzed using the Friedman test, followed by the Mann-Whitney U test where appropriate. Results are expressed as mean ± standard deviation (SD), and values of $P < 0.05$ were considered statistically significant.

Results and discussion

Effects of anesthetic protocols on lacrimal secretion. Tear production was evaluated using the Endodontic Absorbent Paper Point Test (EAPPT) and the Phenol Red Thread Test (PRTT). Both anesthetic combinations produced a temporary reduction in lacrimal secretion following administration. The mean tear production values obtained throughout the study period are presented in Tables 1, 2 and Figure 1 and 2.

Endodontic Absorbent Paper Point Test (EAPPT). Temporal changes in tear production measured by EAPPT are presented in Table 1. Baseline tear production values for the groups were comparable, and no significant intergroup differences were observed before anesthetic administration ($P > 0.05$).

Following anesthesia, tear production gradually decreased in all groups. Significant temporal changes were observed in Group 1 (SC ketamine-medetomidine-midazolam; $P = 0.007$), Group 3 (SC ketamine-dexmedetomidine-midazolam; $P < 0.001$), and Group 4 (IP ketamine-dexmedetomidine-midazolam; $P = 0.002$). In contrast, Group 2 (IP ketamine-medetomidine-midazolam) did not show a significant temporal change ($P = 0.151$).

Compared with baseline values, Group 1 demonstrated significantly lower EAPPT values at 30 and 45 min ($P < 0.05$). Group 3 showed significant decreases at 15, 45, and 60 min ($P < 0.05$), whereas Group 4 exhibited a significant reduction at 60 min ($P < 0.05$). No significant differences from baseline were detected at 24 h in any group.

Intergroup comparisons revealed a significant difference only at the 24-h evaluation point ($P = 0.003$). No significant differences between groups were detected at baseline, 15, 30, 45, or 60 min.

Tab. 1. Temporal changes in tear production measured by the Endodontic Absorbent Paper Point Test (EAPPT) in gerbils receiving different anesthetic protocols

Time point	Group 1 (SC KMM)	Group 2 (IP KMM)	Group 3 (SC KDM)	Group 4 (IP KDM)	Intergroup P
Baseline	4.69 ± 0.60	4.50 ± 1.10	5.25 ± 1.00	4.75 ± 0.86	NS
15 min	3.81 ± 1.17	4.12 ± 0.96	4.50 ± 0.63*	4.56 ± 0.51	NS
30 min	3.44 ± 1.15*	3.56 ± 0.96	4.25 ± 1.00	4.31 ± 0.60	NS
45 min	2.88 ± 1.26*	3.62 ± 1.41	3.75 ± 0.86*	4.12 ± 1.15	NS
60 min	3.56 ± 2.99	3.56 ± 0.73	3.44 ± 0.73*	3.69 ± 1.08*	NS
24 h	4.31 ± 0.60	4.50 ± 0.82	5.50 ± 0.73	4.88 ± 0.62	0.003

Explanations: Data are presented as mean ± SD. Intragroup P values (Friedman test): Group 1 = 0.007, Group 2 = 0.151, Group 3 < 0.001, Group 4 = 0.002. *P < 0.05 compared with baseline value within the same group. NS – not significant; SC – subcutaneous; IP – intraperitoneal; KMM – ketamine-medetomidine-midazolam; KDM – ketamine-dexmedetomidine-midazolam.

Phenol Red Thread Test (PRTT). Temporal changes in tear production measured by PRTT are presented in Table 2. Compared with EAPPT, PRTT demonstrated more pronounced reductions in lacrimal secretion and detected significant alterations in all experimental groups.

Tab. 2. Temporal changes in tear production measured by the Phenol Red Thread Test (PRTT) in gerbils receiving different anesthetic protocols

Time point	Group 1 (SC KMM)	Group 2 (IP KMM)	Group 3 (SC KDM)	Group 4 (IP KDM)	Intergroup P
Baseline	4.31 ± 0.60	4.38 ± 0.50	4.81 ± 0.75	4.38 ± 0.50	NS
15 min	2.88 ± 0.34**	3.69 ± 0.48*	3.69 ± 0.79**	3.62 ± 0.89	0.026
30 min	2.88 ± 0.62**	3.38 ± 0.50*	3.19 ± 0.75**	3.06 ± 0.57**	NS
45 min	2.50 ± 0.52**	2.75 ± 0.58**	3.12 ± 0.72**	2.88 ± 0.62*	NS
60 min	2.38 ± 0.50**	2.99 ± 0.72*	2.69 ± 0.60**	2.62 ± 0.81*	NS
24 h	4.50 ± 0.52	4.06 ± 1.39	5.12 ± 0.81	4.50 ± 0.52	NS

Explanations: Data are presented as mean ± SD. Intragroup P values (Friedman test): Group 1 < 0.001; Group 2 < 0.001; Group 3 < 0.001; Group 4 < 0.001. *P < 0.05 compared with the baseline value within the same group. **P < 0.01 compared with the baseline value within the same group. NS – not significant; SC – subcutaneous; IP – intraperitoneal; KMM – ketamine-medetomidine-midazolam; KDM – ketamine-dexmedetomidine-midazolam.

Significant temporal changes were observed in Group 1 ($P < 0.001$), Group 2 ($P < 0.001$), Group 3 ($P < 0.001$), and Group 4 ($P < 0.001$).

Compared with baseline values, Group 1 demonstrated significantly reduced tear production at 15, 30, 45, and 60 min ($P < 0.01$). Similar findings were observed in Group 3, where all measurements between 15 and 60 min differed significantly from baseline ($P < 0.01$). Group 2 exhibited significant reductions at 15, 30, 45, and 60 min ($P < 0.05$), whereas Group 4 demonstrated significant decreases at 30, 45, and 60 min ($P < 0.05$).

Intergroup comparison revealed a significant difference at 15 min following anesthetic administration ($P = 0.026$). No significant differences between groups were observed at baseline, 30 min, 45 min, 60 min, or 24 h.

Tear production gradually increased during recovery and returned to values comparable with baseline within 24 h in all experimental groups.

Overall findings. Both anesthetic combinations induced transient suppression of lacrimal secretion in gerbils. Although EAPPT detected significant alterations in selected groups at selected time points, PRTT identified significant reductions more consistently throughout the anesthetic period. These findings suggest that PRTT may be more sensitive than EAPPT for detecting anesthesia-induced changes in tear production in gerbils.

The present study evaluated the effects of two injectable anesthetic combinations administered via different routes on lacrimal secretion in gerbils. The findings demonstrated that both ketamine-medetomidine-midazolam and ketamine-dexmedetomidine-midazolam protocols significantly reduced tear production during anesthesia. Decreased lacrimal secretion was observed with both PRTT and EAPPT measurements, although the magnitude and consistency of the changes differed between the two methods. Tear production gradually recovered following anesthesia and returned to values comparable with baseline levels within 24 h.

Compared with many other laboratory rodent species, gerbils present unique challenges in anesthetic management. They possess a relatively high metabolic rate and exhibit marked physiological responses to environmental stressors. Their small body size, rapid metabolism, and limited physiological reserves increase their susceptibility to anesthesia-associated alterations in cardiovascular, respiratory, thermoregulatory, and ocular functions (3, 20). Although gerbils are widely used in neuroscience, auditory physiology, behavioral studies, and experimental surgery, information regarding ocular changes occurring during anesthesia remains limited. Consequently, characterization of anesthesia-induced alterations in tear production may contribute to both refinement of anesthetic protocols and improvement of animal welfare.

Reduction in tear production during anesthesia has been reported in several animal species and is generally attributed to the depressant effects of anesthetic and sedative agents on autonomic regulation of the lacrimal glands. Alpha-2 adrenergic agonists, including medetomidine and dexmedetomidine, suppress sympathetic and parasympathetic pathways involved in tear production and may therefore contribute to reduced lacrimal secretion during anesthesia (11, 13, 14). Similar decreases in tear production have previously been reported in dogs, cats, rabbits, and laboratory rodents receiving alpha-2 agonist-containing anesthetic protocols (23, 24). These findings are in agreement with previous studies evaluating the ocular effects of individual α2-adrenoceptor agonists. Sanchez et al. (19) reported that medetomidine significantly reduced Schirmer tear test values in both dogs and cats shortly after administration, with tear production remaining below baseline throughout the sedative period. Similarly, Herring et al. (12) demonstrated that tear production decreases markedly during general anesthesia, particularly when α2-adrenergic agonists are included in the anesthetic protocol. More recently, Leonardi et al. (18) and Di Pietro et al. (5) reported significant reductions in tear production following dexmedetomidine administration and recommended routine ocular lubrication to reduce the risk of corneal desiccation and exposure keratopathy. The present findings in gerbils are therefore consistent with those reported in other veterinary species, suggesting that suppression of lacrimal secretion is a common pharmacological effect of α2-adrenoceptor agonists.

The marked reduction in tear production observed during anesthesia may be particularly relevant in gerbils because of their behavioral and anatomical characteristics. In conscious animals, grooming activity and frequent blinking contribute substantially to maintenance of ocular surface integrity and tear film stability. During

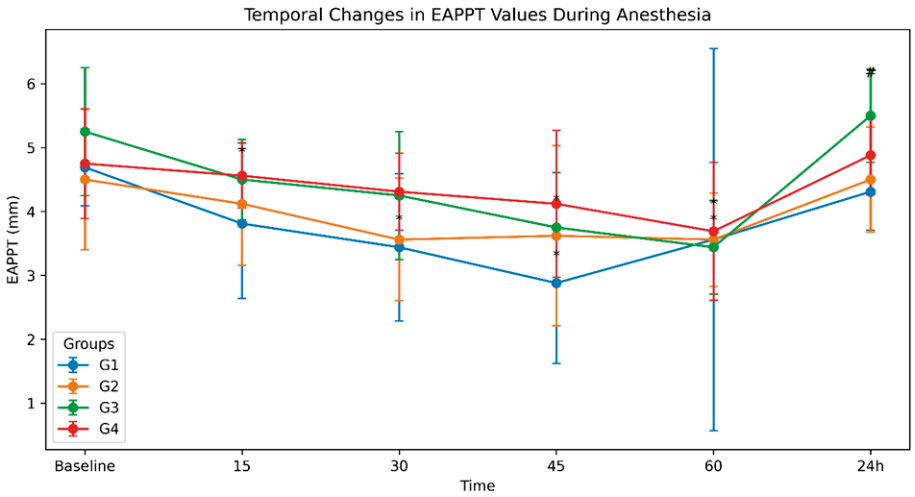

Fig. 1. Temporal changes in tear production measured by the Endodontic Absorbent Paper Point Test (EAPPT) in gerbils receiving ketamine-medetomidine-midazolam (KMM) or ketamine-dexmedetomidine-midazolam (KDM) combinations administered via subcutaneous (SC) and intraperitoneal (IP) routes

Explanations: Data are presented as mean ± SD. * $P < 0.05$ versus baseline within the same group. ** $P < 0.01$ versus baseline within the same group. # Significant intergroup difference ($P = 0.026$). Group 1 – SC ketamine-medetomidine-midazolam; Group 2 – IP ketamine-medetomidine-midazolam; Group 3 – SC ketamine-dexmedetomidine-midazolam; Group 4 – IP ketamine-dexmedetomidine-midazolam. Significant temporal reductions in tear production were observed in Groups 1, 3, and 4, whereas Group 2 did not show statistically significant variation throughout the study period.

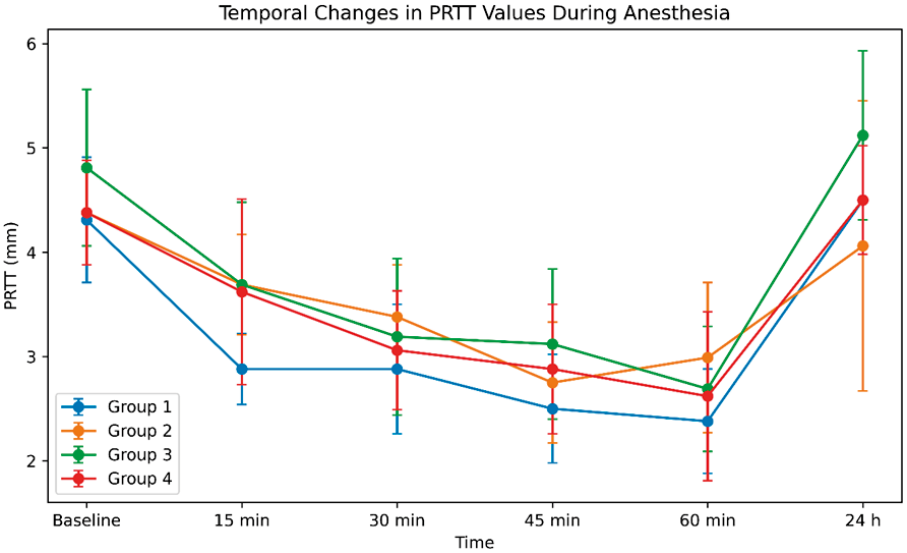

Fig. 2. Temporal changes in tear production measured by the Phenol Red Thread Test (PRTT) following administration of different anesthetic protocols in gerbils

Explanations: * $P < 0.05$ versus baseline within the same group. # Significant intergroup difference ($P = 0.003$). Group 1 – SC ketamine-medetomidine-midazolam; Group 2 – IP ketamine-medetomidine-midazolam; Group 3 – SC ketamine-dexmedetomidine-midazolam; Group 4 – IP ketamine-dexmedetomidine-midazolam. Significant reductions in tear production were observed in all groups during the anesthetic period. The greatest decreases occurred between 15 and 60 min after anesthetic administration. Tear production recovered progressively and returned to baseline values within 24 h.

anesthesia, these protective mechanisms are markedly diminished, increasing susceptibility to corneal desiccation and ocular surface injury. Therefore, reductions in tear production observed during anesthesia may have greater clinical significance than tear measurements alone would suggest.

A notable finding of the present study was that PRTT measurements demonstrated significant reductions in tear production in all experimental groups, whereas EAPPT detected significant changes only in some groups at certain time points. These findings suggest that PRTT may be more sensitive for monitoring anesthesia-induced alterations in lacrimal secretion in gerbils. Similar observations have been reported in ophthalmological studies evaluating tear production in small mammals, where PRTT was considered particularly useful because of its rapid application time, minimal ocular irritation, and ability to detect subtle physiological changes in tear secretion (10, 27). The greater sensitivity observed in the present study may reflect the ability of PRTT to identify transient changes occurring during the dynamic phases of anesthesia.

Although both medetomidine- and dexmedetomidine-containing protocols reduced tear production, dexmedetomidine-treated animals generally exhibited more sustained decreases throughout the anesthetic period. Dexmedetomidine possesses substantially greater α2-adrenoceptor selectivity than medetomidine and produces more profound sedative, analgesic, and sympatholytic effects (17). Consequently, stronger suppression of lacrimal gland activity may be expected. Recent studies have similarly demonstrated that dexmedetomidine-containing anesthetic protocols can significantly influence physiological variables and autonomic responses in laboratory animals and veterinary patients (1, 10). However, the differences observed between dexmedetomidine and medetomidine combinations in the present study were less pronounced than anticipated. This finding may indicate species-specific responses in gerbils. Previous studies in dogs and cats have documented substantial reductions in tear production following administration of α2-adrenergic agonists, but the magnitude of these effects appears to vary among species depending on receptor distribution, dosage, and anesthetic combinations employed (23, 24).

Another important observation was the rapid recovery of tear production following anesthesia. Tear production

values had returned to baseline levels in all experimental groups within 24 h of anesthetic administration. This recovery suggests that the effects of the anesthetic protocols on lacrimal gland function were primarily pharmacological and reversible rather than indicative of permanent glandular dysfunction. The ability of gerbils to regain normal tear production within a relatively short period may reflect efficient physiological recovery following transient autonomic suppression induced by anesthesia.

The route of administration also appeared to influence the temporal pattern of tear suppression. Intraperitoneal administration generally produced earlier reductions in tear production, whereas subcutaneous administration was associated with a more gradual decline. These findings are likely related to differences in drug absorption kinetics. Drugs administered intraperitoneally are rapidly absorbed because of the extensive vascularization of the peritoneal cavity, whereas subcutaneous administration typically results in slower and more prolonged absorption (5). Similar route-dependent differences have been described in rodents and rabbits receiving injectable anesthetic protocols (5, 10).

From the perspective of laboratory animal welfare, the present findings support routine ophthalmic protection during anesthesia in gerbils. Reduced lacrimal secretion may predispose animals to tear film instability, corneal desiccation, and ocular surface injury, particularly during prolonged procedures. Application of artificial tears or ophthalmic lubricants before anesthetic induction may therefore represent a simple refinement strategy to improve perioperative welfare and reduce anesthesia-associated ocular complications. Such measures may be especially important in gerbils because of the substantial reductions in tear production observed during the first hour of anesthesia.

Several limitations of the present study should be acknowledged. First, the sample size was relatively limited, which may have reduced statistical power for detecting subtle differences between anesthetic protocols. Second, only healthy male gerbils were included, so the results may not be directly applicable to females, juvenile animals, or animals with systemic disease. Third, evaluation of corneal integrity, tear film breakup time, and ocular surface pathology was beyond the scope of the study. Future investigations incorporating detailed ophthalmological examinations, larger populations, and additional anesthetic protocols would further clarify the ocular effects of anesthesia in gerbils.

Overall, the results indicate that both ketamine-medetomidine-midazolam and ketamine-dexmedetomidine-midazolam combinations induce transient suppression of lacrimal secretion in gerbils. PRTT detected these alterations more consistently than EAPPT, which suggests a greater sensitivity of the former in monitoring anesthesia-related changes in tear production. Despite significant reductions during anesthesia, tear production returned to baseline values within 24 h in all groups, indicating that the observed effects were temporary and reversible. These findings contribute to the limited literature regarding ocular physiology during anesthesia in gerbils and may assist in the refinement of anesthetic and perioperative care protocols for this increasingly important laboratory species.

Both ketamine-medetomidine-midazolam and ketamine-dexmedetomidine-midazolam combinations produced a temporary reduction in lacrimal secretion in gerbils following subcutaneous and intraperitoneal administration. Tear production decreased significantly during the anesthetic period, particularly between 15 and 60 min after drug administration, and subsequently returned to baseline values within 24 h, indicating that the observed effects were reversible.

Although dexmedetomidine-containing protocols tended to induce more pronounced and sustained reductions in tear production, differences between anesthetic combinations and administration routes were generally limited. The finding that PRTT detected anesthesia-associated alterations in tear production more consistently than EAPPT may be related to methodological differences between the two tests. PRTT requires a shorter measurement period and causes less ocular irritation than paper-based methods, which may reduce reflex tearing and improve its capability of detecting subtle changes in basal tear secretion. Similar observations have been reported in ophthalmic studies involving small mammals, where PRTT was considered a practical and reliable tool for evaluating tear production under clinical and experimental conditions (27).

The greater sensitivity of PRTT may be particularly relevant in gerbils because of their relatively small ocular surface area and limited tear volume. Minor alterations in lacrimal gland function may therefore be more difficult to detect using less sensitive techniques. In the present study, significant reductions in tear production were identified in all experimental groups when assessed by PRTT, whereas EAPPT detected significant changes only at selected time points. These findings suggest that PRTT may be the preferred method for evaluating anesthesia-related ocular changes in this species. Although dexmedetomidine-containing protocols tended to induce more pronounced and sustained reductions in tear production, differences between anesthetic combinations were generally less marked than expected. Dexmedetomidine possesses substantially greater α2-adrenoceptor selectivity than medetomidine and is known to produce stronger sedative, analgesic, and sympatholytic effects (17). Previous studies in veterinary species have demonstrated that dexmedetomidine can significantly reduce tear production through suppression of autonomic pathways regulating lacrimal gland secretion (23, 24). Therefore, the greater reduction observed in dexmedetomidine-treated gerbils is consistent with the known pharmacological profile of the drug.

However, the magnitude of the differences between dexmedetomidine and medetomidine groups remained relatively modest. This observation may indicate that factors other than α2-adrenoceptor selectivity also con-

tribute to the regulation of tear production during anesthesia. The concurrent administration of ketamine and midazolam in all protocols may have reduced the relative contribution of the α2-agonist component, resulting in partially overlapping physiological responses among treatment groups. In addition, species-specific characteristics of gerbils, including autonomic regulation and lacrimal gland physiology, may influence the extent to which tear production is affected during anesthesia. Our findings also support previous pharmacological observations indicating that dexmedetomidine may induce a greater reduction in tear production than medetomidine because of its higher α2-adrenoceptor selectivity. Nevertheless, the relatively modest differences observed between the two anesthetic combinations suggest that species-specific physiological characteristics and the concurrent administration of ketamine and midazolam may have moderated these effects in gerbils.

The influence of administration route was similarly limited. Although intraperitoneal administration generally produced a more rapid onset of tear suppression, long-term patterns of lacrimal secretion were comparable between intraperitoneal and subcutaneous protocols. This finding suggests that drug absorption kinetics primarily affect the timing of the response rather than the overall magnitude of lacrimal suppression. Comparable route-dependent differences have been reported in studies evaluating injectable anesthetic protocols in rodents and rabbits, where intraperitoneal administration resulted in faster systemic drug availability, but did not necessarily alter the overall pharmacodynamic outcome (6, 10). Taken together, these findings indicate that the reduction in tear production observed during anesthesia is associated primarily with the pharmacological effects of the anesthetic agents rather than the route of administration.

From a clinical perspective, the consistent decrease in lacrimal secretion across all groups highlights the importance of ocular lubrication and perioperative eye protection during anesthesia in gerbils, regardless of the specific anesthetic protocol selected. The use of ophthalmic lubricants or artificial tears should be considered, particularly during procedures of moderate to long duration, to minimize the risk of corneal desiccation and ocular surface injury.

Overall, the present study provides novel information regarding the effects of commonly used injectable anesthetic protocols on lacrimal secretion in *Meriones unguiculatus*. These findings may contribute to the optimization of anesthetic management and perioperative ocular care in gerbils used for experimental and clinical purposes.

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