Original Article

Short-term vs Long-term Effects of Latanoprost on Tear Test, IOP, and Pupil Size in Dogs

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ABSTRACT

Background: Glaucoma poses a significant challenge in veterinary medicine, necessitating effective management strategies to mitigate vision loss. Prostaglandin analogs like latanoprost offer promising avenues due to their ability to lower intraocular pressure (IOP). However, a comprehensive understanding of latanoprost's short-term and long-term effects on ocular parameters in dogs remains limited.

Objectives: This study aims to compare the effects of short-acting versus long-acting latanoprost on the Schirmer tear test (STT), IOP and pupil size in clinically normal dogs, highlighting its potential applications in veterinary ophthalmology. By examining both short-term and long-term impacts, this study offers novel insights into the temporal pharmacological effects of latanoprost.

Methods: Twenty healthy adult male crossbred dogs underwent thorough baseline assessments before receiving either latanoprost or saline drops in randomly chosen eyes. The STT, IOP and pupil size were measured at various intervals using standardized protocols. Statistical analyses were conducted to compare treated and untreated eyes.

Results: Short-term analysis revealed a significant IOP reduction at 6 and 8 h post-latanoprost instillation, with no significant changes in STT values. Pupil diameter showed significant differences between treated and untreated eyes. The long-term effects included sustained IOP reduction and pupil constriction after three weeks of latanoprost treatment.

Conclusion: Latanoprost demonstrates rapid and sustained efficacy in reducing IOP in dogs, with potential implications for glaucoma management. Although it does not significantly affect tear production, it modulates pupil size, highlighting its multifaceted pharmacological effects. The study affirms the latanoprost's safety profile and underscores its therapeutic potential in veterinary ophthalmology, urging further exploration of its mechanisms and applications.

Keywords: Dogs, Glaucoma, Intraocular pressure (IOP), Latanoprost, Schirmer tear test (STT)

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Introduction

Glaucoma is a multifactorial ocular disease characterized by elevated intraocular pressure (IOP), which, if left uncontrolled, can lead to irreversible optic nerve damage and vision loss (Graham et al., 2020). In veterinary medicine, glaucoma poses a significant clinical challenge, particularly in dogs, where primary and secondary forms of the condition are encountered. Effective management of glaucoma in dogs often involves using various ocular medications to reduce IOP and preserve ocular integrity (Webb, 2021).

Among the classes of antiglaucoma drugs, prostaglandin analogs have emerged as key therapeutic agents because they enhance uveoscleral outflow, lowering IOP (Plummer et al., 2021). Latanoprost, a member of this class, has been widely utilized in human and veterinary ophthalmology for its potent IOP-lowering effects (Cordeiro et al., 2024). However, while the short-term efficacy of latanoprost in reducing IOP has been well-documented in dogs, this study uniquely addresses this gap by comparing latanoprost's short-acting versus long-acting effects, providing novel insights into its sustained pharmacological impact on canine ocular health (Desai et al., 2022a). Understanding the effects of latanoprost on these parameters over both short-term and long-term durations is crucial for optimizing glaucoma management strategies and ensuring the overall ocular well-being of canine patients.

This study aims to compare the effects of short-acting versus long-acting latanoprost on the Schirmer tear test (STT), IOP and pupil size in clinically normal dogs for potential application in managing glaucoma and other ocular conditions in veterinary practice.

Materials and Methods

Twenty healthy adult, castrated male crossbred dogs were used in this study. Before commencement, all dogs were housed indoors for seven days under controlled environmental conditions, maintaining a constant temperature of 22 ˚C and humidity levels between 40-45%. The lighting regimen followed a 12-hour light and 12-hour dark cycle (Bódizs et al., 2020). The dogs had access to food that met their dietary requirements and were provided water and ad libitum. Before inclusion in the study, each dog underwent a comprehensive physical examination, including a complete blood count and serum biochemical profile assessment, to ensure baseline health status. Furthermore, a thorough ophthalmic examination, encompassing tests, such as the STT, slit-lamp biomicroscopy, fluorescein staining, tonometry, and direct and indirect ophthalmoscopy, was conducted to confirm ocular health and ensure eligibility for participation in the study.

Baseline IOP was assessed in dogs (T0). Subsequently one drop of latanoprost (Latanapost®, Sinadarou Laboratories Company, Tehran, Iran) was administered to each dog in a randomly chosen eye. The other eye received one drop of normal saline as a control. These eye drops were administered every 12 hours for three consecutive weeks.

Each animal was gently restrained in the ventral recumbent position for the duration of the procedure. IOP was assessed using a rebound tonometer (TonoVet®, Jorgensen Laboratories, Loveland, CO, USA) calibrated to 'd'. Care was taken to avoid any head, neck, or eyelid stimulation during the measurement to mitigate potential confounding factors (Klein et al., 2011). Short-term assessment of IOP, STT and pupillary diameter (PD) IOP were measured at 30 minutes, 60 minutes, 90 minutes, 120 minutes, 4, 6, 8, 10, 12, 24 and 36 h. Additionally, for long-term evaluation, measurements were taken every Sunday for three weeks at 2 hours, 4 hours, 6 hours, 8 hours and 12 hours post-morning drug instillation. PD was recorded simultaneously using a Jameson caliper (Storz Ophthalmic, Bausch+Lomb, New York, NY, USA). A single examiner conducted all measurements and ocular examinations to ensure consistency and minimize inter-operator variability.

Statistical analysis was conducted utilizing SPSS software, version 23. All collected values were normalized using the one-sample Kolmogorov–Smirnov test ($P>0.3$). Repeated measures analysis of variance with Bonferroni post hoc correction was employed to compare the means of STT, IOP and PD values between treated and untreated eyes. Statistical significance was defined as a $P<0.05$ (Molazem et al., 2024; Mottaghian et al., 2022; Rassouli et al., 2021; Rezaey & Alizadeh, 2024).

Results

Short-term effects

Significant differences in IOP were observed between the treatment and non-treatment groups at 6 and 8 h post-drop instillation ($P=0.008$, and $P=0.014$, respectively), with a mean of 21±4.5 mm Hg.

However, no significant differences were observed in Schirmer test values between the treated and untreated eyes across all time intervals (mean: 16.3±3.2 mm/min).

A significant difference in pupil diameter was observed between the treated and untreated eyes at all times, except baseline and 36 h post-drop instillation (P<0.001; mean: 0.08 cm) (Table 1).

No significant differences were found in IOP, pupil diameter, or Schirmer test values between the treated and untreated eyes at various time points (P>0.05).

Long-term effects

Baseline IOP values in the treated eyes were (16.6±2.8 mm Hg) and a significant reduction in IOP was observed after 3 weeks of treatment. Similarly, Schirmer test values were 0.6±0.1 cm and no significant difference was observed after three weeks. Also, baseline pupil diameter values were 0.6±0.1 cm and 21.2±1.4 mm/min, and a significant reduction in pupil diameter was observed after 3 weeks of treatment, respectively (Figures 1 and 2).

Discussion

Glaucoma is a prevalent ocular disease in veterinary medicine and poses significant challenges due to its potential for irreversible vision loss (Park & Komáromy, 2021) This study uniquely investigates the differential impacts of short-acting versus long-acting latanoprost on the STT, IOP and pupil size in clinically normal dogs. By providing a novel comparison of these formulations, our study sheds light on the temporal pharmacological dynamics of latanoprost. Our results confirm the rapid IOP-lowering effects and reveal long-term administration's sustained efficacy and safety, which has been less frequently documented in veterinary literature. These results enhance our understanding of latanoprost's temporal effects and ocular tolerability, offering valuable insights for its clinical application in glaucoma management.

The short-term efficacy of latanoprost in reducing IOP in dogs has previously been established (Studer et al., 2000). The results corroborate these results, demonstrating a significant reduction in IOP at 6 and 8 h post-drop instillation. This rapid onset of action aligns with latanoprost's pharmacokinetics, which enhances uveoscleral outflow (Nakagawa et al., 2019). However, despite its potent IOP-lowering effects, no significant changes in the STT values were observed in our study, indicating that latanoprost may not directly influence tear production in clinically normal dogs. This result is consistent with previous human and veterinary literature reports, suggesting that latanoprost primarily targets IOP regulation without affecting tear secretion (Desai et al., 2022b).

This study revealed a significant difference in pupil diameter between treated and untreated eyes at various time points, suggesting a potential role for latanoprost in modulating pupillary dynamics. Observations have underscored the multifaceted pharmacological effects of latanoprost beyond its primary mechanism of IOP reduction (Smith et al., 2010). Further investigations are warranted to elucidate the underlying mechanisms driving these changes in pupil size and their clinical implications.

In contrast to short-term effects, long-term analysis revealed a sustained reduction in IOP and pupil diameter following three weeks of latanoprost administration. These results highlight the therapeutic durability of latanoprost and its potential for long-term glaucoma management in dogs. This study also demonstrated the ocular safety profile of latanoprost, with no significant adverse effects observed on electrocardiography, blood cell counts, or biochemical profiles over both short and long-term intervals. This favorable safety profile further supports the use of latanoprost as a reliable therapeutic option for canine glaucoma.

These results are consistent with previous studies evaluating latanoprost's effects in various animal models, including horses and cats (McDonald et al., 2016; Willis et al., 2001). While ocular adverse effects have been reported in some species, this study provides reassurance regarding the ocular tolerability of latanoprost in dogs. The absence of significant changes in control eyes treated with saline reaffirms the specificity of latanoprost's effects on ocular parameters.

While this study sheds light on latanoprost's short- and long-term effects in dogs, limitations exist. These include a small sample size, a brief observation period of three weeks, and reliance on a fixed dosing regimen. Additionally, the study's focus on healthy dogs may limit generalizability, and using a single examiner could introduce bias. Not all relevant endpoints were assessed, and species-specific differences may impact the applicability beyond dogs. Addressing these limitations in future research will enhance understanding latanoprost's role in veterinary ophthalmology.

Conclusion

In conclusion, this study underscores the efficacy and safety of topical latanoprost in canine glaucoma management. By elucidating its short- and long-term effects on STT, IOP and pupil size, we provide valuable insights for optimizing treatment strategies and preserving ocular health in dogs affected by glaucoma. Future research

Table 1. Mean±SD of measured pupillary diameter, iop and stt post-instillation of latanoprost in 20 healthy adult castrated male dogs during 3 weeks

Groups/Time Points		Mean±SD											
		Hour									Week		
		0	0.5	1.5	2	4	8	12	24	36	One	Two	Three
Pupillary diameter	Untreated eyes	0.8±0	0.8±0	0.76±0.05	0.76±0.05	0.83±0.05	0.73±0.05	0.73±0.05	0.7±0.1	0.71±0.11	0.76±0.05	0.74±0.05	0.78±0.04
	Treated eyes	0.8±0	0.3±0.1	0.26±0.05	0.2±0.1	0.3±0.17	0.2±0.1	0.66±0.11	0.63±0.05	0.65±0.02	0.7±0.12	0.68±0.17	0.68±0.1
IOP	Untreated eyes	21±4.58	20.33±4.72	16.66±3.51	16±1	17.3±3.21	17.66±2.51	19±5.1	21.33±5.68	20.43±2.44	20.6±2.7	20.3±1.49	19.77±2.22
	Treated eyes	19.66±4.5	19±4.58	17.1±1.1	12±1	12.33±1.52	10.1±1.1	17.33±8.09	16.1±1.1	16.5±1.2	16.6±2.88	14.57±1.58	15.57±2.64
STT	Untreated eyes	16.33±3.21	15.66±3.05	24.66±6.8	24.66±6.8	24.66±6.8	19.33±5.13	23.33±5.5	23±5.29	23.1±4.09	22.4±1.34	21±1.87	21.6±1.94
	Treated eyes	19.33±7.57	19.66±6.42	22.66±8.08	22.66±8.08	22.66±8.08	20.33±8.5	25.66±7.09	19.33±7.57	20.32±5.55	20.8±2.04	20.6±1.51	20.8±1.64

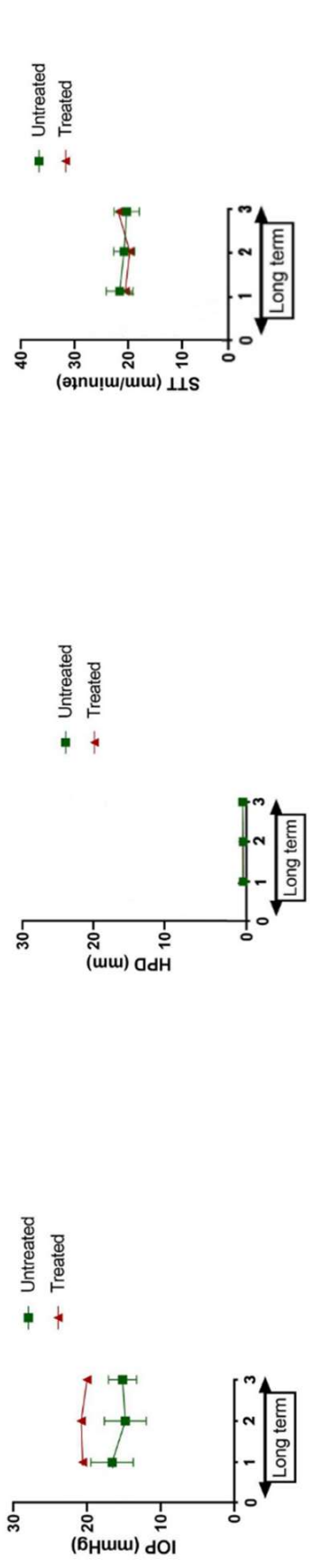

Figure 1. Mean IOP, PD, and STT of T and UT eyes, post-instillation of latanoprost in dogs during three weeks

T: Treated; UT: Untreated.

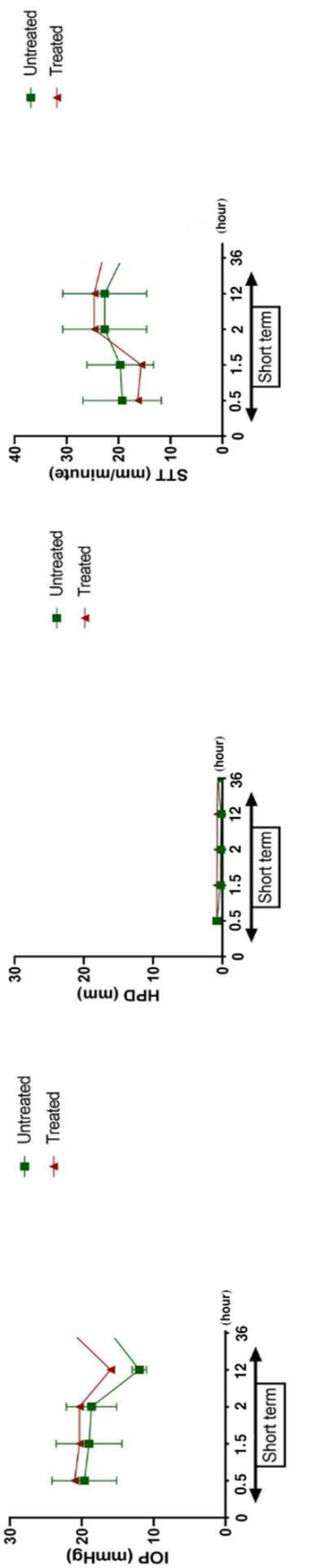

Figure 2. Mean IOP, (PD, and STT of T and UT eyes post-instillation of latanoprost in dogs during first 36 h

T: Treated; UT: Untreated.

should further elucidate the mechanism of latanoprost's effects on pupillary dynamics and explore its potential therapeutic applications beyond glaucoma management.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Science and Research Branch, Islamic Azad University, Tehran, Iran and adhered to the Association for Research in Vision and Ophthalmology (ARVO) statement guidelines for the ethical use of animals in ophthalmic and vision research.

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Authors' contributions

Conceptualization and supervision: Armin Shokoohimand; Methodology, project administration and writing the original draft: Armin Shokoohimand, and Farnoosh Arfaee; Data curation and software: Ehsan Khaksar; Validation: Farnoosh Arfaee, and Armin Shokoohimand; Formal analysis: Ahmad Asghari, and Ehsan Khaksar; Resources: Farnoosh Arfaee, and Ahmad Asghari; Visualization: Ahmad Asghari, and Ehsan Khaksar; Investigation, review and editing: All authors;

Conflict of interest

The authors declared no conflict of interest.

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