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Beyond pressure control: Periorbital impact of prostaglandins vs. laser trabeculoplasty

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ABSTRACT | Purpose: To assess the one-year impact of prostaglandin analog (travoprost) on periorbital appearance and lower eyelid horizontal tension, compared with the contralateral eye treated with Pascal selective laser trabeculoplasty. **Methods:** This nested case-control study was derived from a non-inferiority randomized clinical trial comparing Pascal selective laser trabeculoplasty efficacy with travoprost in fellow eyes over 12 months. One eye received daily travoprost, while the contralateral eye underwent Pascal selective laser trabeculoplasty. Lower eyelid horizontal tension was measured using a validated digital imaging method, and prostaglandin-associated periorbitopathy signs were graded by masked observers. Statistical analyses included generalized estimating equations and the Mann–Whitney *U* test for nonparametric data, with $p<0.05$ considered significant. **Results:** Ten patients met the inclusion criteria for this subanalysis. Travoprost-treated eyes had significantly lower mean lower eyelid distension compared with Pascal selective laser trabeculoplasty-treated eyes (4.32 mm vs. 5.02 mm; mean difference: 0.70 mm; $p<0.001$). Prostaglandin-associated periorbitopathy scores were significantly higher in the travoprost group, reflecting more pronounced changes in ptosis, periorbital hyperpigmentation, and eyelid retraction. **Conclusions:** Chronic use of prostaglandin analogs is associated with notable periorbital changes and increased lower eyelid tension, potentially affecting aesthetics and ocular function. Pascal selective laser trabeculoplasty may offer a safer profile for preserving periorbital anatomy while maintaining effective intraocular pressure control. Laser trabeculoplasty should be considered as an initial treatment when appropriate to minimize cosmetic and functional changes from chronic topical therapy.

Keywords: Prostaglandin analogs; Selective laser trabeculoplasty; Periorbitopathy; Eyelid tension; Glaucoma treatment

INTRODUCTION

Glaucoma comprises a group of diseases causing retinal ganglion cell loss, nerve fiber layer thinning, optic nerve excavation, and progressive visual field loss[1]. It is the leading cause of irreversible blindness worldwide, affecting millions of people. Global prevalence is projected to rise from 60 million in 2010 to 111.5 million by 2040 due to aging populations[2,3]. In Brazil, prevalence among adults over 40 years ranges from 2% to 3%, increasing with age[4].

Elevated intraocular pressure (IOP) is the main modifiable risk factor for glaucoma development and progression. Reducing baseline IOP by 30%–50% is associated with slower disease progression[5]. Prostaglandin F2α analogs (PGAs) are first-line pharmacologic treatments due to potent IOP-lowering effects and once-daily dosing. They enhance uveoscleral outflow, reducing IOP by approximately 25%–35% from baseline[6].

Selective laser trabeculoplasty (SLT) offers additional benefits, including independence from patient adherence, minimal invasiveness, and low complication rates[7–9]. Recent trials, such as SLT/Med and LiGHT, show SLT can achieve 20%–35% IOP reduction comparable with prostaglandins, with lasting effects and fewer side effects; 74% of patients remained medication-free for three years in the LiGHT trial[10].

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The datasets produced and/or analyzed in this study can be provided to referees upon request.

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Our group recently compared Pascal SLT (PSLT), a computer-guided variant of SLT, with travoprost for ocular hypertension (OH) and primary open-angle glaucoma (POAG). Both treatments demonstrated similar IOP reductions over 1 yr, supporting PSLT as a viable alternative (ahead of publication)[11].

Despite their effectiveness, chronic PGA use is associated with prostaglandin-associated periorbitopathy (PAP), including hyperpigmentation, eyelash changes, deepening of the upper eyelid sulcus, ptosis, horizontal tightening, palpebral fissure narrowing, and lower eyelid stiffness, potentially affecting aesthetics and ocular function[12–14].

This study aimed to evaluate the impact of 1-yr travoprost use on eyelid laxity and periorbital aesthetics and function, using a within-subject comparison with PSLT-treated eyes.

METHODS

This nested case-control study was derived from a non-inferiority randomized clinical trial assessing PSLT efficacy (ahead of publication). The study was approved by HCPA (CAAE: 44489320.7.0000.5327) and registered at ClinicalTrials.gov (NCT 05241938). The study adheres to STROBE guidelines[15].

Ten patients met the inclusion criteria. One eye received daily travoprost, and the contralateral eye underwent PSLT. After 1 yr, lower eyelid tension was measured via a validated digital imaging method, and PAP signs were graded by masked observers.

Eligible patients were adults with OH or mild POAG, enrolled from September 2021 to August 2023. Following a one-month washout, eyes were randomized to PSLT or travoprost for 12 months. Exclusion criteria included additional ocular treatments, early discontinuation of travoprost, need for treatment adjustments, or prior eyelid anomalies unrelated to PAP or strabismus (Figure 1). Informed consent was obtained from all participants. Research complied with the Declaration of Helsinki, CNS Resolution 466/2012, and the LGPD.

Lower eyelid tension was assessed using a validated digital technique[16]. Standardized photographs were taken with patients in primary gaze. Vertical traction was applied to the lower eyelids, and measurements were made using ImageJ 1.33µ software. Horizontal eyelid displacement represented eyelid tension (Figure 2).

PAP signs were independently graded by two examiners for hyperpigmentation, eyelash changes, eyelid alterations (ptosis or retraction), and conjunctival/scleral changes. Scores ranged from 0 (*no PAP*) to 4 (*all signs present*).

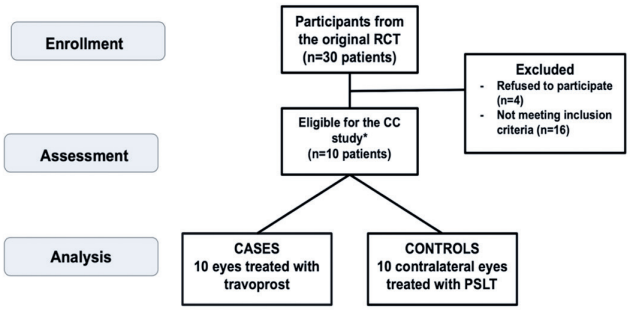

Figure 1. Flowchart of the study methodology.
Eligible for the case-control (CC) study: patients could not have received any additional or alternative treatments other than those assigned to their eyes in the randomized controlled trial (RCT–PSLT or travoprost).

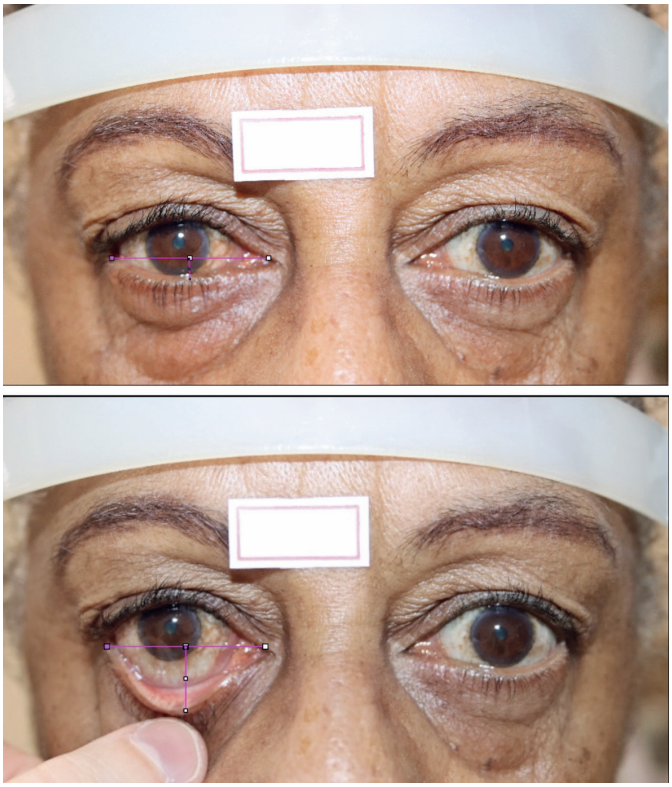

Figure 2. Measurement of lower eyelid tension. Distances were measured from the lowest point of the medial canthus to the lateral canthus in both neutral (top) and tension (bottom) positions. A straight line was then drawn from the midpoint of this baseline to the margin of the lower eyelid to determine eyelid tension (tape was used for scaling purposes). The difference between the two measurements represented lower eyelid displacement, indicating horizontal tension, and was compared between eyes.

Data were managed in REDCap and analyzed using SPSS 11.0 (IBM Corp., Armonk, New York). Categorical variables are presented as frequencies and percentages with 95% confidence intervals. Comparisons used generalized estimating equations for repeated measures and Mann–Whitney *U* tests for nonparametric data. Statistical significance was set at $p<0.05$.

RESULTS

Ten patients met the inclusion criteria for this case-control study. The mean age of participants was 60.2 ± 9 yr, with the majority being women (80%) and 40% identifying as White. Prior to the washout period, patients were using one or two hypotensive eye drops. Most were on beta-blockers (nine patients), while two were using prostaglandin analogs (Table 1).

Patients treated with travoprost exhibited a mean reduction of 0.70 mm in the amplitude of lower eyelid distension compared with eyes treated with PSLT. The average eyelid tension in travoprost-treated eyes was 4.32 mm, whereas laser-treated eyes showed an average tension of 5.02 mm. Statistical analysis revealed a significant difference between the two groups ($p<0.001$; Figure 3).

As expected, higher PAP scores were more frequently observed in travoprost-treated eyes than in laser-treated eyes. Score 0, corresponding to no PAP changes, was observed in only one eye in the travoprost group. Statistical analysis indicated that scores in eyes treated with eye drops were significantly higher than in eyes treated with PSLT ($p=0.005$, nonparametric Mann–Whitney *U* test, Figure 4). In two patients with prior bilateral PGA use, no signs of PAP were observed in the laser-treated eye after one year, while the travoprost-treated eye exhibited persistent periorbital changes. Travoprost-treated eyes could be identified in 70% of cases.

Table 1. Patient characteristics

Mean age (SD)	60.2 (9.0)
Gender (%)	
Female sex	8 (80)
Ethnicity (%)	
White	4 (40)
Black	4 (40)
Other	2 (20)
Systemic diseases (%)	
Hypertension	6 (60)
Diabetes mellitus	2 (20)
Previous use of eye drops, by patient (%)	
Beta-blockers	9 (90)
Prostaglandin analogs	2 (20)
Alpha-2-adrenergic agonists	1 (10)
Carbonic anhydrase inhibitor	0 (0)

SD= standard deviation.

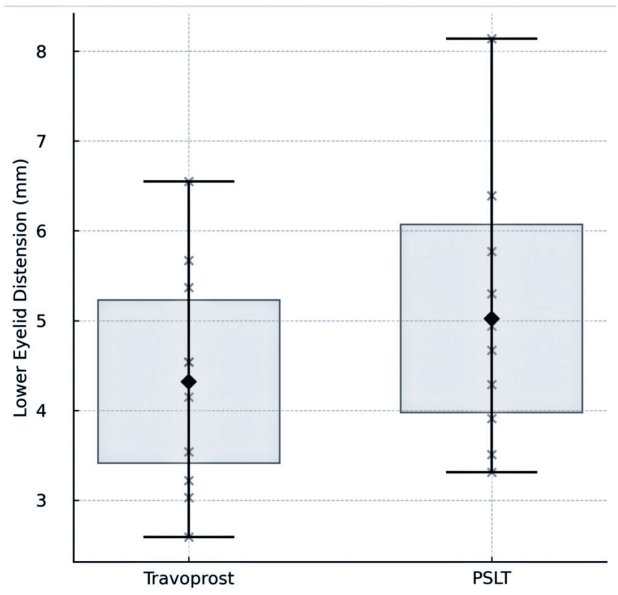

Figure 3. Comparison of lower eyelid distension between travoprost- and PSLT-treated eyes. Data are presented as mean±95% confidence interval, with min–max whiskers and individual data points.

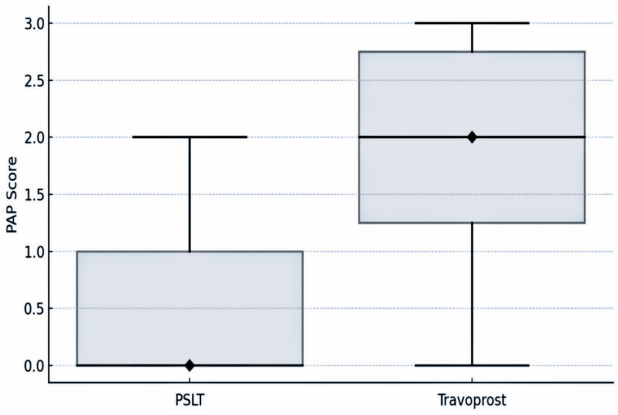

Figure 4. Comparison of PAP scores between eyes treated with selective laser trabeculoplasty (PSLT) and prostaglandin eye drops (travoprost). Scores were analyzed using the Mann–Whitney *U* test, demonstrating significantly higher scores in the eye drop group ($p=0.005$).

DISCUSSION

Since the early 2000s, the clinical spectrum of PAP has become increasingly well-defined. Initially described as a deepening of the upper eyelid sulcus, the syndrome is now recognized to include ptosis, dermatochalasis, orbital fat atrophy, hyperpigmentation, and eyelid tightness[17]. This historical perspective underscores the importance of monitoring the cosmetic and functional consequences of chronic PGA use.

Our study demonstrates that after just 1 yr of prostaglandin eye drop use, signs of PAP were readily noticeable, along with increased lower eyelid tension, compared with the contralateral eye treated with PSLT. This study contributes to the literature by objectively quantifying eyelid tension, an underexplored functional parameter in PAP assessment.

Increased lower eyelid tension may lead to ocular and aesthetic complications. Eyelid retraction can expose more of the sclera, altering appearance and potentially causing ocular surface exposure and dry eye symptoms due to increased tear evaporation. Impaired lacrimal drainage may result in epiphora. Aesthetic changes may create a fatigued or aged appearance, negatively affecting self-esteem. Furthermore, horizontal eyelid tightening can cause malposition and, in severe cases, affect intraocular pressure measurement[18].

Previous studies have highlighted the aesthetic and functional concerns associated with prolonged PGA use[12,19]. SLT, by contrast, is a safe and effective alternative for glaucoma management. Research shows that SLT not only lowers IOP effectively but also reduces the risk of adverse side effects compared with pharmacological therapy. SLT has also proven cost-effective, including within the Brazilian Unified Health System (SUS)[20,21], optimizing resources and improving outcomes. Consequently, many physicians and guidelines now consider SLT a viable first-line option for newly diagnosed open-angle glaucoma. It is important to note that PSLT should not be regarded as inherently protective; rather, it avoids prostaglandin exposure, which drives periorbital changes. Therefore, the observed differences are best understood as consequences of prostaglandin-related adverse effects rather than benefits of PSLT.

This study has several limitations. The small sample size, although sufficient for primary treatment comparison, prevented stratified analyses by age, sex, or prior prostaglandin exposure and may limit generalizability. Two participants had prior PGA use, potentially influencing baseline periorbital features. Nevertheless, the absence of PAP signs in the laser-treated eyes of these patients after 12 months supports the reversible nature of PGA-induced changes, consistent with reports of PAP regression following discontinuation. Complete masking was also impossible; although observers grading PAP were blinded, some clinical signs may have been recognized, introducing subtle bias. Additionally, despite using a validated method, eyelid tension assessment can be examiner-dependent and influenced by age, skin elasticity, sun exposure, and ethnicity, potentially affecting measurement consistency.

Understanding prostaglandin-associated side effects is essential in glaucoma management. Physicians should discuss risks and benefits with patients and consider SLT as a safer alternative. Regular monitoring of intraocular pressure and periorbital features is necessary to optimize ocular health and treatment outcomes. While controlling glaucoma progression is paramount, maintaining periorbital appearance and function can enhance self-esteem, comfort, and treatment adherence.

In conclusion, this study shows that within one year, chronic prostaglandin analog use can induce measurable functional and aesthetic changes consistent with PAP. Despite limitations in sample size and methodology, these findings provide new insights into the broader consequences of PGA therapy and highlight the importance of individualized glaucoma management that considers both visual prognosis and quality of life.

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AUTHORS' CONTRIBUTIONS

Significant Contribution to Conception and Design: Helena M Pakter, Fernando Procianoy. **Data Acquisition:** Leonardo Leivas, Rafaela C. Almeida, Marina M. Pakter, Marcelo V. Fabris, Helena M. Pakter. **Data Analysis and Interpretation:** Leonardo Leivas, Fernando Procianoy, Fábio Lavinsky, Helena M. Pakter.

Manuscript Drafting: Leonardo Leivas, Helena M. Pakter. **Significant Intellectual Content Revision of the Manuscript:** Fernando Procianoy, Rodrigo L. Lindenmayer, Fábio Lavinsky, Daniel Lavinsky, Helena M. Pakter. **Final Approval of the Submitted Manuscript:** Leonardo Leivas, Fernando Procianoy, Rafaela C. Almeida, Marina M. Pakter, Marcelo V. Fabris, Rodrigo L. Lindenmayer, Fábio Lavinsky, Daniel Lavinsky, Helena M. Pakter. **Statistical Analysis:** Helena M. Pakter. **Obtaining Funding:** Helena M. Pakter. **Supervision of Administrative, Technical, or Material Support:** Helena M. Pakter. **Research Group Leadership:** Helena M. Pakter.

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