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West Indies Glaucoma Laser Study (WIGLS) 3. Anterior Chamber Inflammation Following Selective Laser Trabeculoplasty in Afro-Caribbeans with Open-Angle Glaucoma

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Abstract

Purpose: To characterize the prevalence, severity, and duration of anterior chamber inflammation (cells and flare) following selective laser trabeculoplasty (SLT) in Afro-Caribbean eyes with primary open-angle glaucoma (POAG).

Methods: 144 eyes of 72 POAG patients underwent first-time 360-degree SLT treatment following washout of all topical medications in the prospective West Indies Glaucoma Laser Study. No anti-inflammatory therapy was used post-SLT. Anterior chamber cells and flare were characterized pre-SLT after medication washout, and 1 week, 6 weeks, and 3, 6, 9 and 12 months post-SLT using the standardized methodology described by the Society for Uveitis Nomenclature (SUN) in which cells and flare are each graded on a scale of 0–4+ using specific slit-lamp settings.

Results: Mean cell scores in both right and left eyes rose significantly ($p < 0.0001$) from baseline to Week 1 after SLT before returning to baseline values at all subsequent time points. Mean flare scores in right eyes ($p = 0.0185$) but not left eyes ($p = 0.1816$) rose from baseline to Week 1 after SLT before returning to baseline values at all subsequent time points. Cells appeared in 40.3% of eyes and flare appeared in 9.7% of eyes after SLT. One subject developed bilateral symptomatic anterior iritis one day postoperatively and reported a previously undisclosed history of recurrent iritis; the iritis resolved with topical steroid therapy.

Conclusion: SLT in Afro-Caribbean people with POAG is associated with mild, short-lived and self-limited anterior chamber inflammation. Routine anti-inflammatory therapy to suppress post-treatment inflammation after SLT is unnecessary in this population.

Precis

In the absence of prophylactic anti-inflammatory therapy, anterior chamber inflammation (characterized by cells and less commonly flare) is minimal and transient after selective laser trabeculoplasty in Afro-Caribbean glaucoma patients.

Keywords

selective laser trabeculoplasty; inflammation; glaucoma; West Indies

Introduction

Selective laser trabeculoplasty (SLT) effectively and safely lowers intraocular pressure in eyes with open-angle glaucoma (OAG) with a therapeutic effect comparable to prostaglandin monotherapy.^{1,2} Common side effects include transient anterior chamber inflammation occurring in an estimated 50–83% of treated eyes and transient IOP elevations occurring in an estimated 5–25% of eyes.³ Elevations of IOP are undesirable in glaucomatous eyes, and prophylactic pre-treatment with an IOP-lowering medication—commonly brimonidine 0.2%—effectively reduces the risk of IOP elevations after SLT.⁴ The clinical significance of—and the value of prophylactic treatment to prevent—transient low-grade anterior chamber inflammation is less clear. Several randomized trials have demonstrated no difference in anterior chamber inflammation, ocular discomfort, or IOP reduction in eyes undergoing SLT that did and did not receive perioperative anti-inflammatory therapy.^{5–7}

The prevalence of glaucoma and glaucoma-related blindness among black Africans and those of African descent is higher than in people of other ethnicities in other regions of the world.^{8,9} People of African descent are also at higher risk for postoperative inflammation and scarring following glaucoma surgery¹⁰ as well as keloid formation following surgical or traumatic skin incision.^{11,12} The natural history of anterior chamber inflammation following SLT in eyes of people of African descent has not been previously described.

The West Indies Glaucoma Laser Study (WIGLS) was a prospective evaluation of the efficacy and safety of monotherapy SLT in an Afro-Caribbean sample of subjects on the islands of Saint Lucia and Dominica. WIGLS sought to evaluate the role of SLT as monotherapy in reducing blindness from glaucoma in African-derived people. Primary outcomes at 12 months have been previously reported.^{13,14} At baseline and every post-SLT treatment visit, subjects in WIGLS underwent assessment of anterior chamber cell and flare using standardized methodology.¹⁵ Herein, we report the changes in anterior chamber cell and flare during the 12-month period following SLT in eyes of Afro-Caribbean patients with OAG.

Methods

This was a post hoc analysis of data collected in the prospective WIGLS study, which was funded by the National Eye Institute (R01 EY023620), registered on www.clinicaltrials.gov on March 2, 2015 (NCT02375009), and conducted in Saint Lucia and Dominica between March 9, 2015, and September 21, 2018. The study was conducted in accordance with the

tenets of the Declaration of Helsinki. The protocol was reviewed and approved by all appropriate ethics committees. Subjects provided informed consent to participate.

The study methodology has been reported previously.¹⁴ Briefly, a convenience sample of adult subjects with early or moderate open-angle glaucoma by ISGEO criteria¹⁶ was recruited from existing practices in Saint Lucia and Dominica. Key exclusion criteria included advanced glaucoma (cup-disc ratio greater than 0.9 or automated visual field loss within the central 10 degrees in either eye), previous laser or incisional glaucoma surgery, intraocular inflammation within the past 3 months, ocular trauma or surgery within the past 6 months, or IOP outside the range of 18–32 mmHg, inclusive, after washout of all IOP-lowering medications. Qualifying subjects were randomized to immediate versus 3-month or 6-month delay before 6-week washout of topical IOP-lowering therapy followed by SLT treatment using a stepped wedge design.¹⁷ After washout, baseline IOP was determined in two sessions 1–3 days apart, after which SLT was performed using the Lumenis Selecta II portable slit-lamp mounted laser system. Approximately 100 treatment spots were delivered to the full 360 degrees of trabecular meshwork in each eye. No prophylactic anti-inflammatory therapy was used. Post-treatment assessments occurred at 1 hour, 1 week (± 2 days), 1 month (± 5 days), 3 months (± 7 days), and every 3 months (± 7 days) thereafter. Repeat SLT could be performed based on prespecified criteria for failure of initial SLT (IOP above target IOP [target IOP = minimum 20% reduction from post-washout, pre-SLT IOP] on 2 consecutive visits).

Anterior chamber cell and flare were graded at every study visit using the methodology described by the Society for Uveitis Nomenclature Working Group.¹⁵ In a dimly-lit room, using the slit-lamp with a 1mm x 1mm spot size, its brightest light setting, and 16x magnification, the presence of anterior chamber cell was graded on a six-grade scale (Table 1) and flare on a five-grade scale (Table 2) by the principal investigator (TR) who was masked to prior readings after baseline assessment.

In this analysis, the mean cell and flare values at baseline and each visit through 12 months after initial SLT were determined and changes in cell and flare from baseline were evaluated separately in right and left eyes using paired t-tests. The sample size for this study was determined by the primary analysis; for this current analysis, a sample size of 50 eyes provides >93% power to detect a 0.25-unit change in mean cell/flare scores (which is one-half the difference between zero and the minimum detectable value for cell and one-quarter the difference between zero and the minimum detectable value for flare) assuming a standard deviation of 0.5 units and $\alpha = 0.05$. Analyses were performed using SAS v9.4, Cary, NC, and significance was set at $\alpha p < 0.05$.

Results

Overall, 144 eyes of 72 subjects underwent initial SLT. Demographic data and glaucoma-specific and SLT parameters of these subjects are given in Table 3.-SDC All subjects were Afro-Caribbean, most (59.7%) were women, and their mean age was 61.0 ± 11.4 years at the time of enrollment. SLT was delivered with an average of 0.8–0.9 mJ per treatment spot. During the first 12 months of post-SLT follow-up, 21 eyes of 15 subjects failed initial SLT

(and underwent repeat SLT) and 8 eyes of 6 subjects were censored (for loss to follow-up, cataract surgery, etc); these eyes contributed data to this analysis until the time of failure/censor.

At baseline, mean (standard deviation) cell scores were 0.02 (0.13) in right eyes and 0.00 (0.00) in left eyes (Table 4-SDC and Figure 1). By 1 week postoperatively, these values rose significantly to 0.29 (0.33) (a change of +0.27 [0.31]; $p<0.0001$) and 0.24 (0.31) (a change of +0.24 [0.31]; $p<0.0001$) in right and left eyes, respectively. By Week 6, cell scores were back to baseline values in both eyes and remained insignificantly changed from baseline through 12 months (range in right eyes 0.00–0.03, range in left eyes 0.00–0.01; all $p>0.05$). The incidence of anterior chamber cell appearance from baseline was 40.3% (58/144 eyes), with cells present in all 58 eyes at Week 1.

At baseline, mean (standard deviation) flare scores were 0.01 (0.12) in right eyes and 0.04 (0.35) in left eyes (Table 4-SDC and Figure 2). By 1 week postoperatively, these values rose significantly to 0.11 (0.32) (a change of +0.10 [0.34]; $p=0.0185$) and insignificantly to 0.13 (0.38) (a change of +0.09 [0.53]; $p=0.1816$) in right and left eyes, respectively. By Week 6, flare scores were back to baseline values in both eyes and remained insignificantly changed from baseline through 12 months (range in right eyes 0.00–0.03, range in left eyes 0.00–0.02; all $p>0.05$). The incidence of anterior chamber flare appearance from baseline was 9.7% (14/144 eyes), with flare present in all 14 eyes at Week 1.

Only one subject experienced acute symptomatic anterior uveitis following SLT. A 56-year-old man with no baseline cell or flare in either eye was randomized to immediate washout and SLT which was performed bilaterally without complications. On the first postoperative day, he presented with pain, redness, and photophobia in both eyes. Examination revealed 0.5+ cell and 1+ flare in both eyes. Prednisolone acetate 1% ophthalmic suspension was prescribed, at which point the subject proffered a bottle of prednisolone acetate from his pocket and reported that it had been prescribed for similar symptoms several months before study enrollment. Of note, the subject had denied any history of intraocular inflammation at screening, which would have rendered him ineligible for study participation. He was instructed to use the prednisolone acetate four times daily in each eye. At the 1-week safety assessment, his anterior chamber inflammation had resolved and the medication tapered without recurrence.

Discussion

Glaucoma is the second leading overall cause of blindness (behind cataract) and the leading cause of irreversible blindness throughout the world.¹⁸ The burden of glaucoma in Africa and in regions populated by people of African descent represents a significant public health crisis.⁹ Barriers to care in these resource-limited areas result in blindness rates higher than in more developed regions.^{19–21} Among these barriers is cost: for an intervention to be viable for widespread application in low-resource settings, it must be affordable.

SLT addresses many of the barriers to care, and the potential role of SLT in preventing glaucoma blindness in Africa has been described.²² SLT effectively and safely lowers IOP in

people of African descent^{13,23–25} and is cost-effective in low-resource settings.^{22,26} The incremental cost of SLT can be further reduced by minimizing or eliminating the need for routine post-treatment anti-inflammatory medications for prophylaxis of post-SLT inflammation if such treatment can be shown to be unnecessary. In three studies conducted in the developed world with primarily Caucasian subjects, such routine use of post-SLT anti-inflammatory therapy has been shown to be unnecessary from both safety and efficacy perspectives.^{5–7} Less is known regarding the need for post-SLT anti-inflammatory therapy in African-derived populations.

The current study characterizes the natural history of anterior chamber inflammation in Afro-Caribbean eyes undergoing SLT for OAG. In the WIGLS study population, both anterior chamber cell and flare scores peaked 1-week post-SLT and normalized by 6 weeks post-SLT with no anti-inflammatory therapy in the perioperative period. Only one of 72 subjects (1.4%) experienced acute symptomatic anterior uveitis, which resolved with topical steroid therapy, and this patient had an undisclosed history of uveitis that would have prevented his entry into the study had he reported it at screening. In a prior study of SLT in Saint Lucia in which no prophylactic anti-inflammatory therapy was utilized, only 1 of 61 subjects (1.6%) sought care for acute symptomatic uveitis post-SLT.²³ These results demonstrate that routine prophylactic anti-inflammatory therapy is unnecessary following SLT in this population.

The analysis and results presented in this paper are strengthened by several design features of the WIGLS protocol. The decision not to use prophylactic anti-inflammatory therapy in any subject permitted characterization of the natural history of anterior chamber inflammation following SLT in this population. Anterior chamber cell and flare were graded using a schema and examination methodology developed and described by the Society for Uveitis Nomenclature Working Group specifically to standardize the characterization of uveitis and its manifestations in clinical studies.¹⁵ Exam data were collected by an experienced clinician who was masked to all prior data after baseline. One limitation of the study is that the schedule of visits precludes more precise characterization of the time course to onset and resolution of anterior segment inflammation in these eyes. Also, the study was not powered specifically for this analysis; however, the sample size provided adequate power to constrain the risk of Type II errors to below 7% while holding the risk of Type I errors at 5% (as >50 eyes were available for analysis at each time point).

In summary, Afro-Caribbean subjects with OAG undergoing SLT without prophylactic anti-inflammatory therapy experience transient and clinically insignificant increases in anterior chamber cell and flare scores. The incidence of acute symptomatic anterior uveitis following SLT in this population is low (<2%). Routine prophylactic anti-inflammatory therapy after SLT is unnecessary in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Course of anterior segment cell scores through 12-months post-SLT in the West Indies Glaucoma Laser Study. Error bars are standard deviation. Mean cells scores for both right (RE) and left (LE) eyes rose significantly from baseline at Week 1 and returned to baseline levels at every time point thereafter.

Figure 2.

Course of anterior segment flare scores through 12-months post-SLT in the West Indies Glaucoma Laser Study. Error bars are standard deviation. Mean flare scores for right eyes (RE), but not left eyes (LE), rose significantly from baseline at Week 1 and returned to baseline levels at every time point thereafter.

Table 1.

Society for Uveitis Nomenclature Working Group grading scheme for anterior chamber cells.¹⁵

Grade	Cells per Field
0	<1
0.5+	1–5
1+	6–15
2+	16–25
3+	26–50
4+	>50

Table 2.

Society for Uveitis Nomenclature Working Group grading scheme for anterior chamber flare.¹⁵

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)