

RESEARCH ARTICLE



Pseudoexfoliation Glaucoma Selective Laser for Trabeculoplasty Treatment in Vietnam



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Abstract: Introduction: To evaluate the effectiveness of selective laser trabeculoplasty (SLT) in lowering intraocular pressure (IOP) in Vietnamese patients with pseudoexfoliation glaucoma (PXG).

Methods: This prospective, comparative study included a total of 64 eyes from PXG patients who had not previously received any antiglaucomatous medication. Patients were categorized into two groups: Group 1 consisted of 32 eyes treated with SLT as the initial therapy, while Group 2 comprised 32 eyes treated with Tafluprost 0.0015%.

Results: The baseline IOP before treatment ranged from 22 to 26 mmHg. There were no significant differences between the two groups in terms of mean cup/disc (C/D) ratio and retinal nerve fiber layer (RNFL) thickness. At the final visit, the mean percentage reduction of IOP was 26.73% in Group 1 and 27.15% in Group 2.

Discussion: SLT significantly reduced IOP in PXG patients, with outcomes comparable to Tafluprost. Treatment was more successful in eyes with higher trabecular pigmentation and early-stage glaucoma. Structural and functional parameters remained stable over 12 months. Side effects, including mild itchiness, IOP spikes, and anterior chamber reactions, were transient and manageable. No vision-threatening complications occurred, confirming SLT as a safe and effective first-line option for PXG in Vietnamese patients.

Conclusion: SLT can be effectively used as a primary treatment for PXG. In cases of recurrent IOP elevation, a second SLT procedure can be administered alone or in combination with other medications.

Keywords: Pseudoexfoliation glaucoma, intraocular pressure, selective laser trabeculoplasty, antiglaucomatous treatment, secondary open-angle glaucoma, antiglaucomatous medication, cup/disc, retinal nerve fiber layer.

1. INTRODUCTION

Pseudoexfoliation glaucoma (PXG) is the most common secondary open-angle glaucoma (SOAG) characterized by the deposition of a distinct fibrillar extracellular material and histological changes in various tissues, including the eye [1]. Immediate treatment for early open-angle glaucoma can delay the progression of the disease; this is the main reason that explains the importance of an early diagnosis. Today,

glaucoma treatments include eye drops, laser trabeculoplasty, conventional surgery, or a combination of any of these. Antiglaucoma medication (AGM) such as adrenergic agonists, adrenergic antagonists, carbonic anhydrase inhibitors, and cholinergic agents have shown limited efficacy in treating PXG, while surgical interventions carry a high risk of complications [2, 3]. Many treatments have been developed to control intraocular pressure (IOP) and prevent progressive damage to optic nerves in PXG patients [4].

Interestingly, PXG has been associated with single nucleotide polymorphisms (SNPs) in the lysyl oxidase-like 1 (LOXL1) gene on chromosome 15q24.1. Two of these SNPs

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confer a population attributable risk greater than 99% for PXG in the Nordic population, with different manifestations in different populations; the high-risk haplotypes, in fact vary between different populations [5]. The data confirm that LOXL1, whose function in connective tissue maintenance has been confirmed in mice, is one of the groups of enzymes involved in the cross-linking of collagen and elastin in the extracellular matrix. Other candidate genes linked to PXG are those involved in the regulation of lysosomal trafficking, clusterin, adenosine receptors, matrix metalloproteinase-1 (MMP1), and glutathione transferase. In addition, the SNP (G-308A of rs1800629) upstream of the TNF- α promoter site tends to almost permanently activate the expression of TNF- α . In particular, the GA and AA genotypes have been strongly observed with PXG in different cohorts [6-8].

A different cause may be of bacterial origin. *Helicobacter pylori* is a gram-negative spirochete with an estimated 58% colonization rate worldwide [9]. Though commonly associated with gastric diseases, it has also been found to be associated with open-angle glaucoma, due to inflammation, the release of pro-vasoactive factors, and dysfunction of the trabecular meshwork via oxidative stress. Interesting to know *Helicobacter pylori* rate in Vietnam is extremely high, with almost two-thirds of the population having positive serum antibody test results [9-11]. *Listeria monocytogenes* is a gram-positive bacillus commonly active in immunocompromised individuals, older adults, or neonates. Infections can also result in ocular listeriosis, a rare but severe condition manifesting with a dark hypopyon [12], endophthalmitis, elevated intraocular pressure, eye pain, and vision loss [13]. Even in this case, glaucoma in ocular listeriosis may result from inflammatory insults, iris necrosis, and pigment dispersion [12-14]. *Mycobacterium tuberculosis* and *Mycobacterium leprae* are aerobic, acid-fast, gram-positive rods; the former is sadly notorious for tuberculosis (TB), the latter, as an obligate intracellular parasite, is associated with Hansen's disease or leprosy. Although rare, both may be responsible for several ocular manifestations, particularly true in immunocompromised patients, such as patients with AIDS. Outcomes have shown that patients with TB may have elevated intraocular pressure, leading to the development of glaucoma. Glaucoma can occur from chronic anterior uveitis due to TB, including synechial angle closure and pupillary block [14, 15]. *Mycobacterium leprae* is also associated with secondary angle closure and glaucoma due to intraocular inflammation [16, 17].

In fact, prostaglandins are commonly used as the first-line treatment for PXG [17, 18]. However, they have certain drawbacks that hinder patient compliance, such as adverse drug effects, medical costs, or absent-mindedness in old patients. On the other hand, the selective laser trabeculoplasty (SLT) has been proven to be effective with open-angle glaucoma with better outcomes compared to prostaglandins [17, 18]. In PXG, SLT could be used as a first-line therapy in individuals or an alternative treatment along with medications [17]. SLT is useful for patients who have difficulty taking medication and does not affect future surgery results [18].

SLT is a procedure introduced by Latina and Park in the mid-1990s for the treatment of open-angle glaucoma [19]. The SLT consists of a frequency-doubled Q-switched laser with a wavelength of 532 nm and a pulse duration of 3 ns, which allowed targeting only the pigmented cells of the trabecular meshwork without touching other cells [17-19]. While reaching the target cells, several outcomes have shown that SLT is able to reduce intraocular pressure (IOP) between 11% and 40% in various types of glaucoma in the short- and medium-term period [20]. The exact mechanism by which SLT reduces IOP remains unclear. However, it is hypothesized that it induces the presence of essential factors that determine the first regulatory immune response, such as cytokine secretion, matrix metalloproteinase formation, increased cell division, repopulation of burn sites, and recruitment of type 2 macrophages, which are considered responsible for IOP reduction [20, 21].

Although in Vietnam, SLT has been applied in many more facilities to treat open-angle glaucoma, the efficacy and safety of SLT in Vietnamese patients with PXG is still uncertain without conclusive data. Therefore, the aim of this prospective study was to evaluate the efficacy and safety of SLT in lowering IOP in Vietnamese patients with PXG.

2. METHODS

2.1. Patient Selection

PXG patients were enrolled by clinical measurement that could be summarized as follows: fibrillar white flaky deposits on the anterior lens capsule or at the pupillary border in slit-lamp, angles were open on Goldmann 3-mirror gonioscopy (Schaffer's grade III and IV), combined with either a glaucomatous visual field defect or optic disc change.

The inclusion criteria applied were PXG diagnosis, no previous glaucoma treatment by medication, SLT, or surgery. Patients were excluded if there were any intraocular trauma or surgery, corneal scarring, identifiable other open-angle glaucoma, or allergic to prostaglandin drugs.

Treatment Target: The target IOP reduction represents the initial treatment goal for patients with pseudoexfoliation glaucoma, serving as a basis to evaluate the effectiveness of the treatment method and to guide further management toward individualized target IOP for each patient.

2.2. Study Design

This was a prospective, comparative clinical study. Data prospectively recorded for each patient included age, sex, medical history, family history, visual acuity, IOP, C/D ratio, visual field analysis, and retinal nerve fiber layer (RNFL) measurement by OCT. A detailed ophthalmological examination was performed before recruitment for treatment. A Goldmann applanation tonometry IOP assessment, slit-lamp examination, gonioscopy examination, and funduscopy evaluation of cup/disc ratio and pallor were performed.

Sampling Method: All patients included in the study had not received any prior topical or systemic treatment. Patients

were enrolled sequentially based on the order of inclusion in the study. According to the predefined rule, those assigned an odd number were placed in the medication group (Group 1), while those assigned an even number were placed in the SLT treatment group (Group 2).

Approval for the data collection and study analysis was granted by the local ethics committee, with the decision paper number 436/ĐHYD-HĐĐĐ granted by the Vietnam MOH. Informed consent was obtained from all of the patients before each procedure, and the study was conducted according to the tenets of the Declaration of Helsinki.

2.3. Procedure

2.3.1. Group 1: SLTs

The procedures were performed in the hospital glaucoma clinic by a single ophthalmologist. The patients were treated using an Ellex Tango SLT/YAG laser (Ellex, Adelaide, Australia), ND: YAG laser with a beam emission of 532 nm, a pulse duration of 3 ns, and a spot size of 400 μm . The Latina SLT Gonio laser lens (Ocular Instruments, Inc., Bellevue, WA, USA) was used to visualize the angle. Topical Tetracaine 1% was applied for anesthesia. The pigmented trabecular meshwork was targeted, and non-overlapping laser spots were placed in the entire 360° of the trabecular meshwork. The laser energy was initially set at 0.8 mJ with first spot at 12 o'clock and then adjusted in increments of 0.1 mJ until bubble champagne-like formation occurred. When a bubble champagne-like formation was seen, treatment was continued at this minimal energy level. The total number of pulses and the total amount of energy were recorded. After the procedure, the patients received non-steroidal anti-inflammatory medications for 5 days. If IOP increased ≥ 6 mmHg 1 hour post-op, topical Brinzolamide 1% was administered for 5-7 days; if patients experienced pain, Acetazolamide 0.25g q.i.d and Paracetamol 0.5g b.i.d were prescribed for 1-2 days followed by a re-examination on the next day; if the patients had anterior chamber (AC) reaction, topical Indomethacin 0.1% (Indocollyre, Bausch & Lomb) q.i.d to q.4.h was used depending on severity of inflammation.

2.3.2. Group 2: Prostaglandin Medication

The patients were instructed to use Tafluprost 0.0015% (Taflotan, Santen) qd at 8 p.m.

Target IOP $\geq 20\%$ lower than baseline and < 21 mmHg [13] for successful treatment. If the target IOP was not achieved, SLT procedure or Tafluprost 0.0015% qd or other glaucoma medications were provided.

Successful achievement was determined when the target IOP was achieved without using other medications.

2.4. Statistical Analysis

2.4.1. Statistical Tests Used in this Study

- Student's t-test was used to compare continuous quantitative variables.

- Mann-Whitney U test was used for comparing two continuous variables with non-normal distribution or unequal variances.
- Chi-square test or Fisher's Exact test was used to compare proportions.
- Kaplan-Meier curves and Log-rank test were used to compare the success rates between groups over time.
- Scatter plots were used to compare variables before and after treatment.

2.4.2. Sample Size Calculation

Formula for comparing two groups:

$$Z_{1-\alpha/2} - Z_{\beta} = \frac{P_1 - P_2}{\sqrt{\frac{P_1 * (1 - P_1)}{n_1} + \frac{P_2 * (1 - P_2)}{n_2}}}$$

Assuming equal sample sizes for both groups:

$$n = \frac{(Z_{1-\alpha/2} - Z_{\beta})^2 * (P_1 * (1 - P_1) + P_2 * (1 - P_2))}{(P_1 - P_2)}$$

Where,

- $Z_{1-\alpha/2} = 1.96$ for a two-side alpha of 0.05
- $Z_{\beta} = 0$ for 50% power
- P = expected proportion of success: 25.0% (based of Jin A.Song's 16.76% globally)
- $\Delta = P_1 - P_2 = 0.20$ (minimum clinically important difference)

Result: $n \approx 31.4 \rightarrow$ minimum required sample size per group: ≥ 32 eyes

Statistical significance was defined as $p \leq 0.05$.

3. RESULTS

The mean age of the patients was 64.9 ± 13.2 years (range: 34-86 years). The mean age was 69.1 ± 11.7 years in Group 1 and 62.9 ± 14.5 years in Group 2.

Follow-up for both groups were scheduled at 1 week and 1, 3, 6, and 12 months. During each follow-up visit, IOP was measured using a Goldmann applanation tonometer. The mean IOP change and mean percentage decrease in IOP from baseline to the last postoperative visit were calculated.

The mean $\pm$ SD baseline IOP for the entire study was 24.11 ± 0.97 mmHg (range 22-26 mmHg). In comparison, the mean baseline IOP was 24.19 ± 0.97 mmHg for group 1 and 24.03 ± 0.99 mmHg for group 2, which was not a significant difference. The final IOP measurement was 17.79 ± 0.72 mmHg for group 1, while for group 2 was 17.42 ± 0.58

mmHg. The mean percentage reduction of IOP at the last visit was 26.73% for group 1 and 27.15% for group 2.

Overall, the two groups had similar characteristics; however, baseline visual acuity in Group 1 was lower than in Group 2 ($p = 0.02$), a difference that may have resulted from cataract severity, with 62.5% of eyes in Group 1 having grade 3 and 4 cataracts, compared to only 37.5% in Group 2. The change in visual acuity after 12 months of treatment was considered the same in both groups ($p = 0.996$). Only mild changes were reported at 12 months postoperatively, with no significant differences between groups in IOP, C/D, RNFL, MD, PSD, or glaucoma staging at baseline and final visits.

In group 1, the success rate was related to the trabecular meshwork pigmentation. 7/8 failed cases had low pigmentation (1+ and 2+) while 17/24 successful cases had high pigmentation (3+ and 4+). Those differences in pigmentation were significant ($p = 0.01$).

Among the patients, there were 3 individuals (9.38%) who experienced pain after the SLT procedure. However, that feeling prolonged for only 1-3h. 3 cases had IOP elevation (30-32 mmHg) 1h post-op. Additionally, those 3 cases responded well to treatment with topical Brinzolamide 1% q.i.d, and their IOP returned to normal after 1 day. Furthermore, post SLT, 11 eyes had anterior chamber reaction, including mild, moderate, and severe inflammation with 6, 3, and 2 cases, respectively. All those cases that had inflammation were controlled after using topical Indomethacin 0.1% for 3-5 days.

4. DISCUSSION

The results of this study indicated that SLT effectively decreased IOP as a primary treatment in patients with PXG. The mean $\pm$ SD baseline IOP was $24,19 \pm 0,97$ mmHg for group 1 and $24,03 \pm 0,99$ mmHg for group 2, and the final IOP measurement was $17,79 \pm 0,72$ mmHg and $17,42 \pm 0,58$ mmHg, respectively. No significant differences were observed between the 2 groups in the average decrease in IOP (Table 1). Generally, the characteristics of patients of both groups were quite similar. Although the baseline visual acuity of group 1 was lower than group 2 ($p = 0.02$), the difference might be associated with the severity of cataract, with 62.5% of eyes in group 1 had cataract grade 3 and 4, while the number was only 37.5% in group 2 (Table 2). Nevertheless, the changes of visual acuity after 12 months of treatment in both groups showed a slightly better performance of the SLT group with no statistical significance ($p = 0.996$) (Figs. 1-3). There were slight changes in C/D, RNFL, MD, and PSD in the mean numbers of both groups at 12 months post-op. Comparing between 2 groups, no significant differences were observed in IOP, C/D, RNFL, MD, PSD, or staging of glaucoma among patients at the baseline and final visit (Tables 3-7).

SLT may be effective in PXG, since the main reason for increased intraocular pressure in PXG is due to trabecular meshwork pigmentation [20, 21], and melanin has been shown to have a strong absorption rate with laser procedure [20, 21]. In our study, the mean IOP either during or at the end of the research was significantly lower than the baseline (Table 2). This result was shown to be in line with other studies. For instance, Shazly et al [22] found that in 18 PXG patients treated with SLT as primary treatment on 180° trabecular meshwork, the mean IOP was 20.4 ± 4.2 mmHg at 12 months post-op and decreased to 18.3 ± 4.7 mmHg after 30-40 months post-op. The success rate was also 77% similar to our study (around 75%) at the 12-month post-op. These results were also comparable to a study of other studies on 48 primary open angle glaucoma and 37 PXG patients using SLT as a complementary treatment, which had 6.1 ± 3.6 mmHg in IOP reduction and succeeded in 78.4% patients. However, this is inconsistent with several studies which reported a decrease of 4.7 ± 9.3 mmHg, 3.84 ± 4.59 mmHg in IOP with reduction rate 16% and 16.76% at 12 months follow up, respectively [22-24]. These variations can be attributed to differences in the study methodology; our study used SLT as primary treatment, while patients in those studies had used a different treatment prior to the use of SLT. More, in our study, SLT was used on 360° trabecular meshwork in line with different studies, while in those studies SLT was performed on 180° trabecular meshwork.

Although several outcomes suggested that there were no differences in the effectiveness of SLT either on 180° or 360° of trabecular meshwork in open angle glaucoma [25-27], Shibata et al. [28] found that the SLT 360° yielded better results in IOP reduction than the SLT 180°. Meanwhile, in PXG patients, there was no research comparing the effectiveness of these 2 approaches. This aspect should be investigated furtherly to get better information for choosing the appropriate SLT procedure. Overall, in comparison with Tafluprost (group 2), SLT showed the same effect on lowering IOP and decreasing the advance of PXG (Fig. 4).

There were deliberate progresses in C/D, RNFL, MD, and PSD mean numbers of both groups at 12 months post-op. In terms of C/D, the rates were 0.76 for group 1 and 0.77 for group 2, which slightly increased to 0.77 and 0.78, respectively, at the final visit. Regarding RNFL depth, our study found a decrease of $3.03 \mu\text{m}$ in Group 1 and $-1,57 \mu\text{m}$ in Group 2. These numbers were within the allowable limit from 6.4 to $8 \mu\text{m}$ [29, 30]. In relation to RNFL, mean MD reductions of both Groups in our study were $-0,221 \pm 0,12$ and $-0,224 \pm 0,33$ dB lower than 0.5 dB, which was determined as slow progress of glaucoma [24]. The visual acuity at the beginning of the study was significantly lower in group 1 compared to group 2. This could be attributed to the cataract condition, as in group 1, 62.5% had grade 3 and higher cataract, while that was only 32.5% in group 2. The decrease of visual acuity by the time may also involve in cataract progress. Comparing the 2 groups, the decrease was not statistically significant ($p = 0.996$).

Table 1. Characteristics of patients.

Characteristics of Patients	Group 1	Group 2	p-value
Age	69.09 ± 11.67	62.88 ± 14.47	0.113
Visual acuity	-	-	-
Pre-op	0.264 ± 0.14	0.165 ± 0.08	0.02
Change	-0,0183 ± 0,037	-0,0182 ± 0,035	0,996
IOP			
Pre-op	24,19 ± 0,97	24,03 ± 0,99	0.522
Post-op	17,79 ± 0,72	17,42 ± 0,58	0.059
C/D			
Pre-op	0.76 ± 0.1	0.77 ± 0.11	1.0
Post-op	0.77 ± 0.1	0,78 ± 0,11	0.908
Cataract			
Grade 0	2 (6.2%)	2 (6.2%)	0.164
Grade 1 & 2	25 (31.2%)	18 (56.3%)	
Grade 3 & 4	20 (62.5%)	12 (37.5%)	
Trabecular Meshwork Pigmentation			
1+	2 (6.2%)	0	0.433
2+	12 (37.5%)	11 (34.4%)	
3+	16 (50%)	17 (53.1%)	
4+	2 (6.2%)	4 (12.5%)	
RNFL (Micrometre)			
Pre-op	70 ± 10.42	68.41 ± 8.49	0.472
Post-op	66.97 ± 10.64	66.84 ± 8.82	0.634
MD*			
Pre-op	-11.09 ± 2.77	-10.86 ± 3.27	0.778
Change	-0,221 ± 0,12	-0,224 ± 0,33	0.634
PSD**			
Pre-op	6.49 ± 2.70	5.55 ± 2.03	0.294
Post-op	6.87 ± 2.72	5.77 ± 2.00	0.144
Staging***			
Mild	17 (53,1%)	16 (50%)	1.0
Moderate	15 (46.9%)	16 (50%)	

Notes: *MD: mean deviation; **PSD: pattern standard deviation

***Staging of PXG following Hodapp, Parish, and Anderson classification system [10]

Table 2. IOP changes in both groups following time.

Followed up Time	SLT (Group 1)	Tafluprost (Group 2)	P-value
1 week	5.63 ± 1.56 (23.21%, n=32)	7.03 ± 1.44 (29.13%, n=32)	<0.001
1 month	6.72 ± 1.17 (27.67%, n=32)	7.12 ± 1.2 (29.52%, n=32)	0.271
3 months	6.88 ± 1.21 (27.67%, n=32)	7.06 ± 1.38 (29.25%, n=32)	0.724
6 months	6.87 ± 1.11 (28.32%, n=31)	7.22 ± 1.41 (28.70%, n=32)	0.923
9 months	6.81 ± 3.33 (27.97%, n=27)	6.78 ± 1.28 (28.14%, n=28)	0.8
12 months	6.42 ± 1.28 (26.73%, n=24)	6.54 ± 1.24 (27.15%, n=26)	0.56

Note: After one week of treatment, Group 2 had a significantly higher mean reduction in intraocular pressure (7.03 ± 1.44 mmHg) than Group 1 (5.63 ± 1.56 mmHg) ($p < 0.001$), which then remained almost unchanged during subsequent visits, presenting a substantially equal reduction in intraocular pressure.

Table 3. Target IOP success of both groups.

Followed up time	Group 1	Group 2	p-value
6 months	31 (96.9%)	32 (100%)	0.313
9 months	27 (84.4%)	28 (87.5%)	0.719
12 months	24 (75%)	26 (81.2%)	0.545

Note: Although the success of group 1 was lower than that of group 2 at 6, 9 and 12 months the results were not statistically significant ($p=0.313, 0.719, 0.545$).

Table 4. Target IOP success with SLT in different levels of trabecular pigmentation.

Gonioscopy		Group 1		P - value
		Success	Failure	
Pigmentation grading	1+	0	2	0.01
	2+	7	5	
	3+	15	1	
	4+	2	0	
	Total	24	8	

Table 5. Target IOP success with SLT by glaucoma stage.

Staging	Group 1	
	Success	Failure
Mild	16 (94.1%)	1 (6.7%)
Moderate	8 (53.3%)	7 (46.7%)
Total	24	8

Note: The mild stage had higher success rate than the moderate. The difference was significant.

Table 6. Complications and side effects in both groups.

Characteristics		Group 1	Group 2
Pain, Irritation, Itchy		3 (9.38%)	8 (25%)
Prolonged hyperemia		-	7 (21.9%)
IOP elevation 1h post-op		3 (9.38%)	-
Anterior chamber reaction	Mild	6 (18.75%)	-
	Moderate	3 (9.38%)	-
	Severe	2 (6.25%)	-
	Total	11 (34.38%)	-

Table 7. Different features in both groups based on SLT and Tafluprost.

Characteristic	SLT (n=32)	Tafluprost (n=32)	p-value
Age distribution <40 yrs	2 (6.3%)	2 (6.3%)	0.161**
40-<50 yrs	1 (3.1%)	3 (9.4%)	-
50-<60 yrs	3 (9.4%)	10 (31.3%)	-
60-<70 yrs	14 (43.8%)	7 (21.9%)	-
70-<80 yrs	5 (15.6%)	3 (9.4%)	-
≥80 yrs	7 (21.9%)	7 (21.9%)	-
Mean Age	69.09 ± 11.67	62.88 ± 14.47	0.113*
Baseline Visual Acuity (logMAR)	0.264 ± 0.14	0.165 ± 0.08	0.02*
Mean IOP (mmHg)	24.19 ± 0.97	24.03 ± 0.99	0.522*
Average C/D Ratio	0.763 ± 0.1	0.772 ± 0.108	1.0*
Lens Opacities			
- None	2 (6.2%)	2 (6.2%)	-
- Grade 1	1 (3.1%)	4 (12.5%)	-
- Grade 2	9 (28.1%)	14 (43.8%)	-
- Grade 3	16 (50.0%)	7 (21.9%)	-
- Grade 4	4 (12.5%)	5 (15.6%)	0.164**
Angle Pigmentation			
- 1+	2 (6.2%)	0	-
- 2+	12 (37.5%)	11 (34.4%)	0.433+
- 3+	16 (50.0%)	17 (53.1%)	-
- 4+	2 (6.2%)	4 (12.5%)	-
Average RNFL Thickness (μm)	70 ± 10.42	68.41 ± 8.49	0.472*

Table 7 contd.

Characteristic	SLT (n=32)	Tafluprost (n=32)	p-value
Mean Deviation (MD)	-11.09 ± 2.77	-10.86 ± 3.27	0.778*
Pattern Standard Deviation (PSD)	6.49 ± 2.70	5.55 ± 2.03	0.294*
Visual Field Stage			
- Mild	17 (53.1%)	16 (50%)	-
- Moderate	15 (46.9%)	16 (50%)	1.0*

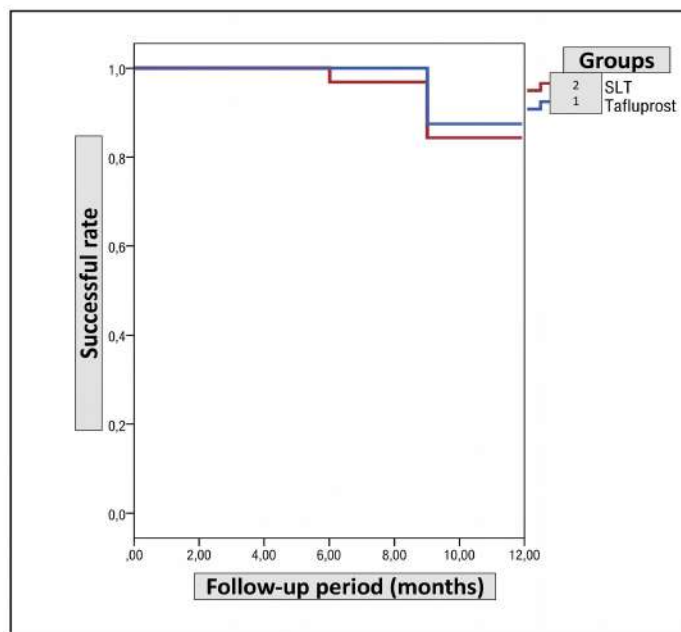


Fig. (1). Kaplan-Meier curve: Used to compare cumulative success probability over time (in months) between groups. Results showed that SLT performed better over time. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

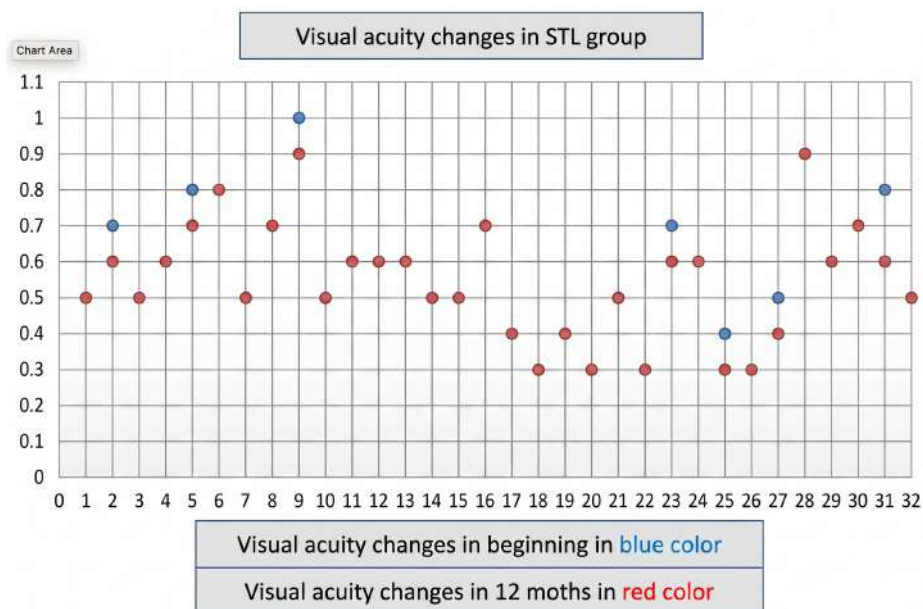


Fig. (2). Visual acuity in SLT group from beginning (red spots) up-to 12 months (blue spots). (A higher resolution / colour version of this figure is available in the electronic copy of the article).

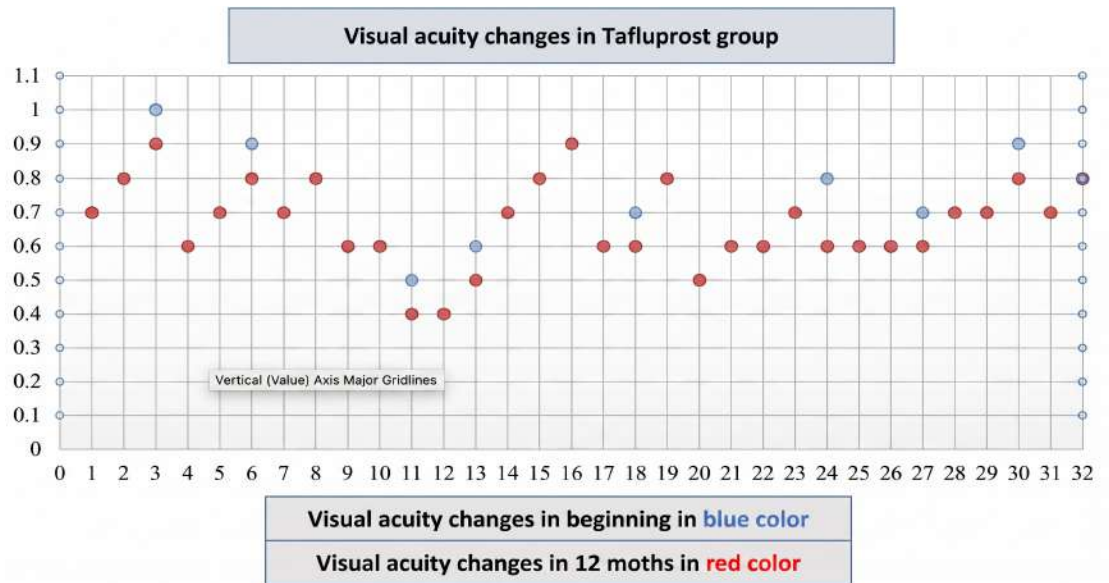


Fig. (3). Visual acuity in Tafluprost group from beginning (red spots) up-to 12 months (blue spots). (A higher resolution / colour version of this figure is available in the electronic copy of the article).

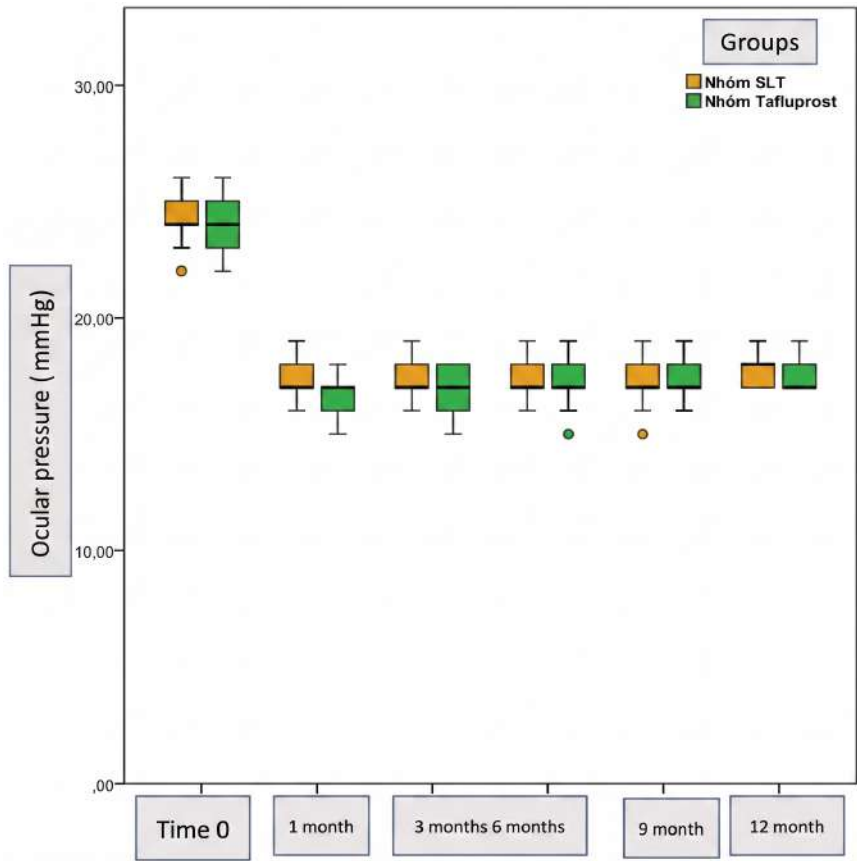


Fig. (4). Comparing the mean intraocular pressure of successful cases between the two groups at different time points. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

Therefore, once the effect of SLT was analyzed, it was found that the success of the procedure was influenced by the level of trabecular pigmentation and the glaucoma staging. In fact, several studies suggested SLT may be more effective in high trabecular pigmentation eyes [29, 30]. Results that are consistent with the outcomes obtained in our study, we observed 70.8% success cases in grade 3+ and 4+ pigmentation eyes while the rate was only 25% in grade 1+ and 2+. In this case, the difference was statistically significant ($p < 0.001$). However, due to the lack of information on the level of trabecular pigmentation in other studies [31], we were unable to give a real conclusion on the possible causes for these differences. Nevertheless, our study found that the mild case had a higher success rate (94.1%) than the moderate ones (53.3%) at the final visit, suggesting the importance of initiating SLT earlier in the mild stage after PXG diagnosis to maximize its treatment effectiveness.

The SLT laser selectively treats specific cells, leaving the untreated portions untouched. This allows for increased drainage of aqueous fluid from the eye, lowering the pressure within the eye. Additionally, SLT is generally a painless procedure or causes only mild discomfort. Latina *et al.* [19] reported that only 5% patients had redness and pain post-SLT, while Kara *et al.* [31, 32] observed that 27% of PXG patients felt itchy after the procedure. In this study, we observed that 9.36% patients reported itchiness, though that feeling just lasted for 1-3 hours. IOP elevation post-SLT was defined as an increase ≥ 6 mmHg one hour after the procedure [33]. Goldenfeld *et al.* [34] and Damji *et al.* [35] found that 3.5 - 4.5% of open angle glaucoma patients had IOP elevation post-op, whereas the number increased to 27 - 28% in PXG patients, as studies by Shazly *et al.* [22] and Kara *et al.* [31]. However, our study found that only 3 cases (9.38%) had this complication, lower than previous studies. Additionally, anterior chamber reaction may generally occur 2-3 days after the SLT procedure. However, this condition regularly resolves after 5 days [36]. Latina *et al.* reported 86% glaucoma patients experienced this complication, while Kara *et al.* observed in just 24.3% of PXG patients, indicating significant variation [19, 31]. On the other hand, our study showed that 34.38% of patients had this complication, which was something in between the two studies. Nevertheless, we observed that the reaction lasted only for 3-5 days and responded well to topical anti-inflammatory medicine. In group 2, 25% of patients experienced itchiness and irritation, and 21.9% had prolonged hyperemia. These side effects were similar to Kuwayama *et al.* [25], who found rates of 20.4% and 26.5% respectively. Besides, these side effects were mild and did not affect the vision of patients. Demonstrating the safety of Tafluprost 0.0015% in the treatment of PXG. SLT was found to be a safe treatment option for Vietnamese PXG patients. The complications and side effects were in line with other studies, and no vision-related complications were eventually found.

All patients included in the study were evaluated for IOP reduction and changes in visual fields and OCT findings. Cataract status was not a primary focus. While pseudoexfoliation syndrome (PEX) is not a new disease in Vietnam, our

study aims to demonstrate the efficacy of SLT in this condition, using Prostaglandin analogues (a first-line treatment group) as the control. The novelty of this study lies in its investigation of SLT effectiveness for PEX in Vietnamese patients. In both groups, degenerative changes were observed in varying degrees. Intracellular and extracellular edema, multilayering, apoptosis, and destroyed cells adjacent to normal cells were described. Although the origin of pseudoexfoliative material has been associated with dysregulation in the process of elastin synthesis, the formation of abnormal aggregates of elastic fibers, accompanied by a significant reduction in collagen fibers, all typical signs of the aging process, in the end, age, sex, and cataract have been shown to be not statistically significant [37-39]. Indeed, degenerative changes and PEX material have been observed, linked to a dysregulated and inflamed microenvironment. Analysis of the aqueous humor (AH) of the eyes of affected patients confirmed the presence of inflammatory factors such as transforming growth factor beta-1 (TGF- β 1), pro-inflammatory cytokines (IL-6, IL-10, IL-1 β , TNF- α), and oxidative stress (ROS) [40]. TGF- β , IL-6, IL-10, IL-1 β , TNF- α , and ROS play a fundamental role in health and disease, and their interaction in inflammation and progression of cellular and tissue degeneration is also well known. The mutual collaboration of these factors is highly complex and, due to their differential roles in degenerative progression, great care should be taken when considering combinatorial targeting in PXG therapies [40-43].

Additionally, several researchers have studied the association of several pathogens as inflammatory promoters of these interleukins and cytokines, raise with susceptibility to PXG, SOAG, and pseudoexfoliation syndrome [13-16, 44]. The results showed that a possible pathogen infestation linked to polymorphism presence may be predictive of PXG pathogenesis, suggesting that this condition could be detected early in the disease if at-risk individuals with specific bacteria, viruses, and interleukin and cytokine genotypes are identified. Interestingly, 26 out of 32 patients (82%) equally distributed between males and females, were affected by *Helicobacter pylori* (data not shown). The hypothesis of the correlation between *Helicobacter pylori* infection and glaucoma originates from the fact that the bacterium causes the release of various pro-inflammatory and vasoactive substances, inducing increased activation and platelet aggregation induced by arteriosclerosis and an impact on the apoptotic process of trabecular meshwork cells. The condition is associated with a cross-immune reactivity between anti-*Helicobacter pylori* antibodies and ciliary epithelium [45]. Therefore, a greater understanding of the role of several SNPs and possible pathogen infection in PXG disorder could open the door to future treatments [13-16, 42, 43].

CONCLUSION

There are many studies that aim to identify the precise origin of PXG, methods to diagnose and treat PXG, and the systemic traits of PXG. As a result, a significant number of discoveries are currently being made public, especially in the field of molecular genetics and regenerative medicine. We are well aware of the practical and theoretical limita-

tions of this study, the small cohort, and the lack of more distinctive assessments regarding SNPs and the role of pathogens in PXG. These will be the topics of the next study to be published soon. We are learning more and more, although the answer to the most important question, how this condition is generated, remains something not completely clear. It is likely that a combination of factors, such as age, environmental insults (bacterial, viral, or fungal infestations, even far from the eye site), inflammatory patterns, with genetic changes, triggers the whole mechanism, which requires further studies to clarify the cause of PXG and the therapeutic possibilities for this condition. Nevertheless, SLT can be used effectively as a primary therapy for the treatment of PXG, and it is advisable to consider performing SLT earlier, at a mild stage of glaucoma, to achieve better results.

AUTHORS' CONTRIBUTIONS

The authors confirm their contribution to the paper as follows: study conception and design: TDK, TTK, TLM; investigation: ATC, GDP, LS; visualization: KCN; draft manuscript: CGI. All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

PGX	=	Pseudoexfoliation glaucoma
IOP	=	Intraocular Pressure
SLT	=	Selective Laser Trabeculoplasty
SOAG	=	Secondary Open-Angle Glaucoma
AGM	=	Antiglaucomatous Medication
C/D	=	Cup/Disc
RNFL	=	Retinal Nerve Fiber Layer
Hp	=	<i>Helicobacter pylori</i>
SNPs	=	Single Nucleotide Polymorphisms
LOXL1	=	Lysyl Oxidase-Like 1
MoU	=	Ministry of Health

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval for the data collection and study analysis was granted by the local ethics committee, with the decision paper number 436/ĐHYD-HĐĐĐ granted by the Vietnam MOH.

HUMAN AND ANIMAL RIGHTS

All procedures performed in studies involving human participants were followed in accordance with the ethical standards of institutional and/or research committee and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from all of the patients before each procedure.

AVAILABILITY OF DATA AND MATERIAL

All data generated or analyzed during this study are included in this published article.

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CONFLICT OF INTEREST

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