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Selective laser trabeculoplasty in primary open-angle glaucoma: Primary versus secondary treatment outcomes

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Objective: To compare the outcomes of selective laser trabeculoplasty (SLT) on treatment-naive, primary open-angle glaucoma (POAG) patients with those of SLT on patients previously treated medically and/or surgically. Secondary objectives: To establish whether age, race or gender influenced SLT outcomes.

Design: A retrospective chart review of patients who received SLT therapy for POAG between June 2011 and January 2015.

Subjects: Group A: Treatment-naive patients (n = 15). Group B: Prior medical therapy and/or prior surgery (n = 69).

Methods: Group A: Patients were treated with SLT therapy as first line, with medical treatment added as needed. Group B: Patients were treated with SLT therapy as additional therapy to medication and/or surgery. All patients were followed up for at least 1 year.

Main outcome measures: A reduction in intraocular pressure (IOP) of at least 20% from baseline was considered significant.

Results: The following percentage reduction in IOP was found in the different groups: Group A 50.7%, Group B 32.0%, Africans 52.2%, Indians 29.8% and Caucasians 28.87%.

Conclusion: In our study patients, SLT achieved significant reductions in IOPs in treatment-naive as well as previously surgically and medically treated eyes with POAG. Statistically significant higher reductions in IOP at 1 year after SLT was seen in treatment-naive eyes, patients older than 70 years when compared with younger patients, female patients (54%) when compared with male patients (30%) and in patients of African (52%) descent compared with Caucasians (30%).

Introduction

There is no simple answer to how to treat primary open-angle glaucoma (POAG). To date, the only proven modality to slow down the disease progression is to lower the intraocular pressure (IOP). Various treatment options exist, ranging from medication to laser treatments and surgical intervention.

This study was conducted to determine if there is a difference in the outcomes of selective laser trabeculoplasty (SLT) therapy in treatment-naive POAG patients compared with those who have had prior medical or surgical therapy. The study also looked at the possible influence of age, ethnicity and gender on the outcomes of SLT. Could SLT therapy be considered a first-line therapy for POAG[1,2,3,4] or should its main role be as a supportive treatment to medical and surgical therapy? What is the survival time of SLT treatment?[5,6]

In order to stop progression of glaucomatous nerve fibre loss, a target IOP should be set before commencing treatment.[1,7] This is generally accepted as a reduction in IOP of 20% from baseline. This figure is only a guideline. The target IOP should be tailored to each patient according to merit and should be adjusted if progression still occurs despite reaching the previous target IOP.

The European Glaucoma Society (EGS) has shown that first-line SLT is effective in 85% of cases. They reported a drop in IOP of 6 mmHg – 9 mmHg.[1] The effect was also shown to last 5 years in 50% – 60% of patients.[3]

Previous cataract surgery does seem to reduce the effect of primary SLT therapy, with a reduced drop in IOP, but levels are comparable in the long term.[8]

SLT has proven its safety and repeatability as seen in the EGS guidelines,[1] building on the research done by the Glaucoma Laser Trial[9] that looked at argon laser trabeculoplasty (ALT). ALT cannot be safely repeated as it causes local destruction of tissue, whereas SLT causes remodelling of the trabecular meshwork.[10]

Research methods and design

The study was conducted as a retrospective chart review of patients who received SLT therapy for POAG over a 5-year period, spanning from 2011 to 2015, at St Aidan's Regional Mission Hospital, Durban, South Africa.

Aims

In this study, we set out to prove the IOP-lowering effect of SLT in South African patients with POAG of the eye. By doing so, we could potentially reduce the need for medical and surgical intervention. Could SLT become the standard primary treatment in POAG?

Specific objectives

The objectives are:

- To determine the outcome of SLT on treatment-naive POAG patients (Group A).
- To determine the outcome of SLT on POAG patients previously receiving topical and/or systemic IOP-lowering agents and/or previously operated upon (Group B).
- To determine, using multiple regression analysis, if SLT outcomes are influenced by ethnicity, gender, age or previous glaucoma treatment.

IOP, medication and surgical interventions were noted at 1, 3, 6 and 12 months after SLT therapy.

Informed consent was not obtained from patients included in this study, as it was a retrospective chart review. Institutional Review Board and Ethics committee approval was obtained from the University of KwaZulu-Natal Biomedical Research Ethics Committee. The described research adhered to the Declaration of Helsinki.

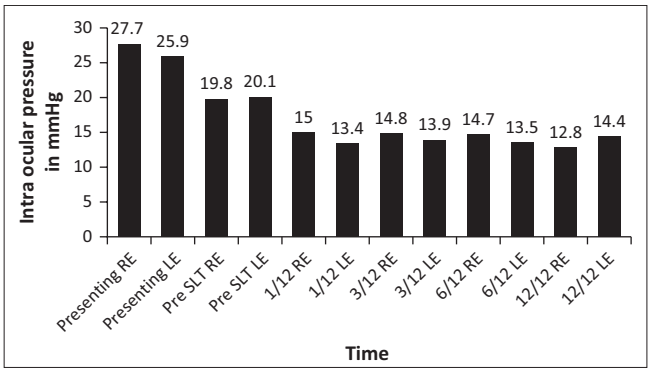
Data were entered into SPSS version 21 (Statistical Packages for the Social Sciences) for analysis. Statistical significance was considered as $p < 0.05$. A descriptive statistical analysis of the data (means, standard deviations, ranges, frequencies and percentages) was conducted before inferential statistics were done. A one-sample *t*-test was used to assess the differences in IOP. Multiple regression analyses were used to ascertain if race, age, gender or previous glaucoma treatment were indicators of glaucoma outcomes. Eighty-four patients (148 eyes) were enrolled in the trial (see Tables 1 and 2 for patient demographic details).

TABLE 1: Age and gender distribution.

Age group	Gender		Total
	Male	Female	
30–39	5	1	6
40–49	4	7	11
50–59	13	13	26
60–69	13	9	22
70–79	6	11	17
80–89	0	2	2
Total	**41**	**43**	**84**

TABLE 2: Ethnic make-up of study sample.

Patient demographic	Group A	Group B
African	11	49
Indian	4	17
Caucasian	0	3
Male	6	35
Female	9	34



RE, Right eye; LE, Left eye; SLT, selective laser trabeculoplasty.

FIGURE 1: Combined chart of mean intraocular pressure over 1 year.

Results

A total of 148 eyes of 84 patients were evaluated. Group A consisted of 29 eyes, while Group B had 119 eyes. A greater than 20% reduction in IOP was achieved in 71% of eyes at month 1, 79% at month 3, 76% at month 6 and 81% at 1 year.

The mean pre SLT IOP was 19.95 mmHg, reducing to a mean IOP at 1 month of 14.2 mmHg (29% reduction), 14.35 mmHg at 3 months (33% reduction), 14.1 mmHg at 6 months (29% reduction) and 13.6 mmHg at 1 year (32% reduction). This result compares favourably to a reduction of 24.3% at 1 year, found by Weinand et al.[5]

The mean reduction in IOP exceeded the required 20% stipulated in the study protocol (Figure 1).

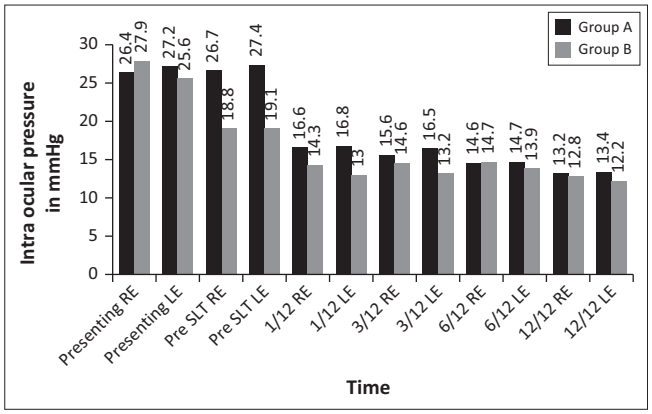
In Group A, the mean pre SLT IOP was 27.07 mmHg; it was 16.76 mmHg at 1 month after SLT, 16.09 mmHg at 3 months, 14.72 mmHg at 6 months and 13.33 mmHg at 1 year. There was a 51% reduction in mean IOP from the baseline value.

The percentage of patients who reduced their IOP by more than 20% was 68% at 1 month, 91% at 3 months, 89% at 6 months and 95% at 1 year (see Table 3 and Figure 2). There was a significantly reduced need for medical therapy in

TABLE 3: Mean intraocular pressure drop Group A versus Group B.

Group ($p < 0.001$)	Time	Mean IOP (mmHg)	Mean IOP reduction	Reduction from baseline (%)
Group A	Pre SLT	27.07	-	-
	1/12 post SLT	16.76	-10.31	38.1
	3/12 post SLT	16.09	-10.98	40.6
	6/12 post SLT	14.72	-12.35	45.6
	12/12 post SLT	13.33	-13.74	50.7
Group B	Pre SLT therapy	18.97	-	-
	1/12 post SLT	13.70	-5.27	-
	3/12 post SLT	14.45	-4.52	27.8
	6/12 post SLT	14.50	-4.47	23.8
	12/12 post SLT	12.90	-6.07	23.5

IOP, Intraocular pressure; SLT, Selective laser trabeculoplasty.



RE, Right eye; LE, Left eye; SLT, selective laser trabeculoplasty.

FIGURE 2: Mean intraocular pressure in Group A versus Group B.

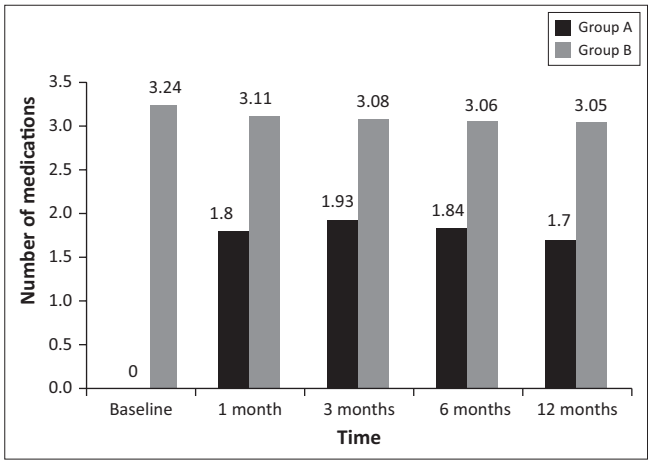


FIGURE 3: Number of medications needed after selective laser trabeculoplasty.

Group A versus Group B, highlighting the effect and sustainability of SLT (see Figure 3).

In Group B, the mean pre SLT IOP was 18.97 mmHg; it was 13.70 mmHg at 1 month, 14.45 mmHg at 3 months, 14.5 mmHg at 6 months and 12.9 mmHg at 1 year. There was a reduction in mean IOP of 32% at 1 year.

The percentage of patients who reduced their IOP by more than 20% was 72% at 1 month, 75% at 3 months, 70% at 6 months and 77% at 1 year.

There was a 15% reduction in the use of acetazolamide. This enforces the need for SLT as a first-line therapy to reduce the use of medication, as Group A required far fewer medications (Table 4).

TABLE 4: Additional therapy needed after selective laser trabeculoplasty in Group A versus Group B.

Month	Medication	Group A (%)	Group B (%)
1 Month	Prostaglandin	53	89
	Beta blocker	53	97
	Alpha agonist	46	82
	Pilocarpine	-	1
	Acetazolamide	26	40
	Repeat SLT	-	1
3 Months	Prostaglandin	60	89
	Beta blocker	53	97
	Alpha agonist	53	82
	Pilocarpine	-	1
	Acetazolamide	26	38
	Repeat SLT	-	1
6 Months	Prostaglandin	53	89
	Beta blocker	53	95
	Alpha agonist	44	80
	Pilocarpine	-	1
	Acetazolamide	15	39
	Repeat SLT	-	3
12 Months	Prostaglandin	50	89
	Beta blocker	50	92
	Alpha agonist	50	82
	Pilocarpine	-	1
	Acetazolamide	20	39
	Repeat SLT	10	1

SLT, selective laser trabeculoplasty.

Analysing the differences in gender, 82% of the male patients (n = 41) had a reduction in IOP of at least 20% at 1 year compared with 77% of female patients (n = 43). Male patients had a 30% reduction in mean IOP from baseline at 1 year compared with a 54% reduction in female patients. This large difference in IOP reduction cannot be fully explained, but is significant. A follow-up trial of a prospective controlled design would be useful to further study these results (see Table 5).

Analysing the different ethnic groups, we found a reduction of IOP of at least 20% at 1 year in 90% of African patients compared with 54% in the Indian subgroup and 83% in the Caucasian subgroup. This supports the theory that SLT directly targets melanocytes in the trabecular meshwork, leading to the conclusion that darker pigmented angles do better with SLT.

TABLE 5: The role of gender in the outcome of selective laser trabeculoplasty.

Gender ($p < 0.001$)	Time	Mean IOP (mmHg)	Mean IOP reduction	Reduction from baseline (%)
Female	Pre SLT	20.59	-	-
	1/12 post SLT	15.07	-12.00	44.3
	3/12 post SLT	14.20	-12.87	47.6
	6/12 post SLT	14.41	-12.66	46.8
	12/12 post SLT	12.58	-14.49	53.5
Male	Pre SLT	20.51	-	-
	1/12 post SLT	14.07	-4.90	25.8
	3/12 post SLT	15.66	-3.31	17.4
	6/12 post SLT	14.70	-4.26	22.5
	12/12 post SLT	13.35	-5.62	29.6

IOP, intraocular pressure; SLT, selective laser trabeculoplasty.

TABLE 6: The role of ethnicity in the outcome of selective laser trabeculoplasty.

Ethnicity ($p < 0.001$)	Time	Mean IOP (mmHg)	Mean IOP reduction	Reduction from baseline (%)
African	Pre SLT	21.64	-	-
	1/12 post SLT	14.67	-12.40	45.8
	3/12 post SLT	15.04	-12.02	44.4
	6/12 post SLT	14.70	-12.37	45.7
	12/12 post SLT	12.93	-14.14	52.2
Indian	Pre SLT	18.35	-	-
	1/12 post SLT	14.41	-4.56	24.0
	3/12 post SLT	14.09	-4.87	25.7
	6/12 post SLT	14.37	-4.60	24.3
	12/12 post SLT	13.32	-5.64	29.8

IOP, intraocular pressure; SLT, selective laser trabeculoplasty.

At 1 year, African patients showed a reduction in their mean IOP of 52% from baseline compared with a reduction of 30% in the Indian group. The small number of Caucasian patients enrolled in the trial precluded their inclusion in this comparison (see Table 6).

Evaluating for age, we found that patients from the 50-year age group had a reduction in their IOP of 37% at 1 year, those in the 60-year group had a reduction of 39% and those in the 70-year group had a reduction of 57%.

Prior to the trial, 36 eyes of 26 patients had undergone surgical intervention for glaucoma. These included 28 trabeculectomies, 3 Ahmed glaucoma valves, 22 phaco-emulsifications and 1 ALT.

By the conclusion of the study, no patient from Group A had required any surgery. In contrast, three of the Group B patients had undergone further glaucoma surgeries including one trabeculectomy and one phaco-emulsification combined with an Express valve implant.

The eyes that underwent surgery prior to or during the trial had a reduction in mean IOP of more than 20% at 1 year in 81% of cases. Interestingly, the same percentage of cases (81%) of those patients never having had any surgery ($n = 58$) also had a reduction in mean IOP of greater than 20% at 1 year. The surgical group had an IOP reduction of 33% at 1 year, despite the advanced nature of their disease and having had multiple treatments in the past.

There was no statistically significant risk of SLT failure in the surgical group compared with the non-surgical group. The surgical group had a reduction in their mean IOP of 4.05 mmHg (22%) at 1 month, 5.5 mmHg (30%) at 3 months, 4.3 mmHg (23%) at 6 months and 6.1 mmHg (33%) at 1 year. These levels were on par with the non-surgical groups and exceeded the 20% drop proposed by the EGS[1] and the American Academy of Ophthalmology.[7]

Discussion

In this study, the best outcomes were seen in older and darker pigmented patients. These comprise the majority of patients treated in our hospital. Ninety percent of African patients had a reduction in IOP of greater that 20%, similar to the findings by Seck et al. who also showed efficiency in 90% of African black patients in their study.[11]

SLT only affects pigmented trabecular meshwork cells, explaining the greater effect in pigmented races. In vitro investigation showed that non-pigmented cells did not experience collateral thermal damage.[12]

SLT laser energy recruits macrophages to the trabecular meshwork by increasing the expression of cytokines and cellular mediator activities. Macrophages remove obstructive proteins and remodel the trabecular meshwork, thus improving aqueous outflow and reducing the IOP.[8]

It is also noted that these biological changes may take up to 6 weeks to take effect.[13] Retreatment before this period is not recommended. It is advised to monitor these patients closely initially until the laser has taken effect. In patients with extremely high IOP, it may be prudent to cover them with medical therapy for the first 6 weeks, followed by a tapering period.

In this study, only patients with a minimum of 1-year follow-up were included. It is not possible to discuss the duration of effect on these patients. Weinand et al. looked at the survivability of SLT and found that around 50% of patients had treatment failure at 2 years,[5] and this finding was reproduced by Bovell et al.[6]

Group A patients required significantly less topical and systemic IOP-lowering medications and had the added benefit of not needing surgical intervention during the study period. Two patients belonging to Group B became pregnant during the trial allowing them to be taken off potentially teratogenic medications.

SLT has a great advantage compared with medical therapy, as it does not rely on compliance. Electronic eye drop monitoring revealed 76% – 86% drop in compliance, and evaluation of prescription claims showed patients had glaucoma drops available to use 69% of the time.[14] This is worrying when dealing with blinding conditions. Taking the compliance out of the equation improves the success rate over time. Reducing the amount of medications and trips to the pharmacy will also improve the quality of life for all these patients. The financial implications connected to the reduced need for medication is important to the patient as well as the government hospitals.

However, it was difficult to wean the Group B patients off their chronic medications, but acetazolamide use decreased by 15%, improving the quality of life of some of the patients. Patients on acetazolamide often complain of debilitating muscle cramps and tingling of extremities and the lips. It is probably the drug that is discontinued first by these patients, a fact that is seldom conveyed to the treating clinician. Seck et al. demonstrated a discontinuation of prostaglandin drops in 60% of study patients.[11] Our study showed no drop in the use of prostaglandins, with 89% of Group B on chronic prostaglandin drops.

It was a surprise to see the disparity between genders. The percentage of patients who had a reduction in IOP of more than 20% were similar in both groups, with 82% of male patients and 77% of female patients reaching the target. The female group had a 54% reduction in IOP from baseline compared with 30% in the male group. This was not the case in other international studies, where no significant difference was found.[15,16,17]

SLT preserves the conjunctiva, should future surgical intervention be needed. It can safely be repeated numerous times and is relatively easy to perform with minimal patient discomfort and minimal side effects. The effect of future drainage surgery is greatly influenced once the conjunctiva has been damaged by other surgical intervention.

Most ophthalmology units have access to argon laser. ALT was found to be as effective as SLT in reducing the IOP, but the laser energy caused permanent tissue damage in the trabecular meshwork and cannot be repeated.[18] SLT has a much better side effect profile and is repeatable as seen by Hong et al.[19] Subsequent treatments are effective even if the initial treatment was not.

Unfortunately, most studies excluded patients with prior glaucoma surgery. In our study, we did show a significant reduction of IOP in patients who had prior trabeculectomies, glaucoma drainage valves, cataract surgery and glaucoma shunts. Only 3 of the 37 eyes in the prior surgical group required further glaucoma surgery. Of note is that none of the patients in Group A required any surgical intervention to lower IOP over the 1-year follow-up.

A mean reduction in IOP of 35% was achieved at 1-year after SLT. It was also found that 80% of these patients had a drop in IOP of greater than 20%.

There is enough evidence to advocate the addition of an SLT unit to all government eye centres as it markedly reduces the need for medication, with its accompanying side effects and compliance issues, as well as the need for surgical intervention, with well-known failure rates and morbidity. It is also technically easier to perform than glaucoma surgery. Even the most junior medical officer or resident can perform the procedure without difficulty. There is no steep learning curve to overcome, as it utilises the slit lamp and a gonioscopy lens, both of which are familiar to the ophthalmologist in training.

This is of particular importance in units with staff shortages, a common theme in most government institutions. The procedure can be completed within a few minutes, making 'same-day treatment' a reality, reducing clinic numbers and patient waiting times.

There are known complications of SLT therapy. The EGS guidelines list anterior chamber inflammation, iritis, anterior chamber bleed, IOP spikes and the formation of peripheral anterior synechiae as possible complications.[1] None of the eyes treated during the trial were noted to have any of the side effects mentioned. Compared with the numerous and sometimes unmanageable side effects of topical and systemic IOP-lowering agents and complications of surgical intervention, SLT seems a much simpler and safer choice. Unfortunately, this study was conducted as a retrospective review, meaning some of the side effects may have been missed.

This study did show that SLT as a first line was a viable option, as seen by Waisbourn.[20] Combined with the reduced need for medication, it is advocated in the treatment of POAG.

This study only included 148 eyes of 84 patients. This is a relatively small sample, but still comparable with international studies. Weinand et al. had a sample size of 52 patients[5] and Seck et al. studied 40 patients.[11] A larger study sample would have been ideal. It would also have been better to have groups

of equal size regarding ethnicity to evaluate the contribution of ethnicity to the eventual efficiency of the SLT laser.

Being a retrospective study, the procedure was not standardised. IOP was not measured at the same time of day by the same examiner using the same tonometer. The exact number of laser burns was not always noted in the patient's chart. Certain doctors preferred to do 180 degrees of laser, while others preferred 360 degrees. Follow-up of all patients can be difficult in the state sector, as attendance can be affected by finances, protest action affecting patient transport and other medical comorbidities that may take preference over eye clinic follow-ups.

The study was done as a retrospective chart review. A prospective randomised controlled trial is advocated in the future to confirm the results.

The ideal test of SLT compared with medical treatment is not easily done. This would entail treating one eye medically and one eye with SLT. The medications instilled or used systemically to control IOP in the 'medical eye' would be absorbed systemically and lower the IOP in the 'SLT eye' as well, leading to exaggerated results, as seen by Lai et al.[21] and Best et al.[22] The only way around this is to treat both eyes medically, measure the IOP and then follow with a 'washout period' where all treatment is stopped. The exact duration varies between medications used. SLT and further monitoring of the IOP could then follow this. Patients are thus without treatment for a period of time.

Conclusion

In evaluating the efficacy, ease of application and favourable risk profile, it is highly recommended that SLT be made commonplace in the treatment of POAG, especially in those patients who present for the first time.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.

Authors' contributions

E.G. was the project leader. E.G. and L.V. were responsible for the experimental and project design. Calculations were performed by B.S.

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