Selective Laser Trabeculoplasty in Patients with Medically Uncontrolled Open Angle Glaucoma

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AIMS: To assess the effectiveness of selective laser trabeculoplasty (SLT, a Q switched, frequency doubled Nd:YAG laser, λ = 532 nm) in lowering the intraocular pressure (IOP) in patients with medically uncontrolled open angle glaucoma attending the glaucoma clinic in the Great river eye hospital, Benghazi .

Methods: A prospective clinical trial was designed. 25 Patients and 30 eyes with open Angle Glaucoma were set to treatment with SLT and were evaluated at 1 hour, 24 hours, 1 week, 1 month and 3 months post-laser.

Results: There were 30 eyes in the SLT treatment group, the mean IOP at baseline, 1 hour, 1 week, and 3 months was 24.56 (SD 3.15), 27.6 (3.85), 27.0 (3.7), 23.8 (3,1), 20.8 (3.0), and 19.7 (2.59) mm Hg, respectively. There was a anterior chamber reaction, 1 hour after SLT in 18 eyes ($p< 0.01$) and one patient with hyphema.

Conclusion: SLT appears to be an important and effective method in lowering intraocular pressures in patients with open angle glaucoma. There is a slightly marked post-laser anterior chamber reaction at 1 hour after SLT. These results are encouraging and suggest that SLT should be investigated further as an IOP lowering treatment in open angle glaucoma. These results need to be confirmed with a larger sample size.

Introduction:

Different types of lasers with various wavelengths are being investigated for laser trabeculoplasty. Recently, a Q switched, frequency doubled Nd:YAG laser (λ = 532 nm) has been described for use in trabeculoplasty[1-3] (Mark A Latina, presented at AAO Annual Meeting. San Francisco, 1997). Though, in North America, Argon laser trabeculoplasty (ALT) has become the standard method of treatment for medically uncontrolled open angle glaucoma, the difference between the two types of laser arc mainly due to the effects of the laser type. Argon laser (λ = 488-5 14 nm) been in use since 1979 when it was first described by Wise and Witler.[4] According to the mechanical theory. ALT causes coagulative damage to the trabecular meshwork, which results in collagen shrinkage and subsequent scarring of the TM. This tightens the meshwork in the area of each burn and reopens the adjacent, untreated intertrabecular spaces.[4-6] Another cellular theory proposes that in response to coagulative necrosis induced by the laser, there is migration of macrophages. which phagocytose debris and thus clear the TM. the Q switched, frequency doubled Nd:YAG laser (λ=532nm) has been demonstrated in tissue cultures that the low power and short duration of this laser can selectively target pigmented TM cells while sparing adjacent cells and tissues from collateral thermal damage and can thus maintain the architecture of the TM.[7] This procedure has thus been termed selective laser trabeculoplastv (SLT). The objective of our study was to assess the efficacy of SLT in lowering the intraocular pressure (IOP) in patients with medically uncontrolled open angle glaucoma in a prospective clinical trial.

Patients and methods:

A prospective clinical trial was conducted by the researcher on 30 eyes and 25 patients [16 males and 9 females] in the Great River Eye Hospital. The patients included in this trial were those referred to the glaucoma clinic. All Patients were included if they had open angle glaucoma (to increase the generalisability of the trial, pigmentary and pseudoexfoliation glaucoma were also included) with uncontrolled IOP (>23 mm Hg) on maximal medical therapy [mean age = 51 years. SD ± 9.5 years], the average time from diagnosis to Laser therapy was 6 months (SD ± 2.5), all had two sighted eyes. Patients were excluded if there was any evidence of glaucoma other than

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open angle glaucoma (if the TM could not be visualized 360 degrees); if an advanced visual field defect (scotoma within 10 degrees of fixation or split fixation on Octopus visual field (24-2, full threshold program) was present in the eye being considered for treatment; if the patient had previous glaucoma surgery done (other than peripheral laser iridotomy (PI)), or required any ocular surgery within 6 months post-laser in the study eye; if there was corneal disease precluding an adequate view of the trabecular meshwork; or if the patient was on systemic steroids or had a concurrent condition warranting treatment with systemic steroids within the study period.

Baseline examinations included variables such as age, sex, history of any risk factors for glaucoma (myopia, hypertension, diabetes, race, thyroid disease, and family history of glaucoma), a history of past and present ocular medication, and history of any ocular surgeries done including any laser therapy (ALT/PI) to the study eye. Ocular assessment included corrected visual acuity, slit lamp assessment of the anterior segment of the eye, and Gonioscopyofthe angle. Trabecular meshwork pigmentation was graded according to a standard scale provided by Coherent Medical (graded from 0 to 4+ where 0 = no pigment and 4+ = dense homogeneous pigment). IOP was measured with a Goldmann applanation tonometer at approximately the same time of day (plus or minus 1 hour) for all follow up visits to minimize diurnal variation of IOP. Stereoscopic optic nerve examination was performed with a Volk 90D lens. On the day of laser trabeculoplasty, IOP was checked and one drop of 2% pilocarpinewas instilled in the study eye. Patients were then treated with SLT [a Q switched, frequency doubled Nd:YAG laser (λ = 532 nm), Visual YAG ‖ from Carl Zeiss ®] 180° of the angle was generally treated using 50 non-overlapping applications, with a spot size of 400 urn (centered on the TM) and pulse duration of 3 ns. The initial energy used was 1 mJ. The energy was increased or decreased until bubble formation appeared and was then decreased by 0.1 mJ for the remainder of the treatment. Average power during treatment ranged from 1 to 1.4 mJ. A drop of 4% pilocarpine was instilled in all treated eyes post-laser. One hour post-laser IOP was checked and the anterior chamber reaction was assessed (cells and flare). If pressure was high, 250 mg of acetazolamide was given to the patient and pressures were checked after an 24 hours. When stable, patients were sent home on betamethasone 1% to be instilled in the treated eye four times a day . An attempt was made to keep the patient on the same glaucoma medications prescribed at the study inception for the duration of the study. The medication was changed only if the pressure worsened significantly from preoperative status, or if an adequate drop in IOP was not seen. Patients were evaluated at end of 1 week, then at approximately 1 and 3 months. At all follow up examinations, the best corrected vision, anterior chamber reaction, IOP. grade of trabecular pigmentation, presence of any peripheral anterior synechiae, and cup to disc ratio were noted.

Statistical analysis:
All statistical analyses were performed with the software **SPSS®** Significant p values were considered to be less than or equal to 0.05. The primary outcome variable was a change in IOP from baseline, Secondary outcomes were anterior chamber reaction and Snellen visual acuity.

Results:
In all, 30 eyes of 25 patients were included, the average follow up time for 1 week, 1 month, and 3 months visit was 7.2 (SD 1.8), 34.6 (6.3), 90.7 (10.0) days, respectively. At the baseline characteristics of these patients are summarized in Table [l]. It was noticed that during SLT, there was nil to mild reaction of the trabecular meshwork at most exposed sites, the treatment was not free of bleeding, with hyphcma seen in one diabetic patient. Patients did not complain of any pain during treatment with laser.

Table No. (1) The baseline characteristics

Age (SD) (years)	51 (9.5)
Male	16
Female	9
POAG [eyes]	25
Pseudoexfoliation glaucoma	2
Pigmentary glaucoma	1
OAG status post PI	1
Aphakic glaucoma	1

Although we tried to keep the patients on a constant regimen of medications during the study period, in 10 eyes a change in medication occurred to control the IOP. The average number of medications at baseline and 3 months was 2.5 and 1.3 respectively in the

SLT group, Table No. [2] shows the percentage of patients with or without medication pre- and post - laser treatment. Table [3] shows the mean intraocular pressure at baseline and after laser trabeculoplasty at 1 hour, 1 week, 1, and 3 months whereas Figure [1] shows the mean reduction in IOP at these time intervals. IOP measurements obtained 1 hour after treatment were higher, although the results were not statistically significant (p= 0.07).

At 24 hours there were 118 patients in the SLT who had post-laser anterior chamber reaction and one patient only with post laser hyphema. At 3 months, there were 21 patients who developed stabilization of the intraocular pressure. Figure [2] shows the trial results in terms of IOP measurements, at 1 hour, 1 week, 1, and 3 months. The mean 3-month IOP was 19.7 (3.0) mm Hg in the SLT group. This difference was not statistically significant (p= 0.064).

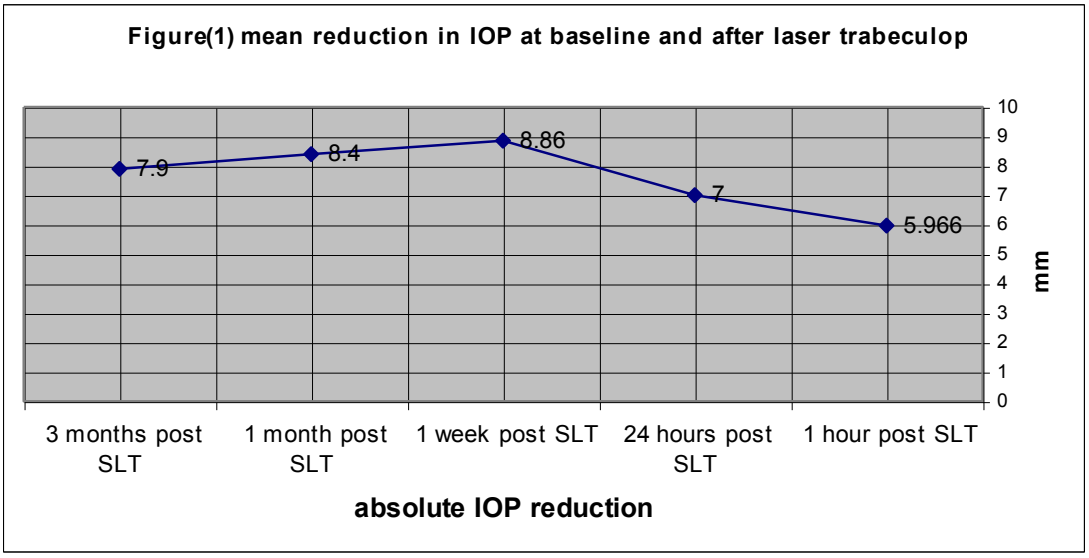
Table No. (2) the percentage of patients with or without medication pre- and post – laser treatment

SLT status	Drug Treatment		
	No drug	Single drug	Two drugs or more
Before SLT	20.64%	40.04%	39.32%
Post- SLT	62.04%	20%	17.96%

A multivariate analyses was done at 3 months taking all baseline characteristics into consideration and analyzing their effect on the final intraocular pressures. It was found that the only predictor of final intraocular pressure at 3 months was the baseline intraocular pressure -that is, patients with lower baseline IOP had lower IOP at 3 months. Secondary outcomes were anterior chamber reaction and Snellen visual acuity. Table [4] shows the anterior chamber reaction in terms of cells and flare 1 hour post-laser. There was significantly higher number of cells in the anterior chamber after SLT ($p < 0.01$). There was no change in visual acuity throughout the study in the study group.

Table No. (3) The main introcular pressure at baseline and after laser trabeculoplasty

Gender	Pre-SLT Mean IOP	Post-SLT Mean IOP				
		1 hour	24 hour	1 week	1 month	3 months
Males	24.31	28.2	28	23.2	20.6	18
Females	25	27.3	26	24.7	20.9	18.5
Average	24.5	27.6	27	23.8	20.8	19.7



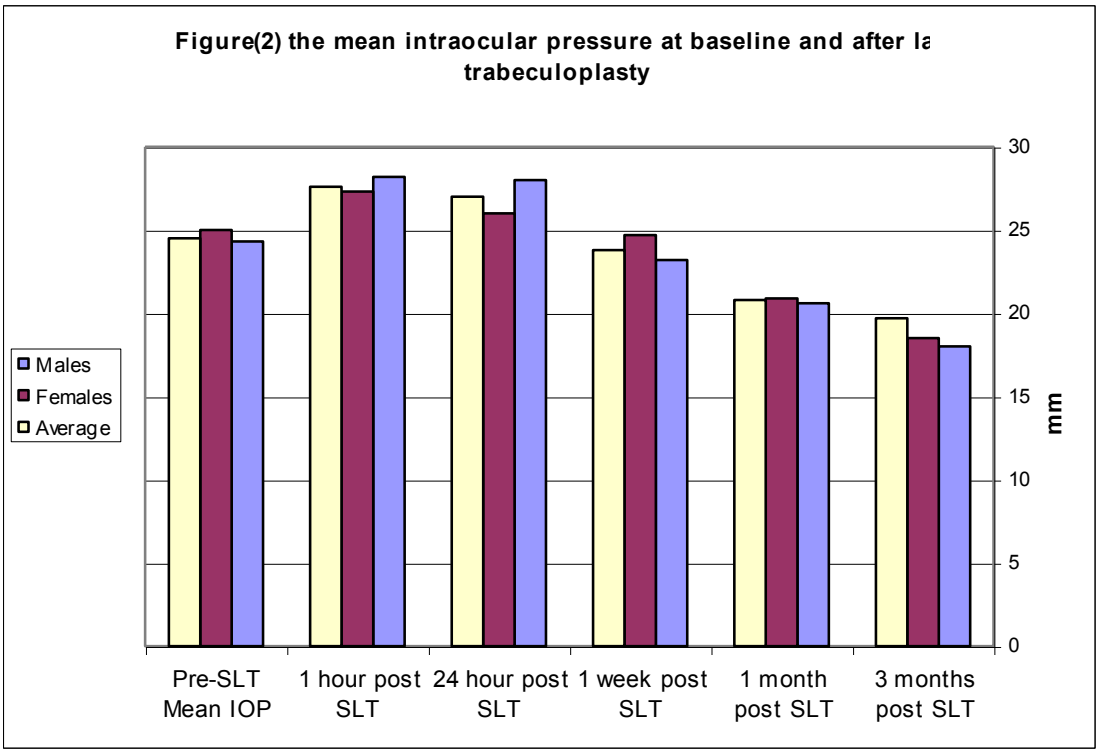


Table No. (4) Anterior Chamber 1 hour post-laser.

Anterior chamber reaction [cells and flare]	
mild	12
moderate	6
Total	18
hyphema	1

Discussion:

In this study we studied the standard Q switched frequency doubled (523 mn) Nd:YAG laser. Our results showed that over 3 months' duration there was statistically significant difference in the intraocular pressures in the group studied. Tabak et al.[2] conducted a prospective randomized trial simultaneously treating one eye of a patient with SLT and the other with ALT. They found an equivalent decrease in IOP at 4 weeks (ALT n=17, SLT n=22) in both the groups. Longer follow up was not reported. Pirnazar et al.[3] conducted a retrospective study comparing ALT (27 eyes) with SLT (30 eyes) and found no difference in IOP drop at I, 6, and 12 months post treatment. ALT has been a standard therapeutic intervention in open angle glaucoma.[4-6,8] The 5 year success rate with ALT is reported to be 50%, with a decrease of 6% to 10% per year.[6] The laser used in this study is a Nd:YAG laser, which is a solid state laser. It has the advantages of less cost, smaller size. longer duration, and high electrical to optical efficiency. The drawbacks of argon gas laser, however, include high cost, large power supply system, large size. Low electrical to optical efficiency, and plasma tube degradation with time.[9] As a possible alternative to this laser a number of other wavelengths are being tested. Although a number of previous studies have been done using Nd:YAG laser trabeculoplasty in animal models and in human glaucomatous eyes.[11-16] these studies used Nd:YAG either in the continuous wave or free running mode with a wavelength of 1064 nm. We used a Q switched, frequency doubled Nd:YAG (532 nm) which combines the advantage of solid state lasers with the emission of monochromatic green wavelength light. In this system, infrared radiation is filtered and only the visible component (532 nm) is used. This uses an effect similar to monochromatic argon green light (514 nm).[9] An additional advantage of 532 nm laser over 1064 nm laser is that optical absorption by melanin increases with the decrease in wavelength, thus lower threshold energy is required for a similar effect.

Frequency doubled Nd:YAG laser with pulse of short duration and low fluence (energy/area) has been found in tissue cultures, to selectively target pigmented TM cells while sparing adjacent cells and tissues from collateral thermal damage. It may thus have the advantage of better maintaining the architecture of the TM compared with ALT.[7]

The exact mechanism of action of this selective laser trabeculoplasty is not known. However, since minimal mechanical damage is thought to occur, a predominately cellular theory has been proposed to explain an improvement in outflow facility. According to Hollo.[11] following ALT, the uveoscleral meshwork is severely destroyed in the area of the laser spots and the surrounding collagen fibres are heat damaged. A membrane is formed by migrating endothelial cells, which covers the meshwork between the laser spots and is responsible for the late pressure rise and treatment failure after ALT. This endothelial membrane and thermal damage was not seen after 532 nm Nd:YAG laser trabeculoplasty.[10] Noeckere et al.[17] studied the morphological changes after SLT and ALT in human postmortem eyes. They found that there was no coagulative damage to the human TM after SLT compared with ALT. This may offer a theoretical advantage for treatment with laser or topical medications if needed in the future.

SLT uses a pulse duration of 3 ns compared with ALT which has a pulse duration in the range of 1 ms or greater. According to Latina and Park,[7] at pulse duration between 10 ns and 1 us energy is deposited within the target (pigmented TM cells) more rapidly than it can diffuse away, hence minimizing damage to the surrounding non-pigmented TM cells. Hence with pulse duration of 3 ns, SLT selectively confines the energy to the pigmented cells, whereas in ALT, heat gets dissipated from the pigmented cells to the surrounding tissues, damaging the non-pigmented cells within the irradiation zone. One interesting observation in our study was almost nil to mild visible reaction on the TM in response to the SLT impacts. This may be the result of deeper tissue penetration of the Nd:YAG laser energy in comparison with argon laser energy, which is deposited near the TM surface.[7]

We also found that the anterior chamber reaction 1 hour post-laser was considerable [18 eyes]. A possible explanation for this may be the larger spot size used for SLT 400 um than that used usually for ALT [50 μm in ALT]. The large spot size in SLT is used to maintain a low fluence (energy/area), which is essential for the selectivity of this laser.[7] Because of such a large spot size, the laser beam probably has an effect on the pigmented cells not only in the TM but also in the ciliary body and surrounding iris. This may be responsible for the increased anterior chamber reaction.

In summary, SLT appears to be an important and effective method in lowering intraocular pressures in patients with open angle glaucoma. There is a slightly marked post-laser anterior chamber reaction at 1 hour after SLT. These results are encouraging and suggest that SLT should be investigated further as an IOP lowering treatment in open angle glaucoma, especially in patients with previously failed ALT. Nevertheless our results need to be verified with a phase III clinical trial.

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