Efficacy and safety of subliminal transscleral cyclophotocoagulation in uncontrolled glaucoma

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Purpose: To determine the efficacy of subliminal cyclophotocoagulation in reducing intraocular pressure (IOP) and to assess the safety profile of the procedure. Methods: We reviewed the charts of all patients who underwent subliminal cyclophotocoagulation between August 2019 and August 2020. The IOP, number of antiglaucoma medications, and visual acuity were compared at baseline and at 6 months. The post-laser complications were noted. Paired t-test, Wilcoxon rank-sum test, and McNemar test were used for analysis. Results: This study included 40 eyes of 40 patients. The most frequent diagnosis was neovascular glaucoma (55%), followed by primary open-angle glaucoma (17.5%). The mean IOP reduced from 32 to 21 mmHg (mean IOP reduction: 32%, 95% confidence interval [CI]: 27%–37%, P < 0.001). Mean number of antiglaucoma medications declined from 3.2 to 1.9 (P < 0.001). Use of oral acetazolamide decreased from 62% to 5% (P < 0.001). The success rate of the procedure at 6 months was 55%. One patient had unexplained visual acuity decline after the procedure. Conclusion: Subliminal sub-cyclophotocoagulation is effective in treating refractory glaucoma in the Indian population. It decreases the medication burden. However, subliminal lasers can also cause vision-threatening complications such as hypotony, uveitis, and optic nerve hypoperfusion. So, clinicians should be cautious when using sub-cyclophotocoagulation in patients with good vision.

Key words: Cyclophotocoagulation, micropulse, SubCyclo, sub-cyclophotocoagulation, subliminal

Methods

Study design, study period, and study setting
This study was conducted in a tertiary care center in South India between August 2019 and August 2020. The research was approved by the Institutional Review Board and done in adherence to the tenets of the Declaration of Helsinki.

Study participants

Inclusion criteria
All patients with glaucoma whose IOP was more than 21 mmHg despite maximal tolerated medical therapy were included in the study. Glaucoma patients with IOP > 21 mmHg who were neither compliant with medications nor willing for trabeculectomy were also included. Six-month follow-up data was mandatory. Only those patients who underwent subliminal cyclophotocoagulation with the standard protocol followed in our institute were included in the study.

Protocol for subliminal cyclophotocoagulation
The procedure is done in the operating room under peribulbar block with 2% lignocaine. The probe used for the procedure is the SubCyclo probe by Quantel Medical Instruments.

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The duty cycle is 31.3% (2 W power, micropulse “on” time 0.5 s, “off” time 1.1 s). The SubCyclo probe is placed 3 mm from the limbus and is moved in a sweeping motion for 80 s in the superior hemisphere and 80 s in the inferior hemisphere (around four sweeps per hemisphere). The 3 o’clock and 9 o’clock positions are avoided (to prevent damage to ciliary neurovasculature).

All antiglaucoma medications are continued up to the day of the laser. Oral acetazolamide is stopped after the laser. Prednisolone acetate eye drops (1%) four times per day is given after the procedure and it is tapered over 1 month. All topical antiglaucoma medications are continued after the laser, and any alteration in topical medications is done only after 1 month.

Exclusion criteria

Patients who underwent SubCyclo with a 25% duty cycle, incomplete laser treatment, and those with incomplete data were excluded.

Data collection

The medical records of all the patients who underwent subliminal cyclophotocoagulation were examined. The demographic details, the type of glaucoma, and glaucoma treatment history were collected. The baseline IOP and the IOP values at 1, 3, and 6 months post-procedure measured by applanation tonometry were recorded. The visual acuity at baseline and at each visit, adverse events following the procedure, and alteration in antiglaucoma drugs were noted.

Outcome

Treatment success is defined as an IOP of less than 21 mmHg or a 30% reduction in IOP, without visual decay due to complications of the procedure and without needing additional medications, retreatment with the laser, or incisional surgery.

Statistical analysis

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) Statistics for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA). Quantitative data is summarized using mean and standard deviation or median and interquartile range, as appropriate. The data was checked for normality using the Shapiro–Wilk test. Depending on the normality, the differences in the continuous measures before and after the laser were analyzed with the paired t-test or the Wilcoxon rank-sum test. The Fisher exact test and the McNemar test were used for analyzing the qualitative data. A two-tailed P value less than 0.05 was considered for statistical significance.

Results

We analyzed the outcomes in 40 eyes of 40 patients. The patients were predominantly male; their age ranged from 26 to 75 years. The most common indication for micropulse laser was neovascular glaucoma, followed by primary open-angle glaucoma. Most patients (32/40) had vision less than 6/60 [Table 1].

Subliminal cyclophotocoagulation lowered the mean IOP by 10.8 mmHg in 6 months (34% reduction). This was statistically significant (t = 9.56, P < 0.001, 95% confidence interval: 8.5–13.1 mmHg) [Table 2]. The maximum IOP reduction occurred within the first month of the laser [Fig. 1].

Patients needed fewer medications 6 months after the laser and this was statistically significant (P < 0.001). Sixty percent of patients could reduce at least one topical antiglaucoma drug after the procedure [Fig. 2].

Success was achieved in 21/40 patients (52.5%, 95% confidence interval: 37.5%–67.5%). We could not find any association between treatment success and baseline clinical characteristics such as the type of glaucoma, the pre-laser IOP, the number of antiglaucoma drugs, and previous trabeculectomy.

The complications encountered at the 1-week follow-up visit included uveitis (four patients), mydriasis (two patients), corneal edema, early hypotony, and unexplained visual loss (one patient each). Uveitis and corneal edema resolved within a month in all the patients.

Hypotony occurred in one patient with Primary Open Angle Glaucoma (POAG) and good central vision. His IOP normalized in 3 months. By the sixth month, his cataract had progressed and his visual acuity reduced by two lines.

Another patient with ocular ischemic syndrome, neovascular glaucoma, IOP 43 mmHg, and a central island of vision had visual acuity decline from 6/24 to hand movements in 1 week. There were no new findings in his anterior and posterior segments. The pre- and post-procedure macular Optical coherence Tomography (OCT) showed no alteration. This patient had multiple systemic vascular risk factors (carotid artery stenosis, prior cerebrovascular accident, and coronary artery disease). We hypothesize that his visual acuity decline after the laser may be due to an acute hypoperfusion of the optic nerve.

The late complications included hyphema and scleral thinning. At the 3-month visit, hyphema occurred in a patient with neovascular glaucoma and no light perception. Scleral thinning was noted at the sixth month visit in a myopic patient (post-retinal detachment surgery) with silicon oil-induced glaucoma.

Discussion

Key findings

We found subliminal micropulse diode laser effective in reducing IOP in the Indian population. The success rate (at

Table 1: Descriptive characteristics of patients undergoing subliminal cyclophotocoagulation

| Descriptive characteristics of patients (N=40) | Median (interquartile range) or n (%) |
|-----------------------------------------------|--------------------------------------|
| Age                                           | 63 (53.5–65.75)                      |
| Male                                         | 31 (77.5%)                           |
| Left eye                                     | 21 (52.5%)                           |
| Previous trabeculectomy                      | 4 (10%)                              |
| Type of glaucoma                              |                                       |
| Primary open-angle glaucoma                   | 7 (17.5%)                            |
| Primary angle closure glaucoma                | 4 (10%)                              |
| Neovascular glaucoma                          | 22 (55%)                             |
| Other secondary glaucomas*                   | 7 (17.5%)                            |
| Central vision >6/24                         | 6 (15%)                              |

*Includes inflammatory glaucoma, silicon oil-induced glaucoma, pseudoexfoliation glaucoma (two cases each), and one case of iridocorneal endothelial syndrome

Table 2: Changes in IOP with subliminal cyclophotocoagulation

| Time (months) | Mean IOP reduction (mmHg) | Median IOP reduction (mmHg) |
|---------------|---------------------------|----------------------------|
| 1             | 10.8                       | 8.5                        |
| 3             | 13.1                       | 10.5                       |
| 6             | 15.0                       | 12.5                       |

The maximum IOP reduction occurred within the first month of the laser.
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Table 2: Postoperative outcome of patients who underwent subliminal cyclophotocoagulation, mean±SD or n (%)

| Clinical characteristic          | Before micropulse laser | 6 months post‑micropulse laser | Mean difference | 95% Confidence intervals |
|----------------------------------|-------------------------|--------------------------------|-----------------|--------------------------|
| Intraocular pressure (mmHg)      | 32±7.4                  | 21.2±5.5                      | 10.8            | 8.5‑13.1                |
| Mean LogMAR visual acuity        | 2.1±0.89                | 2.2±0.84                      | −0.06           | −0.15 to 0.32           |
| Number of antiglaucoma medications| 3.15±1                  | 1.93±0.66                     | 1.23            | 0.91‑1.55               |
| Oral acetazolamide               | 21 (52.5%)              | 2 (5%)                        | *               |                          |
| Treatment success                | 21 (52.5%)              |                                | *               |                          |

*Statistically significant with P<0.001, the paired t-test, Wilcoxon rank­sum test, or McNemar test, as appropriate

Figure 1: Rate of change of intraocular pressure after sub‑cyclophotocoagulation

Figure 2: Dot plot showing number of topical medications used by patients at baseline (a) and at 6 months after micropulse laser (b)

6 months) for the procedure was 55%. Subliminal lasers could curb acetazolamide dependence in 95% of patients and reduce at least one topical antiglaucoma drug in 60% of patients. Visual decay occurred in 5% of patients.

Wide variations exist in the treatment success rates. This can be due to the different criteria used for treatment success, the varying laser parameters in different studies, and exclusion of retreatment from the success criteria. We have listed the studies with laser settings similar to our study and compared the IOP reduction at 6 months [Table 3].

Indian studies on transscleral micropulse lasers are sparse. Ariga et al.[7] conducted a prospective interventional study in 55 eyes with refractory glaucoma (Iridex laser, laser parameters as in this study). They found IOP reduced by 30% in 3 months. A retrospective study by Abbagani et al.[8] (SubCyclo laser by Quantel Medical Instruments, laser parameters as in this study) found a 44% reduction in IOP in 2 months. Our study revealed a 32% reduction in IOP at the 3-month follow-up visit. The short-term results of transscleral micropulse lasers in the Indian population are comparable to those of the Caucasian population.

Complications

The complications we found in this study included uveitis, mydriasis, corneal edema, and hyphema (Neovascular Glaucoma [NVG]). All these complications have been reported by various authors. Prolonged inflammation >1 month and persistent hypotony (IOP<5 mmHg on two visits after 3 months) are the most frequent vision-threatening complications of sub-cyclophotocoagulation. Studies by Williams et al. and Emanuel et al. have reported high rates of persistent hypotony (6%–10%) and prolonged inflammation (27%–46%).[5,15] The average duration time was over 300 s in both these studies. These two complications were also less frequent in studies with laser duration less than 180 s.[16,17] Lower micropulse laser duration may decrease the risk of post-laser inflammation and hypotony.[5] This may be the reason why we did not encounter these complications (the laser duration in this study was 160 s). Interventional comparative studies can help confirm any association between laser duration and complications.

We had only six patients with vision more than 6/24. Among these, one patient developed early hypotony, which resolved with treatment; however, he developed cataract and visual acuity declined. The other patient developed unexplained vision loss within a week, possibly because of optic nerve hypoperfusion. Optic nerve hypoperfusion has been reported following conventional cyclophotocoagulation by Ansari et al.[18] Many studies have reported permanent visual acuity decline of ≥2 lines after micropulse laser, ranging from 16% to 26%.[5,13,15] The reasons for the visual loss included uveitis, hypotony, cystoid macular edema, and cataract progression. Two of these studies have also reported patients with unexplained visual loss following the procedure.[13,15] Hence, more long-term studies assessing the risk–benefit ratio are needed before recommending micropulse lasers in patients with good vision.

Strengths and limitations

This study provides valuable information regarding the efficacy of micropulse in the Indian population. The limitations of this
study include the small sample size, limited follow-up period, and selection bias because of the retrospective nature. Though the standard protocol followed in the institution ensured standardized laser power and duration, different surgeons may have moved the laser probe at varying speeds. Further, there was no uniform protocol for altering the antiglaucoma medications during follow-up.

Implications and further research
We used the micropulse laser with a 31.3% duty cycle for a total of 160 s. Varying the micropulse laser settings may alter the treatment success rates and complications. Randomized controlled trials (comparing laser power and duration) can help decide the optimal laser setting. We must also explore—using large prospective studies—the risk–benefit ratio of micropulse lasers in good vision. More research in these directions can enhance the role of micropulse lasers in managing glaucoma.

Conclusion
Subliminal transcleral cyclophotocoagulation is effective in refractory glaucoma with poor vision. It is useful in all types of glaucoma and can reduce the IOP by 27%–37% in most individuals. It decreases the patient’s medication burden. However, micropulse lasers can cause vision-threatening complications. More research is needed to see whether the benefits of the laser outweigh the risks in glaucoma patients with good vision.

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Conflicts of interest
There are no conflicts of interest.

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