CASE SERIES

Outcomes of Subliminal Transscleral Cyclophotocoagulation treatment in glaucoma

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SUMMARY

Background: Subliminal transscleral cyclophotocoagulation (SL-TSCPC) is a new alternative therapy to reduce intraocular pressure (IOP) safely and effectively. However, there are few studies regarding SL-TSCPC by Supra 810 laser machine and limited data regarding its effectiveness in moderate severity glaucoma that still has good preservation of vision. This study was conducted to evaluate the outcome of SL-TSPCPC in various types of glaucoma including patients with good vision.

Methods: A retrospective, non-comparative, analytical case series of all patients who received SL-TSCPC treatment from October 2018 to April 2019 at Hospital Tengku Ampuan Afzan, Pahang, Malaysia. Data was collected during the second week, sixth week, third month and sixth month follow-up. The primary outcome measure gave success rate at six months post-treatment. Secondary measures were changes in visual acuity, mean IOP reduction, mean number of IOP lowering medications reduced and ocular side effects noted during follow-up.

Results: The success rate was 43.8% (seven eyes out of sixteen eyes) at six months post-treatment. The mean IOP reduced from 43.0mmHg±14.8mmHg pre-treatment to 24.7mmHg±12.0mmHg at two weeks post treatment with 42.6% reduction. Subsequently, mean IOP at sixth week, third month and sixth month were 33.8mmHg±16.9mmHg, 35.2mmHg±14.9mmHg, and 29.0mmHg±16.2mmHg respectively. Vision maintained in 13 patients, two patients had improvement in vision however, five patients had deterioration in vision. No serious ocular side effects were noted.

Conclusion: Subliminal TSCPC is a safe and alternative method of lowering IOP in moderate to advanced glaucoma over 6 months duration of follow-up. As it has good safety profile and repeatability, it is a good treatment option for patients with uncontrolled glaucoma.

KEYWORDS:
Glaucoma, intraocular pressure, subliminal diode laser, transscleral cyclophotocoagulation

INTRODUCTION

Glaucoma is a progressive optic nerve disease characterized by damage of optic disc with associated visual field defects.[1] It is the most common cause of irreversible blindness in the world.[2] Medications, lasers, or surgery are options to treat glaucoma by lowering the intraocular pressure (IOP).[3] Conventional transscleral cyclophotocoagulation (TSCPC) is commonly used to reduce IOP in painful blind eyes or eyes with poor visual potential, failed multiple filtering surgeries, and poor surgical candidates. The mechanism of TSCPC is by destruction of the ciliary body by continuous diode laser delivery, thereby decreasing aqueous production with subsequent IOP reduction. However, complications associated with TSCPC include pain, persistent inflammation, vision loss, hypotony, phthisis bulbi, scleral thinning, macular oedema, intraocular haemorrhage, retinal detachment, aqueous misdirection syndrome and rarely, sympathetic ophthalmia. Occurrence of severe complications is thought to be due to collateral damage to surrounding tissues.[4]

Micropulse TSCPC (MP-TSCPC) or subliminal TSCPC (SL-TSCPC) offers a variety of traditional TSCPC to treat glaucoma. Subliminal TSCPC has a similar mode of action in laser delivery as micropulse TSCPC, where diode laser is delivered in ultrashort and repetitive pulses (on and off time). The major difference between SL-TSCPC and MP-TSCPC are different machine used. SL-TSCPC is delivered by Supra 810 laser machine, Quantel Medical while MP-TSCPC is delivered by IRIDEX laser machine. With this system, short bursts of energy deliver pulses to photocoagulate the targeted tissue (pigmented epithelium of the ciliary body) during the "on-cycle" while surrounding tissue is allowed to cool and remain below the photocoagulation threshold during the "off-cycles". So, it is theoretically able to prevent damage to the surrounding tissue.[5] Some studies have demonstrated that MP-TSCPC is an effective and safe alternative to traditional TSCPC at lowering IOP, with possible decreased rates of complications.[6,7] Subliminal TSCPC shows a good profile that able to reduce IOP safely and effectively.[8] However, more studies are needed to evaluate their safety profile and efficacy. Thus, the aim of this study is to determine the effectiveness and side effects of SL-TSCPC for various types of glaucoma, including glaucoma in patients with good vision.

MATERIALS AND METHODS

This study is a retrospective, non-comparable, analytical medical record reviews of all subjects with various types of glaucoma that received SL-TSCPC treatment from October 2018 to April 2019 at Hospital Tengku Ampuan Afzan,

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Pahang, Malaysia as the SL-TSCPC machine was only available during this period of time. All patients who received SL-TSCPC treatment during this period were recruited and no patients excluded. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the institute. Informed written consent was obtained from all patients prior to their enrolment in this study. Data were collected and analysed each post SL-TSCPC visit. The background characteristics of patients, best corrected visual acuity (BCVA), type of glaucoma, staging of glaucoma, IOP, number of glaucoma medications, ocular history were recorded for each patient. Visual acuity was measured using Snellen chart. Good vision is defined as visual acuity of 6/12 and better. IOP was measured by goldmann applanation tonometry. The SL-TSCPC procedure was performed in an outpatient setting. Subtenon anesthesia with three to four milliliter of 2% lignocaine hydrochloride was given before the procedure. After laser therapy, patients were reviewed at second week, sixth week, third month and sixth month. One to two-week duration of topical steroid and antibiotic were prescribed after the procedure and then tapered accordingly. Each patient had their vision, IOP, number of medications required, and presence of any complications recorded during subsequent follow-up. Outcome measures were the number of patients who achieved surgical success, changes of visual acuity, mean IOP reduction, mean reduction of IOP lowering medications, and documentation of ocular side effects.

The supra 810 laser machine, Quantel Medical was used. It emits infrared diode laser with a wavelength of 810 nm. It delivered 2000mW energy in fast repetitive on and off phase (micropulse mode) for 160s for all patients. The probe was moved in a "to and fro" motion over three mm behind the limbus of upper and lower conjunctiva sparing the three and nine o'clock positions. The duration of treatment for each hemisphere was 80 seconds (s), therefore the total duration of the treatment was 160s. The treatment settings were adjusted individually based on the patient's condition and manufacturer recommendation.[8] There are two treatment settings which are duty cycle of 31.3% (time on 0.5s, time off 1.1s) for patients with no previous history of active ocular inflammation or keratitis, while the duty cycle of 25% (time on 0.62s, time off 1.9s) for patients with active ocular inflammation, good best corrected visual acuity or moderate visual field defects. There was no standard technique for the sweeping motion during application (fast vs. slow).

Surgical success in this study was determined by multiple patient outcomes. Surgical success was defined as an IOP of 6–21 mmHg or a reduction of IOP by 20% from the baseline with antiglaucoma medications.9 Failure was defined as: (1) IOP < six mmHg with hypotony maculopathy, (2) loss of ≥ three Snellen lines, and (3) require further glaucomatous surgical intervention to control the IOP.10 The primary outcome measure was success rate at 6-month post-treatment. Secondary outcome measures were changes of visual acuity, IOP reduction, and ocular side effects noted during each visit.

RESULTS

A total of 20 eyes of 18 patients were treated with subliminal TSCPC in this study. The mean age of treated patients was 58 years old with the range from 12 to 75 years old. There were nine male patients (50.0%) and nine female patients (50.0%). Most patients were Malays (n=13, 72.2%), followed by Chinese (n=4, 22.2%) and Indians (n=1, 5.6%). Twelve patients had treatment in the right eye (66.7%), four patients had treatment in the left eye (22.2%) and two patients had treatment in both eyes (11.1%). There were five eyes (25%) with good vision (6/12 and better) which underwent SL-TSCPC with duty cycle 25% while another 15 eyes (75%) underwent SL-TSCPC with duty cycle 31.3%. All patients were on medical glaucoma therapy prior to treatment and six patients (33.3%) had undergone prior incisional glaucoma surgery [Table I]. Neovascular glaucoma was the predominant diagnosis (n=10, 50%), followed by primary open angle glaucoma, steroid-induced glaucoma, and others [Table II]. The average duration of follow-up post-treatment was 5.7 ± 2.7 months. Percentage of follow-up was initially 19 (95%) eyes at second week visit; 15 (75%) eyes at sixth weeks; 18 (90%) eyes at third month; and 16 (80%) eyes at sixth month. The reason attributing to dropout was defaults on clinic appointments and missing documents on patients follow up.

The success rate was 43.8% (seven eyes out of sixteen eyes) at sixth month post-treatment in this study [Figure 1]. Four eyes were excluded as they defaulted follow up at sixth month post-treatment. Half of the neovascular glaucoma patients were in the failure group (six out of twelve eyes). The reasons of treatment failure are shown in Table III.

In this study, the mean IOP was reduced from 43.0mmHg ± 14.8mmHg pre-treatment to 24.7mmHg ± 12.0mmHg at second week post-treatment, a 42.6% reduction. Subsequently, mean IOP at six weeks, three months, and six months post-treatment were 33.8mmHg ± 16.9mmHg, 35.2mmHg ± 14.9mmHg, and 28.7mmHg ± 16.7mmHg respectively. The IOP reduction from baseline was 21.4% at six weeks, 18.1% at three months and 33.2% at six months. Meanwhile, the mean number of topical antiglaucoma eyedrops maintained the same from 3.5 pre-treatment to 3.5 at second week but further reduced to 2.8 at six weeks, 2.6 at three months, and 3 at six months post-treatment. Besides, the mean number of systemic IOP lowering agents were 0.4, 0.1, 0.2, 0.1, and 0 at pre-treatment, second week, six weeks, three months, and six months post-treatment respectively. Percentage of patients on systemic medication were 35% pre-treatment, 26% at second week, 20% at six weeks, 11% at three months and none of patients were on systemic IOP lowering medications after six months post-treatment. Table IV summarizes the mean IOP, IOP reduction, the mean number of medication and percentage of patient on systemic medication at each follow-up for all patients.

Vision changes after SL-TSCPC were common. Visual acuity changes at six months post-treatment were 5% (n=1) of eyes gained three Snellen lines of vision and 5% (n=1) improved two Snellen lines. Vision maintained unchanged for majority of the patients (65%, n=13). However, 15% (n=3) of eyes dropped one Snellen line, and 5% (n=1) of eyes decreased two

Table I: Demographic data

Demographic Data	n
No. of eye (No. of patients)	20 (18)
Mean age ± SD (years)	58 ± 16
Male : Female	9 : 9
Ethnicity, N (%)	
• Malay	13 (72.2%)
• Chinese	4 (22.2%)
• Indian	1 (5.6%)
Laterality of the eye	
• Right eye	12 (66.7%)
• Left eye	4 (22.2%)
• Both eyes	2 (11.1%)
Prior history of ocular glaucoma procedure	6 (33.3%)
• Trabeculectomy+ mitomycin C	3 (15%)
• Conventional TSCPC	3 (15%)
Visual acuity	
• 6/12 and better	5 (25%)
• <6/12 - 6/18 (early visual impairment)	0 (0%)
• <6/18 – 6/60 (moderate visual impairment)	1 (5%)
• <6/60 – 3/60 (severe visual impairment)	1 (5%)
• <3/60 (blind)	13 (65%)
Staging of glaucoma based on standard automated perimetry	
• Stage 1: early defect , mean deviation (MD) <-6 dB	3 (15%)
• Stage 2: moderate defect, MD -6 to -12 dB	1 (5%)
• Stage 3: advanced defect, MD -12 to -20 dB	0 (0%)
• Stage 4: severe defect, MD > -20 dB	2 (10%)
• Stage 5: end-stage defect	14 (70%)

Table II: Distribution of types of glaucoma

Types of glaucoma	n (%)
Neovascular glaucoma secondary to	10 (50%)
• Proliferative diabetic retinopathy	7 (35%)
• Retinal vein occlusion	2 (10%)
• Ocular ischemic syndrome	1 (5%)
Primary open angle glaucoma	4 (20%)
Steroid-induced glaucoma	2 (10%)
Juvenile open angle glaucoma	1 (5%)
Primary angle closure glaucoma	1 (5%)
Phacomorphic glaucoma	1 (5%)
Plateau iris syndrome	1 (5%)
Total	20 (100%)

Table III: Reasons of eye with treatment failure

Reasons	Number of eyes, n (%)
Glaucoma drainage device implantation	3 (18.8%)
Intraocular pressure	
• Static	3 (18.8%)
• Increased	1 (6.2%)
• Less than 20% reduction	1 (6.2%)
Three snellen lines vision loss and more	1 (6.2%)
Total	9 (56.2%)

Table IV: Comparison of mean IOP, IOP reduction, mean number of medications and percentage of patient on systemic medication among pretreatment (Tx), post Tx during each follow up at second week, sixth week, third month and sixth month

Duration post / treatment	0	2 weeks (W) ± 1W	6 weeks ± 3W	3 months (M) ± 6W	6 months ± 6W
Number of eyes	20	19	15	18	16
Mean IOP ± SD	43.0 ± 14.8	24.7 ± 12.0	33.8 ± 16.9	35.2 ± 14.9	29.0 ± 16.2
IOP reduction	0	18.3(42.6%)	9.2(21.4%)	7.8(18.1%)	14.0(32.6%)
Mean number of medication	topical 3.5 systemic 0.4	topical 3.5 systemic 0.1	topical 2.8 systemic 0.2	topical 2.6 systemic 0.1	topical 2.8 systemic 0
Patient on systemic medication (%)	35	26	20	11	0

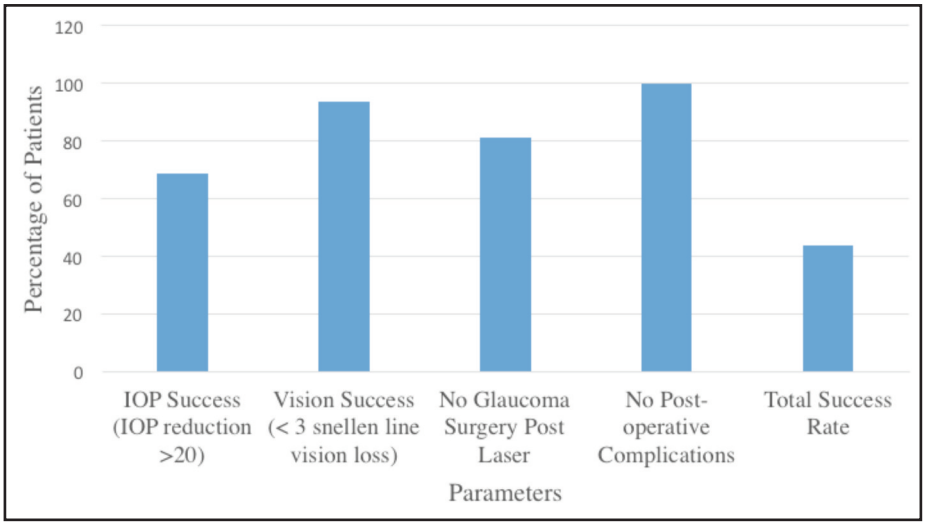

Fig. 1: Percentage of patients with intraocular pressure (IOP) success, vision success, no post laser surgery, no post-operative complications and total success rate.

Snellen lines. There was one eye (5%) with plateau iris syndrome that had visual deterioration by more than three lines from 6/12 to hand movement. Thirteen eyes (65%) pre-treatment vision was blind (range from hand movement to non-perception of light), two eyes had severe visual impairment and five eyes vision were 6/12 and better.

Out of the 20 eyes treated with SL-TSCPC, six eyes (30%) required further laser or surgical intervention for adequate IOP control; three eyes underwent glaucoma drainage device (Ahmed tube) implantation, with surgery proceeded for one eye two weeks post SL-TSCPC, while two eyes had surgery done three months post SL-TSCPC. Two eyes required re-treatment with subliminal TSCPC at four months post first laser treatment. Needling procedure was performed in one eye with advanced primary angle closure glaucoma after five months.

All patients developed slight conjunctival injection and anterior chamber inflammation post treatment. This resolved by the second week post-treatment in all patients following treatment with topical steroids. There was no serious ocular side effects documented during any of follow-up visits such as hyphaema, hypotony, scleral thinning, scleral perforation, sympathetic ophthalmia, and phthisis bulbi.

DISCUSSION

In this study, the success rate was 43.8% at six months follow-up. This success rate is lower compared to other studies such as Alice et al. who found that the success rate of micropulse TSCPC treatment was 66% at six months.9 Higher rates of treatment success were observed by Tan et al. and Aquino et al. who found that the success rate in MP-TSCPC treated eyes at 18 months was 80% and 52% respectively.[5,7] The lower success rate in our study population is attributed to a higher proportion of neovascular glaucoma among all our patients (50%) compared to other studies. Besides, different laser machine was used, all the above studies were using IRIDEX laser machine whereas Supra 810 laser machine was used in our study. Furthermore, five eyes underwent laser treatment with duty cycle of 25% as their vision was good or had a history of uveitis. Out of these five eyes, three eyes were in the treatment failure group which may be due to the lower delivered energy compared to that used in the above studies. Keilani et. al. study stated that SL-TSCPC at 31.3% duty cycle (83.5% success rate) is more effective than the 25% duty cycle SS-TSCPC (65% success rate).[11] One patient with phacomorphic glaucoma contributed to the failure rate as her refusal of cataract extraction left her IOP uncontrolled, due to unresolved pathology of the intumescent cataract. Our mean IOP reduction at six months post-treatment was 17.6mmHg which is similar to Lutic et al.'s study.8 Our study has shown that the subliminal TSCPC can maintain the IOP lowering effect for at least six months. This procedure can be repeated as it is not cyclodestructive and has limited collateral damage. The result of 43.8% success rate has shown to be similar to traditional TSCPC in Matthias et al. study which reported a 42% success rate (IOP 4-18 mm Hg, 20% IOP reduction, and no major complications) at a six month period.[12]

In this study, a drastic drop in IOP was seen in early visits followed by slight increment of IOP until the third month, where it then decreased to around 33% IOP reduction at six months post-treatment. The reduction in IOP seen is due to enhanced uveoscleral aqueous outflow as well as reduced aqueous humor production. Two studies have shown increased uveoscleral outflow post transscleral photocoagulation therapy over the pars plana area.[13,14] After that, the IOP increment during sixth weeks and third months post-treatment are due to the withdrawal of systemic and topical IOP lowering agents. In view of repeated procedures (additional SL-TSCPC laser and surgical interventions) were mostly performed three months post initial SL-TSCPC, the mean IOP at six months of follow-up is lower than mean IOP at six weeks and three months post initial treatment.

In the six months of follow-up post-treatment, the vision of majority of patients remained stable in this study. Only one eye (5%) had a decrease of more than three Snellen lines and one eye (5%) reduced two Snellen lines. Emanuel et al. study

reported 8.2% of patients experienced more than three Snellen lines loss at third month following MP-TSCPC treatment15 while 20% of eyes worsened by two or more lines in another study.[16] Our patient with plateau iris glaucoma that lost more than three Snellen lines of vision had significant cataract, development of central retinal vein occlusion with neovascular glaucoma secondary to uncontrolled IOP which further contributed to vision loss.

There was no serious side effect noted during follow-up such as prolonged inflammation, hypotony, scleral perforation, and phthisis bulbi. These results showed SL-TSCPC had a better safety profile compared to the traditional TSCPC. Thus, subliminal transscleral cyclophotocoagulation may provide an alternative option of bridging the gap between medical therapy and surgical options such as minimally invasive glaucoma surgery (MIGS), and traditional glaucoma-filtering surgery.

The limitations of this study include the small sample size and incomplete data collection as several patients defaulted on follow-up clinic visits. Patients with uneventful events after SL-TSCPC treatment are more likely to default clinic follow-up because of the logistic issues and waiting time in the clinic. As a result, bias may be introduced to the data leading to lower success rates and higher complication rates. Therefore, this study should be repeated with as a multicentre trial with larger sample size and longer study duration to determine the effectiveness, duration of the SL-TSCPC effect and detect late complications.

CONCLUSION

Subliminal TSCPC is a safe method to reduce the IOP in moderate to advanced glaucoma patients during this study's 6 month monitoring. Since it is a repeatable procedure, it can prolong the time for invasive glaucoma surgery in patients who refuse or not fit for surgery. It is an option for glaucoma patients that are refractory to medication and with good vision. With a good safety, efficacy profile and superior patient comfort during application, subliminal TSCPC can be offered as an alternative for patients with uncontrolled glaucoma who have difficulty in compliance to eye drops, or are unable to afford MIGS devices. However, patients should be well informed regarding possible complications that may occur.

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CONFLICT OF INTEREST STATEMENT

There is no any potential financial and non-financial conflicts of interest that could have appeared to influence the work reported in this paper.

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