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Efficacy and Safety of Micropulse Trans-Scleral Cyclophotocoagulation in Cambodian Patients with Glaucoma

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Abstract

Objective: To evaluate the treatment outcomes of micropulse cyclophotocoagulation in Cambodian glaucoma patients. Materials and Methods: 14 patients were enrolled in this retrospective study that was conducted with the consent over a 14-month period. The medical records were analyzed for variables such as intra-ocular pressure, the number of anti-glaucoma drugs used, visual acuity, pain level, and complications during and after treatment. The main outcome was whether or not there was success or failure, with success being defined as a pressure level between 6 and 21 mmHg and a 30% decrease in IOP by week 24 (with/without drugs). Results: In our study, the mean age of patients was 52.36 ± 9.98 years old (42 to 75 years old). The mean intra-ocular pressure before treatment was 41.00 ± 12.26 mmHg, which decreased to 21.60 ± 8.11 mmHg (41.56% reduction) and 16.94 ± 5.46 mmHg (56.04% reduction) in the 12th and 24th weeks ($p < 0.001$), respectively, with a success rate of 86%. Anti-glaucoma medications in average pre-treatment were 3.45 ± 0.89 (2 to 5 drugs), dropped to 1.85 ± 1.19 (1 to 3 drugs), and 1.46 ± 1.15 (none to 3 drugs) in weeks 12 and 24, with a mean reduction of 2, $p < 0.001$. The number of eyes with complications is limited to 3 (22.43%), but there has been no significant change in visual acuity. Conclusion: Micro-pulse trans-scleral cyclophotocoagulation is a safe and effective method for lowering pressure in any stage of disease without the use of invasive surgeries.

Keywords

Photocoagulation, Glaucoma, Efficacy, Safety, Intra-Ocular Pressure, Micro Pulse

1. Introduction

Glaucoma is one of the main causes of irreversible blindness worldwide [1] [2]. Glaucoma treatment involves the use of medicines, lasers, and surgical surgery to reduce pressure. When intraocular pressure is difficult to regulate with drugs, surgery is essential to protect optic nerve function. Alternatively, in glaucoma, laser therapy is increasingly becoming a method for improving intra-ocular pressure control and preventing additional damage to the visual nerves [1]-[3].

According to a global estimate given by the World Health Organization (WHO) in 2010, there are 39 million individuals worldwide who are blind and 285 million who have visual impairment. Overall blindness fell by 15.40% in 2020, according to WHO, but the number of people with visual impairment and avoidable blindness grew by 31.50% and 10.80%, respectively [2] [4]. Glaucoma is also responsible for 8.30% of Cambodia's avoidable blindness in 2019 [Rapid Assessment of Avoidable Blindness 2019].

MicroPulse® is a laser delivery modality for laser photocoagulation that allows for precision control of photo thermal effects [5]. Micropulse technology was used to denature the target tissue while reducing collateral tissue damage in a new type of trans-scleral diode laser cyclophotocoagulation (CPC). Several retinal illnesses, including diabetic retinopathy and maculopathy, have been successfully treated with micropulse diode laser technology. Based on its mechanism of action, micropulse diode laser CPC is expected to deliver IOP-lowering efficacy comparable to classic diode CPC without the pain and inflammation. The micropulse CPC is a revolutionary trans-scleral diode laser CPC platform that, in comparison to conventional CPC, has a higher safety profile. It has been mentioned in a number of current trending peer-reviewed articles and researches, making it one of the most reputable and reliable sources of clinical data [6]-[15], with IOP reductions ranging from 20% to 50%.

The micropulse CPC appears to be a promising new technology that offers excellent pressure control and a low risk of side effects. The goal of this study was to evaluate the micropulse CPC's treatment outcome in lowering glaucoma patients' pressures, as well as its effects on changes in pressure-lowering drugs required, pain experiences, and changes in visual acuity, frequency of complications, and its adverse effects in Cambodian glaucoma patients.

2. Materials and Methods

2.1. Study Site and Study Design

The study used a retrospective, observational chart review of all patients who had proceeded micropulse P3® cyclophotocoagulation (MP3 CPC) at the Department of Ophthalmology, Khmer-Soviet Friendship Hospital, Cambodia.

2.2. Study Population and Eligibility Criteria

A total of 14 out of 27 patients (14 eyes) were conveniently selected. This review investigated back over a period of 14 months, from 1st March 2018 to 1st May

2019. Cambodian patients with glaucoma (18 years old or older) who meet the following criteria are eligible: 1) inadequate control of IOP (22 mmHg or more) despite maximally tolerated medical therapy, 2) deterioration as a result of rapid progression of glaucomatous damages (as evidenced by fundus photography of the optic disc and/or peri-metric visual field status), 3) intolerance to medical therapy or poor compliance, 4) patient who is a poor candidate for filtering surgery. Exclusion criteria include 1) patients with significant scleral thinning (defined as thinning of more than one clock hour observed on scleral trans-illumination), 2) patients who had previously undergone conventional trans-scleral cyclophoto-coagulation, 3) patients who had any intraocular surgery within 2 months of enrollment, and 4) patients who refused retreatment for better intraocular pressure control after the failure of the first procedure.

2.3. Study Instruments

Medical records of the patients have been reviewed using the tools as structured questionnaires which were developed by the researcher based on previous literature reviews [6] [8] [9] [12]-[14].

2.4. Clinical and Therapeutic Measurements

Pre-procedure evaluation:

Age, sex, previous history, visual acuity, baseline pressure, anti-glaucoma drugs before treatment, etiology/severity of glaucoma, and slit-lamp examination findings, pain level, and complications associated with laser treatment were all collected from medical records.

- Visual acuity: Snellen E-chart was used to determine the best-corrected visual acuity (BCVA), which was then translated to LogMAR.
- Intraocular pressure at baseline: The air-puff tonometer was used to measure intraocular pressure at baseline and at each follow-up. The intra-ocular reading was taken from the scale and entered into the medical records. At the very least, the average of two measurements with a five-minute interval were collected.
- Anti-glaucoma drugs: Medical therapy was gradually reduced at first, and if pressure reduction was not achieved, the drugs were adjusted, beginning with oral acetazolamide.
- Glaucoma severity was rated using the *American Academy of Ophthamology*'s glaucoma severity scale in addition to visual field defects and/or clinically optic disc head examination.

Intra-procedure evaluation:

Pain grading: The amount of pain experienced by the patient was recorded and additional peri-bulbar anesthesia was administered as required intra-operatively. The severity of eye pain measured using the verbal analog scale was adopted from the earlier series [15]. Pain scoring was based on a verbal analog scale from previous studies [15] [16] being described as follow:

- None: no subjective feeling of pain.
- Mild: pain tolerable and not requiring the use of oral analgesia.
- Moderate: pain tolerable with regular use of oral analgesia.
- Severe: pain despite regular dosing of oral analgesia.

Post-procedure evaluation:

After surgery, patients were patched for one day and given tobramycin-dexamethasone ointment. All patients were given topical prednisolone acetate 1% (PredForte eye drop) six times daily for five days, as well as oral acetaminophen-caffeine 500 - 65 mg (Cafenol) for five days, as well as topical prednisolone acetate 1% and acetazolamide 250 mg (Diamox 250) 1 tablet three times daily for five days, as indicated, but were tapered post Most notably, topical prednisolone was reduced to four times per day in the first week following surgery, and then to once to three times per day as needed from weeks three to six. Prior to therapy, all required anti-glaucoma drugs were not discontinued and tapered with evidence of well-controlled pressure based on the clinician's judgment.

Clinical and therapeutic evaluation:

- The primary outcome measures were intraocular pressure at 1, 3, 6, 12, and 24 weeks after the intervention, changes in anti-glaucoma medication at 12 and 24 weeks, visual acuity at the final visit, complications and the need for any additional surgery within the 24-week timeframe, and pain experiences. The pressure was measured using the Goldmann Applanation Tonometer. Two measurements with a 5-minute gap were averaged. Best-corrected visual acuity was calculated using the Snellen chart and then converted to LogMAR. A vocal analog scale was used to assess pain.
- The follow-up period lasted from the first day after the treatment to six months afterward. The follow-up period included the first-day post-procedure to the 6 months postoperatively.

Criteria for success:

- IOP between 6 and 21 mmHg and at least a 30% reduction in IOP at the end follow-up (24 weeks) with or without IOP lowering medicines were considered successful. Any requirement for additional surgical operations, an increase in IOP at 12 weeks, any imminent complications, or an increase in anti-glaucoma drugs were all considered failures.
- A less than 30% reduction in IOP from baseline after 3 months on 2 consecutive follow-up visits separated by an interval of 1 week was the basis for the second treatment session. Re-treatment was performed at least 6 - 8 weeks (or on the 12^{th} weeks) after the first treatment session. The third treatment was carried out when necessary according to the same criteria as the second treatment.

2.5. Laser Setting

A treatment session of micropulse trans-scleral cyclophotocoagulation in the af-

fected eye, using the MicroPulse® P3 Glaucoma Device (MP3) powered by the CYCLO G6™ Glaucoma Laser System (IRIDEX Corp., Mountain View, CA, USA) [15].

The following laser settings were programmed: 2000 mW infrared diode laser with an average wavelength of 810 nm set on micropulse delivery mode; micropulse "on" duration 0.5 ms; micropulse "off" time 1.1 ms; duty cycle (percentage of each cycle during which the laser is on): 31.33% From 9:30 to 2:30 and 3:30 to 8:30, the laser probe was used in a continuous sliding or painting motion. At all times, the probe will be applied perpendicular to the limbs, with the edge of the probe directly on the limbs (fiberoptic tip at 1.5 - 2 mm posterior to the limbus). With these settings, the MP3 probe was swept with firm pressure across the upper hemisphere of the afflicted eye 1.5 - 2 mm posterior to the limbus in 10-second continuous sweeps for 90 seconds from the 9:30 to 2:30 position (superior hemisphere). These 10-second sweeps were then repeated across the lower hemisphere for 80 seconds (inferior hemisphere) from the 3:30 to 8:30 clock position for a total treatment time of 170 seconds. This equates to 62,500 micro-pulses given over a 0.5 ms on and 1.1 ms off period (duty factor 31.3%). Each eye received a total of 62.6 J of energy in this way. During application, there was no conventional procedure for the sweeping action (fast vs. slow). Any areas where past filtering operation had been performed were avoided. Regardless of iris color or glaucoma severity, no treatment duration will be modified. In the operating theatre, each case was performed by a single glaucoma specialist at a time. Before the procedure, 3 mL of 2 percent lidocaine hydrochloride 100 mg/5 mL of retro-bulbar anesthesia and 1 mL of peri-bulbar anesthesia were given.

2.6. Data Management and Analysis

Data was double-checked and entered Microsoft Excel 2016 (Windows 8), and STATA v. 14.2 was used for statistical analysis. Student's paired *t*-test and single-factor ANOVA were used to for analysis. Statistical significance was defined as a *p*-value of less than 0.05.

2.7. Ethical Considerations

The study followed the tenets of the Declaration of Helsinki, and was approved by the institutional review board of the University of Health Sciences, Cambodia and Khmer-Soviet Friendship Hospital. The patient detail was kept confidential and anonymous.

3. Results

A total of 27 patients (27 eyes) were enrolled in this study. Among those, 13 patients were excluded from the study including 1 patient treated with cyclocryocoagulation (CCC), 3 patients treated with G-Probe CPC, and other 9 patients being on the waiting list (**Supplemental Table S1**).

3.1. Baseline Characteristics

In this study, among 14 patients included into this study, there were 9 women (64%) and 5 men (36%). The mean age is 52.36 ± 9.98 years old (42 to 75 years old). In 14 eyes, there are 5 eyes are right sided (35.71%) and 9 eyes in the left (64.29%). 5 eyes (35.71%) have done phacoemulsification more than 6 months ago, while 2 eyes (14.29%) have done trabeculectomy +/− mitomycin-C augmented on the same laterality, and other 8 eyes (57.14%) have never done any intra-ocular intervention before. The primary open angle glaucoma comprises of the majority of the patients, 8 eyes (POAG, 57.14%), while 4 eyes are neo-vascular glaucoma (NVG, 28.57%) and 2 others are primary angle closure glaucoma (PACG, 14.29%). Supplemental Table S2 presents baseline characteristics.

Related to severity, 6 eyes were diagnosed as severe (42%), and 5 eyes (37%) as moderate and 3 eyes (21%) as mild. There were no severe cases in both PACG and NVG sub groups. There were 1 mild case and 1 moderate case in PACG as there were only 1 mild case and 3 moderate cases in NVG sub groups. By contrast, there were 6 severe cases in POAG, and 1 mild case and 1 moderate case.

3.2. Primary Outcome

The mean intra-ocular pressure before treatment is 41.00 ± 12.26 mmHg decreased to 21.60 ± 8.11 mmHg ($p < 0.001$), and 16.94 ± 5.46 mmHg ($p < 0.0001$) in 12th and 24th weeks, respectively, with success rate of 86%. In overall, pressure was reduced 41.56% and 56.04% in week 12 and 24, respectively (Figure 1). The mean IOP at 3- and 6-months post-treatment was significantly lower than the baseline IOP ($p < 0.001$), paired *t*-test (Supplemental Table S3).

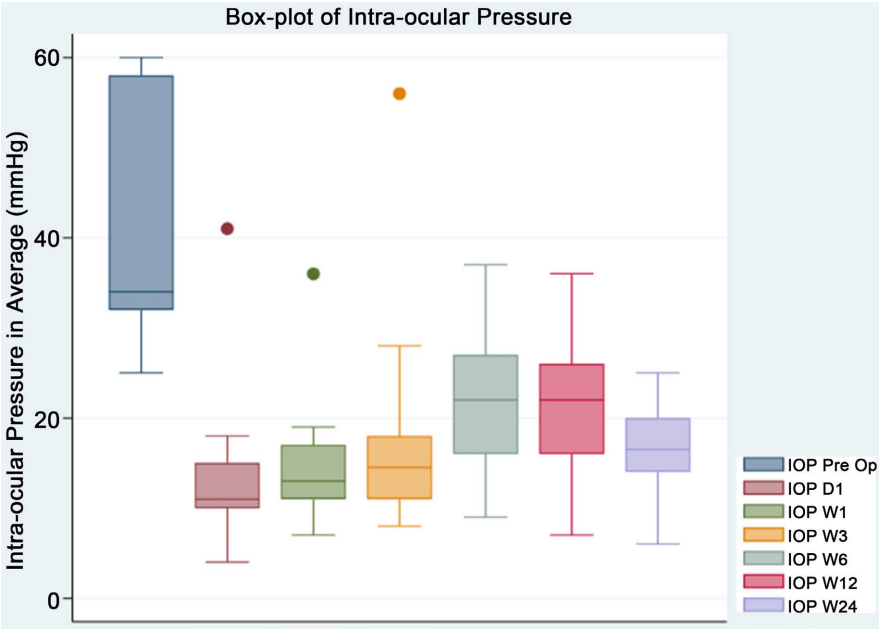

Figure 1. Mean IOP (± SD) progression curve in mmHg over the consecutive follow-up periods. The X-axis represents the different follow-up periods, and Y-axis represents mean IOP (±SD). IOP indicates intraocular pressure.

3.3. Secondary Outcomes

Effects on Anti-Glaucoma Drugs

Initially, number of drugs averaged 3.45 ± 0.89 (2 to 5 drugs) and reduced to 1.85 ± 1.19 (1 to 3 drugs, $p = 0.984$) and 1.46 ± 1.15 (none to 3 drugs, $p = 0.339$) in weeks 12 and 24, with a mean drug drop of 2, $p < 0.0001$ at all follow-up visits (Supplemental Table S4).

Pain Level, Visual Acuity, Complications, Retreatment and Success Rate

4 patients (28.57%) reported pain, all of which were tolerable and did not require any additional anesthesia. Only three patients (21.43%) reported mild pain on the first postoperative day, which resolved thereafter or until the end of week one. None of them were in moderate or severe pain.

Despite some changes throughout the study, there are no significant changes in visual acuity. Pre-treatment visual acuity ranged between 1.00 and 0.78 logMAR. At the final visit, none of the patients' vision had deteriorated.

There are only three complications (22.43%): 1 eye (7.14%) developed hyphema, 1 eye (7.14%) also developed choroidal effusion and 1 eye (7.14%) has vitreous hemorrhage. Those three patients experienced decreased vision but all of them regained BCVA back to the baseline after the complication eventually resolved.

All patients had mild post-operative inflammation at day 1 in the form of anterior chamber reaction 1+ with slight conjunctival hyperemia. These resolved by 2-week post-treatment in 11 eyes (78.57%). There were no cases of scleral perforation or thinning, prolonged anterior chamber inflammation (>2 weeks), phthisis bulbi, endophthalmitis or sympathetic ophthalmia.

However, in the remaining 3 eyes (21.43%) had persistent complications post procedure. In addition, 1 eye (7.14%) developed hyphema post laser (which is a patient with NVG) and resolved in 5 weeks' time post operatively. Another eye (7.14%) also developed choroidal effusion after laser and resolved in week 12 post procedure after an intense compensating treatment and resulted in stable and adequate pressure control and did not require any further laser session, whereas another eye (7.14%) developed a vitreous hemorrhaged, and the condition get totally resolved after 9 weeks of treatment.

Of the 14 patients treated with MP3 CPC, only 1 treated patient (7.14%) required further laser intervention (at a 15-week follow up visit) for adequate pressure control, and the pressure remained adequately low at the final visit. No eye received more than two treatment sessions. In average, throughout the period of study, all eyes required 1.07 sessions to achieve an adequate IOP control at 24-week follow-up. A retreatment session was contemplated no sooner than 3 months (12 weeks) after the initial treatment for patients who failed to respond on 2 consecutive follow-ups.

The number of patients with lowered pressure was up and down over the period of study. It started to remain stagnant, in which 12 out of 14 patients at day 1 post operatively, and this condition stayed stable for three consecutive fol-

low-ups until week 1, and it began to slow down to 86% (n = 12), 64% (n = 9), and 43% (n = 6) at weeks 3, 6, and 12, respectively. Finally, only 86% (n = 12) got the satisfying outcomes with at least 30% reduction of pressure from baseline at the end of the study, week 24.

Significantly, the success rate was 86% (n = 13) for the entire study period. After adjustment for diagnoses, the highest failure rate was observed in week 12 post-operatively, mainly due to the nature of high pressure prior to procedure (mostly more than 40 mmHg). The most lowering pressure effects were found amongst patients with mild to moderate glaucomas (8 out of 14 eyes). One patient (7%, n = 1) underwent a second treatment at 15-week follow-up, and the pressure was adequately under control since then. More severe eyes and/or significantly greater pressure before treatment tended to respond less than those in the early stages (Figure 2).

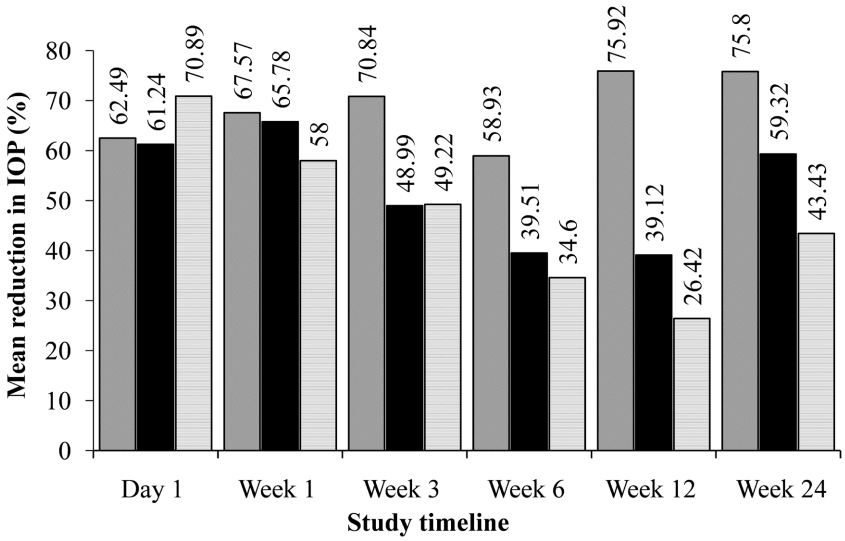

Figure 2. Mean reduction of IOP at various timeframes according to each severity sub-groups.

4. Discussion

This MP3 CPC was found to be both effective and safe in our retrospective study of patients with mild to severe glaucoma. The success rates varied, ranging from 100% at the 1-week follow-up to 43% at the 12-week follow-up and rising to 86% at the final follow-up (at 24 weeks). There were significantly decreased anti-glaucoma medications reported at variable follow-up periods, from 3.46 ± 0.84 at baseline to 1.46 ± 1.12 at 24-week follow up visits (mean drug drops, 1.93 ± 1.12, 55.83%). Only three patients developed complications, but none of them developed serious adverse effects following optimal treatment. Only one patient required a second session of laser treatment, and the pressure was soon under control.

Continuous-wave CPC has traditionally been designated for patients with advanced glaucoma and reduced visual potential, as well as for the relief of painful

eyes. As a result, it's been utilized to treat advanced refractory glaucoma as a last resort [16]. MP3 CPC has proven to be satisfactory for a long length of time in terms of lowering pressure and minimizing the need for anti-glaucoma drugs in glaucoma patients with a wide range of glaucoma severity. More recent trials, in particular, have focused on the safety and efficacy of MP3 CPC as a prospective therapy alternative for glaucoma patients with good visual acuity early in the course of the disease [17] [19]. Several studies have compared the success rate and safety profile regarding the application of MP3 CPC [6]-[9] [11]-[15] (**Supplemental Table S5**).

In a study by Aquino *et al.* [8] on 48 patients with refractory glaucoma, during the 18-month period, mean age are 63.50 years old and pressure mean drop was only 52% (from 36.5 to 20.0 mmHg, $p = 0.70$), and success rate was 52%. The setting was set to 2000 mW with 100 s in each hemisphere.

Tan *et al.* [15] also studied on refractory glaucoma. 40 eyes were included in the study during 18 months of follow up (mean length of 16.3 months) with same setting previously, but the success rate was higher than Aquino *et al.* but less than our study, 72.2% with 1.3 sessions in average. Mean age was 63.2 years old. Pressure mean drop was only 35% (from 40.1 ± 11.6 to 24.6 ± 9.1 mmHg, $p < 0.001$) and mean drug drop was 0.8, decreasing from 2.1 to 1.3 drugs).

By initial results of micropulse CPC in refractory glaucoma by Emanuel *et al.* [9] in 84 eyes during a shorter period, man follow up of 4.3 months. Mean age of patients was 74 years old. IOP mean drop was only 41.2% (from 27.7 ± 10.3 to 16.3 ± 9.5 mmHg, $p < 0.001$), and drug mean drop was 1.35 (3.3 reduced to 1.9 drugs) and these were less than our study. The main outcome in Emmanuel *et al.* was that the mean pressures were 15.5 mmHg and 18.0 mmHg at 6 and 12 months, respectively. Although the mean power in laser setting is similar to ours (1,999 mW vs. 2000 mW) but with longer duration (160 s vs. 80 - 90 s).

According to another study by Cecilia *et al.* [20] 14 patients with refractory glaucoma with mean age of 59.9 years old were included. The mean pressure drop was only 39% but in longer mean duration up to 78 months in total. The success rate was only 67% and mean drug drop was 0.7 (decreased from 1.8 to 1.1 drugs) in each patient. The setting was 2000 mW with 100 s applied to each hemisphere.

In a study of Kuchar *et al.* [6] in 19 eyes with refractory glaucoma, the success rate was quite similar to our study, comprising of 73.7% in 1st session of procedure, and this increased up to 89.5% within the 2nd session (repetition), with laser setting power remained the same as 2000 mW in average but with much longer period, 100 - 240 s. However, the follow-up duration is much less, as it was only 60.3 days in average comparing to our study, 6 months. Mean age of the patient was greater than ours (71.2 vs. 52.36 years old). Mean pressure drop was 41% throughout the study and mean drug drop was 1.35 (ranging from 2.6 to 1.9 drugs).

In another initial out report by Chew *et al.* [13] 12 eyes with mild to moderate glaucomas, achieved only 35.9% of pressure reduction while maintaining the

same setting as in our study. The mean follow-up length was 4.8 months, and this is shorter than in our study (at least 6 months). The patients have only mild to moderate stage with mean age 63.5 years old. The mean drug drop was 0.8 (reduced from 3.2 to 2.4 drugs, in average).

Lee *et al.* [7] studied on moderate to refractory glaucoma on 36 eyes achieved much similar success rate (72.2% vs. 84%) in much longer period (12 months). The laser power is identical but applied on longer duration (160 s vs. 80 - 90 s in each hemisphere). However, the mean pressure reduction was only 33.2% (from 28.41 ± 8.32 to 18.98 ± 6.45 mmHg), and this is less than that of our study, 56.04%. It is noted that the baseline pressure was lower but the final visit pressure was instead higher than ours.

Noeker *et al.* [12] also studied on mild to moderate glaucomas but on larger sample size, 95 patients. With the same laser power and duration as ours, they achieved only 30.3% pressure reduction (from 25.1 ± 5.3 to 17.5 ± 5.1 mmHg, $p = 0.004$) at mean follow up of 12 months. Another study by Radcliffe *et al.* [14] in mild to late-stage glaucomas, 48 eyes only achieve 29.8% reduction in pressure (from 25.8 to 17.1 mmHg, $p = 0.027$) in 3 months. Success rate was only 29.8% among all. Zaarour *et al.* [21] also reported in 75 moderate-to-severe glaucomatous eyes, with same setting (2000 mW, 90 s in each hemisphere), achieved 35.4% reduction of pressure (from 26.01 ± 6.92 to 14.78 ± 5.32, $p < 0.001$), and success rate as high as 66% in 15 months.

Strength and Limitations

It is one of Cambodia's first and most comprehensive studies on many aspects of current glaucoma laser therapy, including evidence-based treatment outcomes. Second, the inclusionary rule is strictly followed by the selection criteria. As a result, almost every patient who received this laser therapy during this time period required variables such as age, gender, glaucoma diagnosis and/or severity, laterality, or previous surgery history. The study also required complete data because no follow-up data from the subjects was lost during the 6-month period. Last but not least, because this is the first study of its kinds in Cambodia, and this procedure demonstrates to be reliable and safe for patients in various stages of glaucoma; this indicates the effectiveness of the novel non-invasive technique. However, its retrospective nature and small sample size were also drawbacks. Furthermore, the information was gathered at a single tertiary medical center. Some information was omitted, such as how drugs are counted differently between oral, topical, and fixed combination preparations. Furthermore, there was insufficient information about the family history of glaucoma-related conditions.

As a result, further research with a larger sample size and more randomly assigned sample size selection is required, as is a prospective evaluation of the MP3 CPC in additional tertiary centers. Furthermore, because our study only included data up to 6 months after treatment, future research will need to include a longer follow-up period to determine the success rate and longevity of laser

therapy, as well as the occurrence of late complications. Finally, the laser settings are pre-programmed and adhere to the IRIDEX guidelines.

As the MP3 CPC laser becomes more popular as a treatment modality, changes to treatment protocols (regarding power, duration of treatment, and/or method of treatment) may be required in determining improved efficacy and safety while maintaining a similar safety profile from the current studied protocols, despite some controversies. To summarize, a small sample size and a convenient sampling technique in nature may not effectively represent the completely defined outcomes of the entire population, but it may be representative of the effectiveness and additional in-depth insight of this laser therapy in a comparable setting within our study.

5. Conclusion

In glaucoma of any stage and/or type, micropulse cyclophotocoagulation is a safe and effective laser treatment for lowering pressure and avoiding more invasive surgical procedures. In comparison to other conventional laser procedures, the above-mentioned technique has the advantage of being repeatable, with a higher success rate and fewer intra-operative complications, all while providing improved safety and efficacy and, as a result, superior pressure management outcomes.

Conflicts of Interest

The authors declare no conflict of interest and declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplemental Table

Supplemental Table S1. Summarized evaluated parameters at consecutive follow-up visits.

Variables	Baseline	Day 1	Week 1	Week 3	Week 6	Week 12	Week 24
No. Eyes	14	14	14	14	14	14	14
Retreatment	-	0	0	0	0	0	1
Lost to follow-up	-	0	0	0	0	0	0
IOP Mean (SD) mmHg	41.00 (12.26)	14.29 (8.35)	14.65 (6.89)	18.32 (11.90)	22.51 (8.18)	21.60 (8.11)	16.94 (5.46)
Percentage of IOP decrease (%)	-	64.87	62.83	53.77	41.57	41.56	56.04
Percentage of patients with IOP decrease (%)	-	100	100	93	93	93	100
Percentage of procedure success (%)	-	100	100	86	64	43	86
No. anti-glaucoma drops mean (SD)	3.45 (0.89)	2.61 (0.91)	2.22 (1.06)	2.15 (1.10)	2.61 (1.12)	1.85 (1.19)	1.46 (1.12)
Mean BCVA (logMAR)	3.26	3.26	3.26	3.26	3.26	3.26	3.26

Supplemental Table S2. Patient's characteristics at baseline.

No. patients (number of eyes)	14 patients (14 eyes)
Age [mean (± SD)] (y)	62.36 (± 9.98)
Gender [n (%)]	
Female	9 (64.29%)
Male	5 (35.71%)
Laterality [n (%)]	
Right	5 (35.71%)
Left	9 (64.29%)
Diagnosis [n (%)]	
Primary open-angle glaucoma	8 (57.14%)
Primary angle-closure glaucoma	2 (14.29%)
Neovascular glaucoma	4 (28.57%)
Prior history of ocular procedures (n* = 15 eyes)	
None	8 (57.18%)
Prior trabeculectomy	2 (14.29%)
Prior cataract surgery	5 (35.71%)

*A patient previously received cataract surgery and trabeculectomy to control intra-ocular pressure in more than 6 months before proceeding micropulse cyclophotocoagulation.

Supplemental Table S3. IOP before and after micropulse diode laser trans-scleral cyclophotocoagulation.

Patient N°	Intra-ocular Pressure (mmHg)							Diagnosis
	Baseline	Day 1	Week 1	Week 3	Week 6	Week 12	Week 24	
1	41	11	12	12	16	16	15	NVG*
2	30	15	19	18	22	28	24	POAG**
3	32	15	15	15	15	16	6	NVG*
4	58	18	18	56	37	32	24	POAG*
5	60	41	36	28	24	19	18	NVG
6	30	18	13	15	37	26	17	NVG*
7	34	8	9	11	21	26	25	POAG**
8	58	15	11	14	27	10	16	PACG
9	45	4	8	8	9	7	10	POAG**
10	33	11	14	14	28	36	20	POAG**
11	34	9	7	11	10	25	17	PACG*
12	34	11	17	15	26	16	16	POAG**
13	60	11	11	10	22	14	9	POAG
14	25	10	13	27	19	25	14	POAG**
Mean	41.00	14.07	14.50	18.14	22.35	21.14	16.50	
(±SD)	(±12.72)	(±8.66)	(±7.15)	(±12.34)	(±8.49)	(±8.42)	(±5.66)	
p-value	-	<0.0001	<0.0001	<0.0001	0.0001	0.0005	<0.0001	

*It indicates the diagnosis in a moderate stage of glaucoma. **It indicates the diagnosis entity in an advanced or severe stage. The *p*-value was calculated using Student's paired t test of pressure at each visit comparing to the baseline pressure.

Supplemental Table S4. Mean number of anti-glaucoma drugs pre- and post-treatment with micropulse CPC.

No. Drug Required	Baseline IOP	Day 1	Week 1	Week 3	Week 6	Week 12	Week 24
Range (Min-Max)	2 - 5	1 - 4	1 - 4	1 - 4	0 - 4	0 - 3	0 - 3
Mean	3.45	2.61	2.22	2.15	2.16	1.85	1.46
(±SD)	(±0.89)	(±0.91)	(±1.06)	(±1.10)	(±1.12)	(±1.19)	(±1.12)
p-value	-	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Note: The average number of IOP-lowering medications pre-treatment was 3.45 ± 0.89. Treatment reduced the number of medications that need to control IOP at all post-procedural time points. The *p*-value was calculated using Student's paired t test of pressure at each visit comparing to the baseline pressure.

Supplemental Table S5. Evaluated parameters of different relevant peer-reviewed studies at consecutive follow-up visits.

Authors	Glaucoma severity	Sample size	Mean age ± SD (years old)	Laser setting (each hemisphere)	IOP (mean reduction, %)	Pressure at baseline (mmHg)	Pressure at final visit (mmHg)	*p*-Value	Reduction of anti-glaucoma drug (average)	Main outcome (Success rate)	Treatment sessions (mean)	Follow-up length
Out study	Mild to severe	14 eyes	62.36 ± 9.98	2000 mW (80 - 90 s)	56.04%	41.00 ± 12.26	16.59 ± 5.46	<0.001	2 (3.45 to 1.46)	84%	1.07	6 months
Aquino, *et al.*	Refractory	48 patients	63.5	2000 mW (100 s)	52%	36.5	20.0	0.70	-	52%	-	18 months

Continued

Emmanuel, *et al.*	Refractory	84 eyes	74 ±16	1939 mW* (319 s)*	41.2%	27.7 ± 10.3	16.3 ± 9.5	<0.001	1.35 (3.3 to 1.9)	-	-	4.3 months*
Kuchar, *et al.*	Refractory	19 eyes	71.2 ± 12.5	2000 mW (100 - 240 s)	41%	37.9	22.7	-	0.7 (2.6 to 1.9)	73.7% (1st) 89.5% (2nd)	-	60.3 days*
Cecilia, *et al.*	Refractory	14 patients	59.9 ± 15.7	2000 mW (100 s)	39%	43.3 ± 16.8	24.8 ± 11.0	-	0.7 (1.8 to 1.1)	67%	-	78 months*
Chew *et al.*	Mild to moderate	12 eyes	63.5 ± 15.7	2000 mW (100 s)	35.9%	22.3 ± 4.5	17.0 ± 3.4	<0.05	0.8 (3.2 to 2.4)	63.6%	-	4.8 months*
Zaarour, *et al.*	Moderate to severe	75 eyes	55.5 ± 22.9	2000 mW (90 s)	35.4%	26.01 ± 6.92	14.78 ± 5.32	<0.001	-	66.0%	-	15 months
Tan, *et al.*	Refractory	40 eyes	63.2 ± 16.0	2000 mW (100 s)	35%	40.1 ± 11.6	24.6 ± 9.1	<0.001	0.8 (2.1 to 1.3)	72.7%	1.3	16.2 months
Lee, *et al.*	Moderate to refractory	36 eyes	60.6 ± 17.7	2000 mW (160 s)	33.2%	28.41 ± 8.32	18.98 ± 6.45	<0.0001	0.5 (3.0 to 2.5)	72.2%	-	12 months
Noecker, *et al.*	Mild to moderate	95 patients	-	2000 mW (90 s)	30.3%	25.1 ± 5.3	17.5 ± 5.1	0.004	1.6 (3.0 to 1.4)	-	-	12 months*
Radcliffe, *et al.*	Mild to late-stage	48 eyes	-	2000 - 2250 mW (50 - 90 s)	29.8%	25.8	17.1	0.027	0.9 (3.3 to 2.4)	29.8%	-	3 months
Masis *et al.*	Mild to late-stage	57 patients	67.0 ± 9.4	2000 - 2500 mW (90 s)	28.9%	23.9 ± 8.0	17.0 ± 6.0	0.002	0.2 (3.5 to 3.3)	-	-	21.5 months*

*Calculated as mean.