• Clinical Research •

Efficacy and safety of micropulse laser trabeculoplasty for primary open angle glaucoma

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Abstract

• AIM: To evaluate the efficiency and safety of micropulse laser trabeculoplasty (MLT) for primary open angle glaucoma (POAG) patients.

• METHODS: Retrospective study. POAG patients undergoing MLT in Peking University Third Hospital from June 2016 to November 2017. Seventy-two eyes of 72 POAG patients were enrolled. Only one eye of each patient was treated by MLT. The intraocular pressure (IOP) before MLT and at 1d, 1, 4, 12 and 24wk and glaucoma medication before and after treatment were compared.

• RESULTS: The IOP was 20.6±5.9 mm Hg before MLT and 20.8±6.8 mm Hg at 2h after MTL. The IOP at 1d, 1, 4, 12 and 24wk was 17.9±4.4, 18.0±4.3, 17.5±3.4, 17.0±2.7, and 16.5±2.9 mm Hg, respectively. The IOP before and after MLT demonstrated a statistically significant difference by ANOVA analyses (F=5.797, P<0.001). Least significant difference t-tests showed there was no statistically significant difference between pre-MLT IOP within 2h after MLT (P=0.207). The statistically significant difference was confirmed between the pre-MLT IOP at 1d, 1, 4, 12 and 24wk after MLT (P=0.006, 0.009, 0.001, <0.001, <0.001, respectively). The number of glaucoma medications before MLT was 1.7±1.4 and 1.5±1.4 24wk after MLT with a significantly statistical difference (t=2.219, P=0.031)

• CONCLUSION: MLT is effective and safe for POAG patients. No patient experienced IOP spikes after MLT. The IOP 6mo after treatment decreased significantly with less glaucoma medication.

• **KEYWORDS:** micropulse laser trabeculoplasty; intraocular pressure; primary open angle glaucoma
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INTRODUCTION

Glaucoma is the first reported irreversible blindness disease in the world[1]. Currently, it can be treated by consistent use of glaucoma medication, laser, or surgery[2]. Long-term usage of hypotensive eye drops might be safe but need to be used several times a day. The ocular surface may be harmed by the preservative, and the reduction of the intraocular pressure (IOP) is limited to 30%, with IOP fluctuations occurring[3]. Surgery can achieve a lower IOP; however, there are risks and complications associated with surgery[4]. Laser therapy is more widely used because of its efficacy and safety[5-8].

Laser trabeculoplasty (LTP) for open angle glaucoma (OAG) includes Argon laser trabeculoplasty (ALT), selective laser trabeculoplasty (SLT), micropulse laser trabeculoplasty (MLT), and Titanium-Sapphire Laser Trabeculoplasty[5-10]. MLT technology, which was innovated 10 years ago, uses a duty-cycle algorithm that delivers subthreshold treatment to ocular tissues without scar formation[11]. MLT has been applied to the treatment of macular edema in retinal vein occlusion, diabetic retinopathy, and central serous chorioretinopathy[12-14], and is now used for the treatment of OAG[5-9]. MLT has a theoretical advantage over other laser therapies by not destroying the pigmented trabecular meshwork cells[11,15-17].

The purpose of this retrospective study was to evaluate the efficacy and safety of MLT on primary open angle glaucoma (POAG) patients. The IOP and glaucoma medications were compared before and after MLT.

SUBJECTS AND METHODS

Ethical Approval The study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Peking University Third Hospital (PUTH; No.2014166). All patients had been fully informed of the purpose and methods of the present study and provided written informed consent from themselves.

Subjects A series of Chinese POAG patients treated with MLT at Peking University Third Hospital Ophthalmology Department from June 2016 to November 2017 were enrolled. One eye of each patient was randomly treated by MLT.

This retrospective study included 72 eyes of 72 POAG patients, including newly diagnosed cases and cases with prior glaucoma medication. Inclusion criteria were as follows: 1) age>18y; 2) IOP>21 mm Hg; 3) open angle on gonioscopy (Shaffer grading >1 in 270); and 4) glaucomatous visual field loss and optic nerve fiber defects[11,15-17]. Cases were excluded if they involved angle closure, corneal pathologies, or if the patients had received prior laser trabeculoplasty.

Micropulse Laser Trabeculoplasty Therapy and Post Laser Management MLT was performed with the IRIS Medical OcuLight SLx 532 IQ Laser System (IRIDEX Corporation, Mountain View, CA, USA). Two drops of topical anesthesia (0.4% oxybuprocaine hydrochloride eye drops; Santen Pharmaceutical Co., Ltd., Osaka, Japan) was applied prior to MLT. No IOP-lowering drugs were used prior to MLT procedure. MLT was performed by the first author (Hong Y) with the same laser settings. Patients were seated at the slit lamp and a special MLT lens was placed on the eye to be treated with an inner face guide that allowed the surgeon to deliver exactly 10 confluent laser shots per clock hour. The MLT setting was 300 μm spot size diameter, 1 W power, 300ms duration with 15% duty cycle. The laser was carefully focused on the anterior trabecular meshwork and 120 laser spots were evenly distributed around 360° in the trabecular meshwork.

The IOPs at 2h, 1d, 1, 4, 12 and 24wk after MLT were recorded. IOP was always measured between 08:00 and 10:00 a.m. to minimize the effects of diurnal variations. Glaucoma medication was recorded at follow-up time points and adjusted by the IOP from 4wk post-MLT. The complications during and after MLT were observed. The complications included cornea side effects, hyphema, trabecular meshwork burn, peripheral anterior synechiae, and IOP spikes. An IOP spike was defined as an IOP increase of at least 5 mm Hg after MLT[18-19].

Statistical Analysis Statistical analyses were performed using SPSS, version 22.0 software (SPSS Inc., Chicago, IL, USA). The IOP and the numbers of antiglaucoma eye drops were presented as the mean±standard deviation (SD). Repeated measurement analysis of variance (ANOVA) was performed to compare the mean IOP at different follow-up time points to baseline. Post hoc LSD *t*-tests were performed to compare all pairs of independent variables. Paired samples *t*-tests were performed for the antiglaucoma eye drops before and after MLT. *P* values <0.05 were considered statistically significant.

RESULTS

Patients' Characteristics There were 72 eyes of 72 patients enrolled, including 42 male patients and 30 female patients.

Table 1 Pretreatment patient characteristics

Characteristics	Number
Gender	
M	42
F	30
Age (y, mean±SD)	48.7±17.8 (23-85)
BCVA (logMAR)	0.2±0.3 (0-1.0)
IOP (mm Hg)	20.6±5.9 (11-44)
Glaucoma medication	1.7±1.4 (0-4)
0	19 (26%)
1	9 (13%)
2	19 (26%)
3	16 (22%)
4	9 (13%)
Including	
β-blockers	3
PGs	6
PGs+β-blockers	9
PGs+α_2-agonists	3
α_2-agonists+CAI	3
PGs+CAI	4
PGs+β-blockers+α2-agonists	7
PGs+β-blockers+CAI	9
PGs+β-blockers+α2-agonists+CAI	9

BCVA: Best corrected visual acuity; PGs: Prostaglandins; CAI: Carbonic anhydrase inhibitors.

The average age was 48.7±17.8y with a range of 23-85y. The best corrected vision acuity (BCVA) was logMAR 0.2±0.3 (range 0-1.0), the IOP was 20.6±5.9 (range 11-44) mm Hg, with 1.7±1.4 glaucoma medications (range 0-4). The IOP was measured between 8:00 and 10:00 a.m. Glaucoma medications included β-receptor blockers, α-agonists, carbonic anhydrase inhibitors (CAI) and prostaglandins. Fixed combination medications were counted as two types of glaucoma medications (Table 1).

Intraocular Pressure IOP was 20.6±5.9 mm Hg before MLT and 20.8±6.8 mm Hg at 2h after MTL. The IOP at 1d, 1, 4, 12 and 24wk was 17.9±4.4, 18.0±4.3, 17.5±3.4, 17.0±2.7 and 16.5±2.9 mm Hg, respectively. The IOP before and after MLT demonstrated a statistically significant difference by ANOVA analyses (F=5.797, P<0.001). LSD *t*-tests showed there was no statistically significant difference between pre-MLT IOP at 2h after MLT (P=0.207) which indicated there was no IOP spike after MLT. The statistically significant difference was confirmed between the pre-MLT IOP at 1d, 1, 4, 12 and 24wk after MLT (P=0.006, 0.009, 0.001, <0.001, <0.001, respectively). However, the comparisons between the IOPs at 1d, 1, 4, 12 and 24wk after MLT did not show any difference (P=0.866, 0.693, 0.386, 0.165, respectively). The results indicated that the IOP was reduced 1d after MLT and

Table 2 The IOP before and after MLT

Parameters	Pre-MLT	2h post-MLT	1d post-MLT	1wk post-MLT	4wk post-MLT	12wk post-MLT	24wk post-MLT
Mean IOP (mm Hg)	20.6	20.8	17.9	18.0	17.5	17.0	16.5
SD (mm Hg)	5.9	6.8	4.4	4.3	3.4	2.7	2.9
Range (mm Hg)	11-44	11-45	10-32	11-31	12-30	12-23	10-22
P		0.207	0.006	0.009	0.001	<0.001	<0.001

Table 3 The summary of recent research

Research	No.	Study design	Diagnosis	Wavelength (μm)	Range (degree)	Reduction (%)	Side effect	Follow-up
Detry-Morel *et al*[9], 2008	16	Prospective	POAG/OH/PXG	810	180	12.2	None	3mo
Fea *et al*[15], 2008	20	Prospective	Uncontrolled OAG	810	180	21.3	IOP spike in one pigmentary glaucoma eye	12mo
Rantala and Välimäki[16], 2012	40	Retrospective	POAG/EG	810	180	17.4	None	Avg 12mo
Babalola[17], 2015	30	Retrospective	Medical uncontrolled OAG	810	180	17.2	Max IOP increased 4 mm Hg at 1h after MLT	Avg 160d
Lee *et al*[11], 2015	48	Prospective	POAG/NTG	577	360	19.5	None	6mo
Current study	72	Retrospective	POAG	532	360	19.9	None	6mo

OH: Ocular hypertension; PXG: Pseudoexfoliation glaucoma; POAG: Primary open angle glaucoma; EG: Exfoliation glaucoma; NTG: Normal tension glaucoma.

was maintained at a 19.9% IOP reduction at the 6mo follow-up (Table 2).

Glaucoma Medications The number of glaucoma medications before MLT was 1.7±1.4 (range 0-4), including β-blockers, α_2-agonists, prostaglandins, and CAI. Among them, 19 cases were initial POAG patients without any medication, 9 cases used one glaucoma medication, 19 cases had 2 medications, 16 cases had three medications, and 9 cases had 4 glaucoma medications. Six months after MLT, the number of glaucoma medications was 1.5±1.4 (range 0-4). Among them, the number of patients without glaucoma medications was 25, and the numbers with 1, 2, 3, or 4 kinds of glaucoma medications were 12, 9, 19, and 7 patients, respectively. The number of glaucoma medications was decreased after MLT with a significantly statistical difference (t=2.219, P=0.031).

Complications No intra- or postoperative complication occurred. In this study, the IOP of the patients' 2h post-MLT was 20.8±6.8 mm Hg without IOP spikes. There was no intraocular pain, postoperative inflammation, corneal infection, hemorrhage, or trabecular meshwork burning reported in our study.

DISCUSSION

Currently, LTP is one of the treatment options for POAG. Both ALT and SLT reduce the IOP and reduce the number of glaucoma medications used, so that some patients can eliminate the risk of surgery. However, ALT and SLT both may induce injury of the local trabecular meshwork, and IOP spikes after laser treatment may occur in some patients[5-8]. Recently, a newer laser therapy named MLT has been shown to reduce the IOP of POAG patients by 12.2%-21.3%[9,11,15-17].

The current study is a retrospective study in a single university hospital. In our study, the IOP before MLT was 20.6±5.9 mm Hg, and the mean IOP 2h post-laser therapy was almost the same, with a baseline IOP of 20.8 mmHg (P=0.207). No IOP spike after MLT treatment was confirmed, which differed from other laser trabeculoplasty reports showing that 7%-27% of the patients experienced IOP spikes after ALT and SLT[20-22]. The IOP decreased significantly from 1d after MLT and was stable until the 24-week follow-up. The number of glaucoma medications was decreased from 1.7 to 1.5, with a significant difference (P=0.031). These results suggest that MLT is effective in the treatment of POAG, and that there are no complications, including IOP spikes after MLT, which further indicate the safety of MLT. Recent MLT studies showed the efficacy of MLT in variable OAG ranged from 12.2% to 21.3%[9,11,15-17]. Detry-Morel *et al*[9] demonstrated that MLT may decrease the IOP of OAG patients up to 12.2%, while Fea *et al*[15] confirmed that the reduction of IOP was up to 21.3% after a 12-month follow-up in patients with uncontrolled OAG, including POAG and pigmentary glaucoma. The study of Rantala and Välimäki[16] showed MLT decreased the IOP of POAG and exfoliation glaucoma to 17.4% at a 6-month follow-up. The study of Babalola[17] found the IOP decreased 17.2% around 5mo after MLT. Lee *et al*[11] showed that 6mo after MLT for OAG and normal tension glaucoma, the IOP was reduced to 19.5%. The aforementioned studies showed variable IOP reductions, which might be induced by the different types of glaucoma and laser wavelengths (810 nm or 577 nm). There was almost no IOP spike or other laser complication in similar studies which is in accordance to our results (Table 3).

However, an IOP spike was the most common complication after SLT, which was not found in our study[20].

The mechanism of LTP is not fully understood. ALT could open the conduit through intervening perforations, but it causes visible histological changes including coagulation damage and scarring to the trabecular meshwork[21,23-26]. SLT was called "selective" for its targeting of pigmented trabecular meshwork cells, and histological studies showed there was minor coagulative damage and structural changes of the meshwork[24,27].

MLT uses a laser pulse with a duty-cycle algorithm to the ocular tissue without scar formation. A major advantage of MLT is the subthreshold therapy effect on the pigmented cells without the burning effect of the trabecular meshwork or damage to adjacent tissues[9]. The principle of LTP may be explained by several mechanisms, including the mechanical pulling open of the uveoscleral trabecular meshwork and Schlemm's canal, cellular mechanisms that stimulate cell division, and biochemical mechanisms that alter cytokines and stimulate the macrophage-like capacity of trabecular lining cells[21,23]. Current research favors a cellular biomechanical cascade[28]. The threshold of the laser-induced cellular cascade is unclear, but variable cells could be activated by a nonlethal thermal insult, which constitutes the principle of laser therapy. The higher photothermal effect may damage the adjacent tissues, as was seen by ALT or SLT. The gentle photothermal effect may be enough to trigger a cellular response without visible damage or complications during or after laser therapy. That could be why MLT reduced IOP, but without visible changes[11,15-17].

Another advantage of MLT is that it achieves its therapeutic aim by repetitive energy pulses, and not through continuous pulses, which allows the temperature of the trabecular meshwork to return to normal at the interpulse separations. There was no trabecular meshwork traction or shrinkage after ALT, or pigmented trabecular meshwork cell damage after SLT[27]. There was also no IOP spike or other complications after MLT, and the process could be repeated.

There was a lack of clinically visible morphological changes during or after MLT, which is quite different from the "bubble" appearance noted when performing SLT[11,16-17,20]. The lack of visible tissue changes constitutes a clinical challenge, because, in the absence of a visible endpoint, the treatment relies on the surgeon's skill, which could be a variable. We chose one surgeon (Hong Y) to perform all the MLT therapies to reduce any systematic errors.

A limitation of our study was the limited number of the patients and the limited follow-up time. The cases enrolled included primary cases and cases with medical treatments. The baseline IOPs of the patients varied, and the patients were on different preoperative medical treatments. There was also an absence of a control group. In the future, we will enroll more cases and follow-up for a longer time to better evaluate the efficacy and safety of MLT.

In summary, MLT reduced the IOP of POAG patients and the number of glaucoma medications without IOP spikes.

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