

Effect of the Transscleral Diode Laser Cyclophotocoagulation Treatment in Refractory Glaucoma Patients

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ABSTRACT

Purpose: Transscleral diode laser cyclophotocoagulation is preferred in patients refractory to medical and surgical treatment modalities. In our study, it was aimed to assess efficacy of diode laser cyclophotocoagulation in reducing intraocular pressure in refractory glaucoma patients.

Material and Methods: The study included patients followed with diagnosis of refractory glaucoma; newly diagnosed refractory glaucoma patients presented to our glaucoma clinic between January 2008 and May 2011. In all patients, visual acuity, intraocular pressure as measured by Goldmann applanation tonometry, findings of slit-lamp examination and fundus examination, glaucoma type, number of medications, previous glaucoma surgeries were recorded at baseline. In all patients, intraocular pressure was measured at baseline and on day 1, on week 1 and 6, and at month 3, 6 and 12 after treatment.

Results: The study included 49 of 49 patients (18 female, 29 male). Mean age was 61.4±12.8 years. In the study group, there were 25 patients (%51.2) with neovascular glaucoma, 9 patients (%18.4) with primary open angle glaucoma, 6 patients (%12.2) with primary angle closure glaucoma, 4 patients (%8.2) with pseudoexfoliation glaucoma and 5 patients (%10.2) with secondary glaucoma. Mean intraocular pressure was 44.1±11.3 mmHg at baseline, which reduced to 17.0±9.8 mmHg at year 1 (%63.4) (p<0.05). £22 mmHg intraocular pressure was achieved in 37 of 49 eyes (%75.5) while an intraocular pressure reduction by ≥30% from baseline was achieved in 33 of the 49 eyes (%87.8).

Conclusion: Transscleral diode laser cyclophotocoagulation is a safe and effective treatment modality for refractory glaucoma patients with poor prognosis and uncontrolled intraocular pressure with medical and surgical treatment modalities.

Keywords: Refractory glaucoma management, Intraocular pressure, Transscleral diode laser cyclophotocoagulation.

INTRODUCTION

The cyclodestructive procedures are alternative treatment modalities employed in refractory glaucoma cases with poor potential of vision in which conventional filtration surgeries or tube shunt interventions are failed and medical treatment cannot ensure desired reduction in intraocular pressure (IOP).¹ These methods basically lead reduction in humor aqueous production as a result of coagulation necrosis occurring stroma of ciliary body due to absorption of laser energy by pigment epithelium of ciliary body.² By reduction in IOP, the need for anti-glaucomatous treatment is decreased and it is also aimed to relieve headache due to elevated IOP. To date, many cyclodestructive methods

have been developed. Owing advances in technology, preliminary treatment modalities with high complication rates such as cyclectomy or cyclodiathermy have been replaced by safer procedures such as ND:YAG laser cyclophotocoagulation, diode laser cyclophotocoagulation and, recently advanced ultrasound cyclophotocoagulation. The laser energy was first use for cyclophotocoagulation as ruby laser in 1970s; subsequently, ND-YAG laser system was used via contact and non-contact route, followed by transscleral diode laser system applied via contact route. In recent years, the use of diode laser energy for endoscopic and micro-pulse transscleral cyclophotocoagulation is the latest advance.³

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Transscleral diode laser cyclophotocoagulation (TDLCP) has become increasingly during 1990s due to efficacy and safety with ease-to-use and portability.⁴ The TDLCP decreases humor aqueous production by inducing coagulation necrosis in ciliary epithelium via semi-conductive diode laser probe at wavelength of 810 nm; in addition, it increases uveoscleral efflux by enhancing permeability of ciliary body and sclera.⁵ The efficacy of TDLCP has been proven in many studies and it is currently used in clinical practice.³⁻⁴

In our study, it was aimed to reduce IOP by TDLCP in refractory glaucoma cases unresponsive to other therapeutic approaches with worsened quality of life and to assess efficacy of TDLCP.

MATERIAL AND METHOD

The study included glaucoma patients with uncontrolled IOP (IOP \geq 22 mmHg despite maximal medical treatment) who were followed at or presented to Glaucoma Clinic of Ophthalmology Department of Celal Bayar University, Medicine School between January 2008 and May 2011. The patients failed in previous filtration surgery, those ineligible for filtration surgery, patients declining surgical treatment, those with headache due to elevated IOP and those with visual acuity up to 0.5 were included. The study was approved by Ethics Committee.

Before laser treatment, data regarding age, gender, IOP, visual acuity, findings of slit-lamp examination and fundus examination, type of glaucoma, number of anti-glaucomatous drugs used and previous glaucoma surgery were recorded for all patients. The IOP was measured using Goldmann applanation tonometry at baseline and in control visits.

In all patients, following peribulbar anesthesia (2% lidocaine hydrochloride and 0.5% bupivacaine) and insertion of eyelid speculum, TDLCP was performed by transscleral application of laser energy (810 nm) via semi-conductive laser diode laser system (IRIS Oculight SLx, IRIS Medical Instruments Inc., Mountainview, CA, USA) using fiberoptic G probe at operating room. All probes were sterilized using ethylene oxide after every procedure. One probe was used for maximum 15 applications. The anterior margin of G probe was placed to border of limbus, positioning center of probe 1.5 mm beneath limbus in order to focus probe center over pars plicata of ciliary body (Figure 1). Initial laser settings were 1500 mW of power and 1500 msec of duration, which was gradually increased by 250 unit increments (maximum 2000 mW and 2000 msec) until pop sound indicating tissue destruction. After detection of pop sound, energy level returned to previous

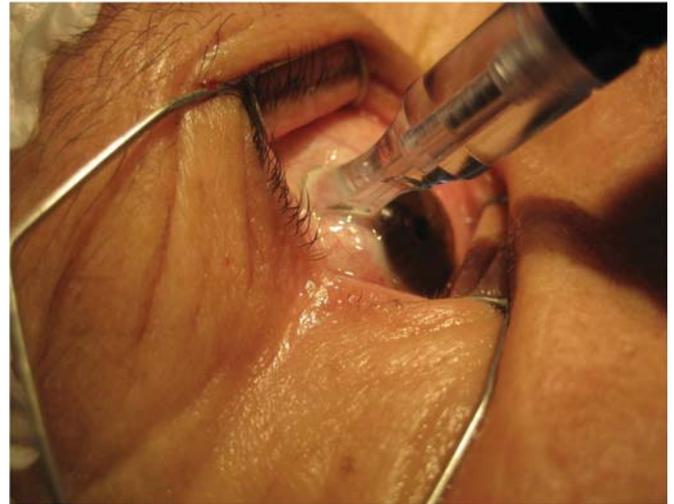


Figure 1: G probe application over eye.

level and laser application was completed at this energy level. If no pop sound was detected, laser application was completed at maximal settings (2000 mW and 2000 msec). In one session, overall 15-20 pulses were applied as being 5-6 pulses at each quadrant. Absence or presence of pop sound was recorded in all patients. The laser therapy was given to an area of 270 degrees by preserving 3 and 9 o'clock directions where long ciliary arteries are located; in patients with history of glaucoma surgery, area of previous surgery was preserved and laser therapy was given to an area of 180 degrees.

After laser treatment, the patients continued to use their anti-glaucomatous medications which was tapered based on IOP monitoring during follow-up visits. A topical steroid agent (prednisolone, 4x1 over 15 days) and a cycloplegic agent (cyclopentolate, 3x1 over 15 days) were prescribed to patients. Patients developing uveitis after laser treatment maintained topical steroid and cycloplegic agents over one month.

According to study protocol, IOP was measured at baseline and on day 1, on week 1 and 6, and at months 6 and 12. The clinical course was monitored by IOP and, when needed, a second session was applied minimum 6 weeks after first session. The success criteria was defined as IOP \leq 22 mmHg or $>$ 30% IOP reduction from baseline regardless of topical anti-glaucomatous treatment. The IOP \leq 5 mmHg was defined as hypotonia.

Statistical analyses were performed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). Data are presented as mean \pm standard deviation. For repeated variables in the groups, normality was tested using Kolmogorov-Smirnov test. Variables with normal distribution were analyzed using ANOVA while those with

skewed distribution were analyzed using Kruskal-Wallis test. Paired samples t test was used to compare pretreatment and post-treatment results. A p value <0.05 was considered as statistically significant.

RESULTS

Demographics

Mean age was 61.4±12.8 years. In the study, 49 eyes of 49 patients (32 men, 17 women) were treated. Most common type of glaucoma was neovascular glaucoma (NVG) detected in 25 patients (51.2%). Mean follow-up duration was 12 months. Of the patients, 26.5% (n=13) had previous history of glaucoma surgery. Table 1 summarizes demographic findings. A second session of treatment was applied in 7 patients (14.3%) who experienced IOP elevation following varying intervals after first session.

Intraocular Pressure

Mean IOP was measured as 44.1±11.3 mmHg at baseline whereas 28.4±10.8 mmHg on day 1, 24.3±13.3 mmHg on week 1, 24.5±12.1 mmHg on week 6, 21.3±11.5 mmHg at month 3, 18.4±9.6 mmHg at month 6 and 17.0±9.8 mmHg at year 1 after TDLC. The IOP reduction was found to be statistically significant for each time point (p <0.005) (Table 2).

In whole study population, the IOP was decreased to ≤22

Table 1: Demographic characteristic of patients underwent TDLC.

Characteristic	Count (n)	Percent (%)
Gender		
F	17	34.6
M	32	65.3
Eye		
Right	25	51.0
Left	24	48.9
Diagnosis		
NVG	25	51.2
POAG	9	18.4
PNAG	6	12.2
PEX	4	8.2
Secondary	5	10.2
Traumatic	3	6.1
Aphakic	1	2.0
Silicone-related	1	2.0
Surgery		
Trabeculectomy	11	22.4
Molteno tube	2	4.0

TDLC: Transscleral Diode Laser Cyclophotocoagulation, NVG: Neovascular Glaucoma; POAG: Primary open-angle glaucoma, PNAG: Primary narrow-angle glaucoma, PEX: Pseudo-exfoliation glaucoma, F: Female, M: Male

mmHg in 37 of 49 eyes (75.5%) while ≥30% IOP reduction from baseline was observed in 43 of 49 eyes. Table 3 presents success rate according to glaucoma subtypes.

Table 2: Success rate in glaucoma subtypes.

Glaucoma type	Number of patients (n)	IOP ≤ 22 mmHg	IOP ≤ %30
NVG	25	19/25 (%76)	23/25 (%92)
POAG	9	6/9 (%66.7)	7/9 (%77.8)
PNAG	6	5/6 (%83.3)	5/6 (%83.3)
PEX	4	4/4 (%100)	4/4 (%100)
Secondary	5	3/5 (%77.8)	5/5 (%100)
Traumatic	3	2/3 (%66.6)	3/3 (%100)
Aphakic	1	0/1(%0)	1/1 (%100)
Silicone-related	1	1/1 (%100)	1/1 (%100)

IOP; Intraocular pressure, NVG: Neovascular Glaucoma; POAG: Primary open-angle glaucoma, PNAG: Primary narrow-angle glaucoma, PEX: Pseudo-exfoliation glaucoma.

Table 3: Mean energy level used in patients achieved ≤22 mmHg IOP and ≥30% IOP reduction at year 1.

	Energy given(J)	p value
IOP≤22 mmHg (37/49)	60.7±23.0	0.593
IOP≥22 mmHg (12/49)	56.7±20.5	
IOP≤%30 (33/49)	60.8±21.8	0.614
IOP≥%30 (16/49)	57.4±23.9	

P <0.05 was considered as statistically significant, IOP: Intraocular pressure, Independent t test

Mean IOP value was decreased from 44.8±11.6 mmHg at baseline to 15.5±11.15 mmHg in patients with NVG (p=0.000) whereas it was decreased from 46.4±11.4 mmHg to 22.6±5.9 mmHg in patients with POAG (p=0.001). In remaining glaucoma subtypes, no statistical analysis was performed due to limited number of patients in the groups.

Laser Parameters

Mean energy used was 59.7±22.3 J. No significant correlation was found between energy given and ≤22 mmHg IOP or ≥30% IOP reduction from baseline (Table 4). Again, no significant correlation was detected between energy given and extent of IOP reduction (p=0.101) or final IOP value (p=0.092). All patients underwent 270° treatment except 9 patients underwent 180° treatment. The pop sound was recorded in 27 patients (55.1) while no pop sound was recorded in 22 patients (44.9%). No significant correlation was detected between pop sound and IOP reduction (p>0.05).

Anti-glaucomatous agents

Mean number of anti-glaucomatous agents was 1.8±0.9 before laser treatment and decreased to 1.3±1.0 after laser treatment, indicating significant difference (p=0.000). No change was observed in the number of anti-glaucomatous agents in 24 patients while it was decreased by one drug in 15 patients (30.6% and by 2 drugs in 7 patients (14.3%).

Visual acuity

At baseline, visual acuity was P (-) in 28 patients (57.1%), P (+) in 8 patients (16.3%), hand movement in 5 patients (10.2%), finger counting at 1 meter in 2 patients (4.1%) and ≥0.1 in 6 patients (12.2%). After laser therapy, it was decreased from hand movements to P (-) level in one patient while no change was observed in patients with visual acuity of P (+), finger counting at 1 meter and ≥0.1

Table 4: Complication rates following TDLCP.

Complication	Count (n)	Percent (%)
Hyphema	5	10.2
Hypotonia	7	14.2
Uveitis	3	6.1
Phthisis	3	6.1
Corneal epithelium defect	2	4.0
Decreased visual acuity	1	2.0
Bullous keratopathy	1	2.0
Corneal perforation	1	2.0

TDLCP: Transscleral Diode Laser Cyclophotocoagulation

at baseline. When considering whole study population, overall loss of vision was 2.0%.

Complications

No complication was detected in 30 patients (61.2%) while several complications, mainly hypotonia, were observed in 19 patients (38.7%) (Table 5). Of 7 patients with hypotonia, phthisis was developed eventually in 3 patients (6.1%). Corneal perforation occurred following TDLCP in one of 3 patients with phthisis (2.0%) and corneal tissue was repaired using tissue adhesives and ocular integrity was preserved. All patients with hyphema had NVG and hyphema was regressed by medical treatment and rest. . The patient with bullous keratopathy had previous history of failure in trabeculectomy surgery and anterior chamber was shallow with endothelial contact before laser therapy. No significant correlation was detected complications and energy level used or presence of pop sound.

DISCUSSION

TDLCP has become increasingly popular and accepted modality of treatment over last 2 decades due to its high efficacy in refractory glaucoma patients as well as being feasible and repeatable.⁶ The aim of the treatment is to reduce IOP with minimal damage in surrounding tissues than those in other cyclodestructive procedures. It seems that effectiveness of laser energy depends on melanin absorption.⁷

Table 5: The TDLCP success rate and IOP reduction rates in the literature.

Study	Success rate (%)	IOP reduction rate (%)
Iliev & Gerber ⁴	69.5	55
Bloom et al. ⁸	69	41
Ansari & Gandhewar ¹²	82	45.1
Vernon et al. ¹³	88.1	50.3
Grueb et al. ¹⁴	36.7	23.8
Shah et al. ¹⁵	82.1	51.2
Kramp et al. ¹⁶	76.4	21.5
Pucci et al. ¹⁷	76	35
Noureddin et al. ¹⁸	72.2	53
Murphy ve ark. ¹⁹	79.5	52.6
Schlote et al. ²⁰	32.8	74.2
Sahin et al.	75.5 / 87.8	61.5

TDLCP: Transscleral Diode Laser Cyclophotocoagulation, IOP: Intraocular pressure

In this prospective study, we defined success criterion as IOP reduction to 22 mmHg or below regardless of anti-glaucomatous medication or $\geq 30\%$ IOP reduction from baseline. In the literature, success criterion was defined as either ≤ 22 mmHg or $\geq 30\%$ IOP reduction alone in some studies while both 22 mmHg and $\geq 30\%$ IOP reduction were used as success criterion.⁸⁻¹¹⁻¹³

In the literature reporting long-term outcomes for TDLCP success rate ranged from 36.7% to 88.1%.^{13,14} In our study, mean IOP value was decreased from 44.1 \pm 11.3 mmHg at baseline to 17.0 \pm 9.8 mmHg at year one (61.5%). In our study, the IOP was decreased to 22 mmHg or below in 37 of 49 eyes treated (75.5%) in agreement with literature. Again, IOP was decreased by 30% or more from baseline in agreement with literature (Table 6). In the series presented in the table, there is a remarkable difference among success rates although successful outcomes were shown with TDLCP in these studies. Thus, direct comparison of percent IOP reduction will provide more valuable information regarding efficacy of the procedure.

In our study, we used laser energy titrated according to pop sound for each patient, rather than a standard treatment protocol. The pop sounds micro-blowout in uveal tissue and occurs as a result of bubble-up of fluid within tissue.²¹ An increase was reported incidence of postoperative iridocyclitis by increased pop sounds.⁷ It is undesired since excessive destruction in ciliary body may result in

complications such as hypotonia or phthisis. On the other hand, there are studies identifying a standard treatment procedure.^{13,18} In our study, mean energy used was 59.77 \pm 22.3 J in first session and no significant correlation was observed between energy level and IOP ≤ 22 mmHg or $\geq 30\%$ IOP reduction. Similarly, laser energy level ranged from 30 J to 126 J in many studies in the literature.^{18,22} Kaushil et al. proposed that standard parameters cannot be used in TDLCP therapy and that energy requirement will change based on race, degree of pigmentation and glaucoma subtype. Authors reported success rate of 78% and re-treatment rate of 16.7% by 87.8 J energy in average, attributing these rates to lower energy requirement due to extensive pigmentation in Indian race.²³ In our study amount of energy given in first and second sessions were lower when compared to the literature; however, success rate was considerably high in our study, This seems to support hypothesis of Kaushik et al. who proposed that lower energy levels may be sufficient in races with extensive pigmentation.²³

As similar to other cyclodestructive procedures, NVG is the major indication for TDLCP. Moreover, in some studies, it was reported that the greatest IOP reduction and lowest complication rate were achieved by diode laser in patients with NVG.^{8,20,24} In our study, $\geq 30\%$ IOP reduction was achieved in 23 (92%) of 25 patients with NVG. In NVG subpopulation, mean IOP reduction was 29.3 mmHg at year 1 when compared to baseline, indicating

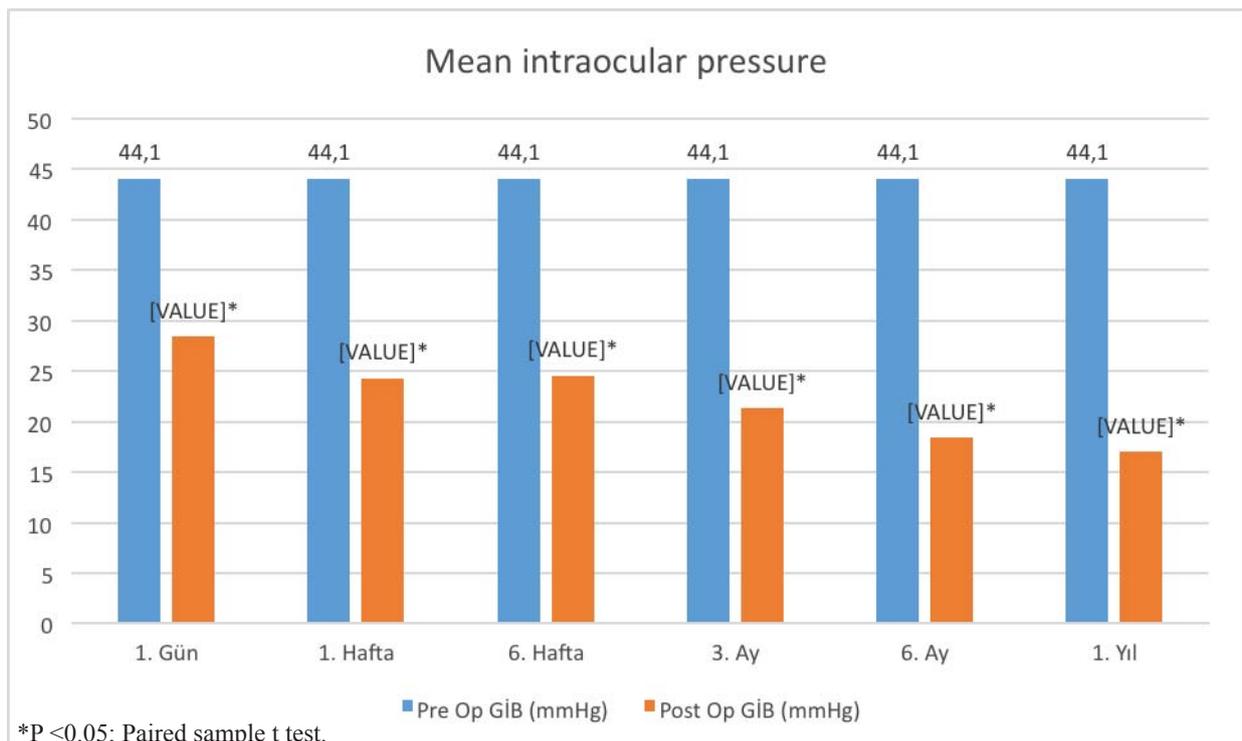


Figure 2: Amount and percent of IOP reduction at different time points when compared to baseline.

statistically significant reduction. This finding is in agreement with literature and supports the hypothesis that TDLCP is choice of cyclodestructive treatment in patients with NVG. In recent years, combined treatments have been used by taking advantage of rapid effect of intravitreal bevacizumab on anterior segment neovascularization in addition to IOP lowering effect of TDLCP. In studies on TDLCP plus intravitreal bevacizumab combination, it was suggested that the combination treatment will provide symptomatic relief by rapid control of anterior segment neovascularization and IOP in NVG treatment.²⁵ On the other hand, in a recent study comparing TDLCP alone and TDLCP plus intravitreal bevacizumab for IOP reduction in patients with NVG, it was found that TDLCP alone group (11 patients) achieved IOP reduction by 33.5% while TDLCP plus intravitreal bevacizumab group (20 patients) achieved IOP reduction by 23.7%, indicating that TDLCP alone was effective and addition of intravitreal bevacizumab caused no significant change in treatment outcomes.²⁶

Different outcomes have been reported in other glaucoma subtypes. In POAG, success rate varies from 89.5%²⁰ to 73.3%.²⁴ In our study, the success rate was found as 66.7% for ≤ 22 mmHg IOP and 77.8% for $\geq 30\%$ IOP reduction in 9 patients with POAG. In POAG subpopulation, mean IOP reduction was 23.8 mmHg at year one when compared to baseline, indicating significant reduction. In a study comparing TDLCP and cyclocryotherapy in patients with POAG, both methods provided mild IOP reduction by low complication rate.²⁷ There is a relative scarcity for outcomes in PNAG; in one study, success rate was reported as 66.7%.²³ In our study, success rate was found as 83.3% for PNAG. Similarly, in 4 patients with PEX glaucoma, success rate was 100% by both criteria, which is higher than those (54.5-66.7%).^{4,20} In a study on 66 patients with POAG and 24 patients with PEX treated with TDLCP, the success rate was reported as 40.9% and 25%, respectively, and no serious complication was observed, suggesting that diode laser therapy may be choice of surgical treatment in these glaucoma subtypes.¹⁴ It was reported that TDLCP is relatively limited in secondary glaucoma subtypes such as traumatic, aphakic or silicone-related glaucoma.

Experimental studies showed that ciliary body atrophy develops approximately 4 weeks after cyclophotocoagulation.²⁸ In many studies, it was reported response to TDLCP takes 4-6 weeks.^{19,20,23} In our study, second session decision was made according IOP elevation to baseline levels during follow-up and none of the patients underwent second session of TDLCP before week 6. Successful response was achieved in all patients underwent

second session and no other session was required. In the literature, it was reported that diode laser can be applied up to 6 sessions in adult patients.¹³

In TDLCP, decreased visual acuity is one of the most concerning complications. In our study, rate of visual acuity loss was found as 2.0%, which rather low when compared to literature. This might be due to fact that visual acuity was hand movement or poorer in 83.6% of patients. Five patients with persistent IOP elevation despite maximal drug therapy and visual acuity ranging from 0.1 to 0.4 were included to the study due to lack of alternative treatment option and no visual acuity reduction was observed in any of these patients. Another reason for lower rate of visual acuity loss was balanced energy titration as a result of individualized protocol rather than standard treatment protocol. In a recent, remarkable study, efficacy and safety of TDLCP was investigated in patients developed refractory glaucoma following penetrating keratoplasty and it was reported that visual acuity improvement was reported in 81% despite poor visual acuity at baseline.²⁹ In another study, TDLCP was applied to a group of patients with visual acuity $>20/40$ and uncontrolled IOP by medical therapy or filtration surgery and visual acuity loss of ≥ 2 lines was observed in 33.3%.³⁰ This rate is similar to those previously reported with tube surgery (32%) and trabeculectomy (33%), emphasizing that advantages of TDLCP such as easy application, lack of intraoperative complications and being choice of treatment in older individuals in whom filtration surgery and glaucoma drainage implant are contraindicated.³¹

It is desired to achieve reduction in number of topical agents following TDLCP therapy.^{8,13,14,17,20,33} In our study, there was a decrease in the number of drugs used in agreement with literature.

Attempting to reduce IOP by decreasing aqueous secretion is associated with risk for hypotonia. In the literature, it was shown that risk for hypotonia and phthisis is directly associated with laser energy given during treatment.¹³ Hypotonia and phthisis are uncommon in protocols using <60 J energy in each session while they become more common in protocols using >60 J energy.¹³ In our study, rates of hypotonia and phthisis were relatively high according to mean energy level of 59.7 ± 22.3 J used in the treatment and no significant correlation was observed between hypotonia and energy used. The finding that hypotonia rate was higher than expected despite mild laser energy parameters used initially and individualized treatment may be attributed to cycloablation applied $>180^\circ$ at first session. In another study, treatment was given with

180° in patients with baseline IOP<25 mmHg while it was given with 270° in patients with IOP>25 mmHg and no case of hypotonia was observed [24]. The mean IOP was 36.4 mmHg in patients developed hypotonia in our study and none had baseline IOP<25 mmHg. In a study comparing micro-pulse TDLCP targeting ciliary body pigment epithelium and continuous wave TDLPC, it was reported that both methods were effective in reducing IOP but micro-pulse TDLCP is method with more consistent and predictable outcomes but complications such as hypotonia and loss of visual acuity are still observed despite lower rates.³² In conclusion, the overreaction against TDLCP and hypotonia development cannot be predicted at individual level; however, low energy level and less treatment will decrease risk for hypotonia and it should be considered that treatment response can be lower in these cases.

HypHEMA, another complication was reported to be 0.7-1.6% in the literature²⁴ while it was found as 10.2% in our study. All cases developed hypHEMA had NVG subtypes and it was an expected complication in eyes with rubeosis iridis.

In our study, bullous keratopathy was observed in one patient (2.0%), which hasn't been reported in the literature so far. We think that bullous keratopathy was a complication secondary to previous trabeculectomy and chronic IOP elevation rather than being associated with TDLCP; since anterior chamber was shallow with endothelial contact before laser therapy in the patient.

In conclusion, our study supports that TDLCP is an effective, safe and non-invasive method to decrease IOP in patients with advanced, refractory glaucoma who cannot be controlled IOP despite medical and surgical treatments and have limited visual prognosis, intolerability to filtration or shunt surgery and poor quality of life due to headache secondary to IOP elevation.

REFERENCES

1. European Glaucoma Society. Terminology and guidelines for glaucoma. 4. Savona: Publi Comm; 2014.
2. Feldmann RM, El-Harazi SM, LoRusso FJ, et al. Histopathologic findings following contact transscleral semiconductor diode laser cyclophotocoagulation in a human eye. *J Glaucoma*. 1997;6:139-40.
3. Dastiridou AI, Katsanos A, Denis P, et al. Cyclodestructive Procedures in Glaucoma: A Review of Current and Emerging Options. *Adv Ther*. 2018;35:2103-27.
4. Iliev M E, Gerber S. Long-term outcome of trans-scleral diode laser cyclophotocoagulation in refractory glaucoma. *Br J Ophthalmol* 2007;91:1631-5.
5. Mistbelger A, Liebman JM, Tschiderer H, et al. Diode laser transscleral cyclophotocoagulation for refractory glaucoma. *J Glaucoma* 2001;10:288-93.
6. Kosoko O, Gaasterland DE, Pollack IP, et al. The Diode Laser Ciliary Ablation Study Group. Long-term outcome of initial ciliary ablation with contact diode laser transscleral cyclophotocoagulation for severe glaucoma. *Ophthalmology* 1996;103:1294-302.
7. Rebolledo G, Munoz FJ, Murube J. Audible pops during cyclodiode procedures. *J Glaucoma* 1999;8:177-83.
8. Bloom PA, Tsai JC, Sharma K, et al. "Cyclodiode". Trans-scleral diode laser cyclophotocoagulation in the treatment of advanced refractory glaucoma. *Ophthalmology* 1997;104:1508-19.
9. Spencer AF, Vernon SA. "Cyclodiode": results of a standard protocol. *Br J Ophthalmol* 1999;83:311-6.
10. Pucci V, Marchini G, Pedrotti E, et al. Transscleral diode laser cyclophotocoagulation in refractory glaucoma. *Ophthalmologica* 2001;215:263-6.
11. Egbert PR, Fiadoyor S, Budenz DL, et al. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. *Arch Ophthalmol*. 2001;119:345-50.
12. Ansari E, Gandhewar J. Long-term efficacy and visual acuity following transscleral diode laser photocoagulation in cases of refractory and nonrefractory glaucoma. *Eye* 2007;21:936-40.
13. Vernon SA, Koppens JM, Menon GJ, et al. Diode laser cycloablation in adult glaucoma: long-term results of a standard protocol and review of current literature. *Clin Exp Ophthalmol*. 2006;34:411-20.
14. Grueb M, Rohrbach JM, Bartz-Schmidt KU, et al. Transscleral diode laser cyclophotocoagulation as primary and secondary surgical treatment in primary open-angle and pseudoexfoliative glaucoma. Long-term clinical outcomes. *Graefes Arch Clin Exp Ophthalmol*. 2006;244:1293-99.
15. Shah P, Lee GA, Kirwan JK, et al. Cyclodiode photocoagulation for refractory glaucoma after penetrating keratoplasty. *Ophthalmology* 2001;108:1986-91.
16. Kramp K, Vick HP, Guthoff R. Transscleral diode laser contact cyclophotocoagulation in the treatment of different glaucomas, also as primary surgery. *Graefes Arch Clin Exp Ophthalmol* 2002;240:698-703.
17. Pucci V, Tappainer F, Borin S, et al. Long-term follow-up after transscleral diode laser photocoagulation in refractory glaucoma. *Ophthalmologica* 2003;217:279-83.
18. Noureddin BN, Zein W, Haddad C, et al. Diode laser transscleral cyclophotocoagulation for refractory glaucoma: a 1 year follow-up of patients treated using an aggressive protocol. *Eye* 2006;20:329-35.
19. Murphy CC, Burnett CA, Spry PG, et al. A two centre study of the dose-response relation for transscleral diode laser cyclophotocoagulation in refractory glaucoma. *Br J Ophthalmol* 2003;87: 1252-7.
20. Schlote T, Derse M, Rassmann K, et al. Efficacy and safety of contact transscleral diode laser cyclophotocoagulation for advanced glaucoma. *J Glaucoma* 2001;10:294-301.

21. Kumar N, Chang A, Beaumont P. Sympathetic ophthalmia following ciliary body laser cyclophotocoagulation for rubeotic glaucoma. *Clin Experiment Ophthalmol* 2004;32:196-8.
22. Wong EY, Chew PT, Chee CK, et al. Diode laser contact transscleral cyclophotocoagulation for refractory glaucoma in Asian patients. *Am J Ophthalmol* 1997;124:797-804.
23. Kaushik S, Pandav SS, Jain R, et al. Lower energy levels adequate for effective transscleral diode laser cyclophotocoagulation in Asian eyes with refractory glaucoma. *Eye* 2008;22:398-405.
24. Frezzotti P, Mittica V, Martone G, et al. Longterm follow-up of diode laser transscleral cyclophotocoagulation in the treatment of refractory glaucoma. *Acta Ophthalmol* 2010;88:150-5.
25. Ghosh S, Singh D, Ruddle JB, et al. Combined diode laser cyclophotocoagulation and intravitreal bevacizumab (Avastin) in neovascular glaucoma. *Clin Experiment Ophthalmol* 2010;38:353-7.
26. Fong AW, Lee GA, O'Rourke P, et al. Management of neovascular glaucoma with transscleral cyclophotocoagulation with diode laser alone versus combination transscleral cyclophotocoagulation with diode laser and intravitreal bevacizumab. *Clin Experiment Ophthalmol*. 2011;39:318-23.
27. Gorsler I, Thieme H, Meltendorf C. Cyclophotocoagulation and cyclocryocoagulation as primary surgical procedures for open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol*. 2015;253:2273-7.
28. Latina MA, Patel S, de Kater AW, et al. Transscleral cyclophotocoagulation using a contact laser probe: a histologic and clinical study in rabbits. *Laser Surg Med* 1989;9:465-70.
29. Rodríguez-García A, González-González LA, Carlos Alvarez-Guzmán J. Trans-scleral diode laser cyclophotocoagulation for refractory glaucoma after high-risk penetrating keratoplasty. *Int Ophthalmol*. 2016;36:373-83.
30. Shah P, Bhakta A, Vanner EA, et al. Safety and Efficacy of Diode Laser Transscleral Cyclophotocoagulation in Eyes With Good Visual Acuity. *J Glaucoma*. 2018;27:874-9.
31. Gedde SJ, Herndon LW, Brandt JD, et al. Surgical complications in the Tube Versus Trabeculectomy Study during the first year of follow-up. *Am J Ophthalmol*. 2007;143:23-31.
32. Aquino MC, Barton K, Tan AM, et al. Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: a randomized exploratory study. *Clin Exp Ophthalmol*. 2015;43:40-6.
33. Dursun O, Yılmaz A, Dinç E, et al. Outcomes of Transscleral Diode Laser Cyclophotocoagulation in End-Stage Glaucoma Patients. *Journal of Glaucoma Cataract*. 2020;15: 113-7.