Micropulse Transscleral Cyclophotocoagulation in Keratoplasty Eyes

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Purpose: To assess the outcomes of micropulse transscleral cyclophotocoagulation for intraocular pressure (IOP) control in keratoplasty eyes.

Methods: Outcomes of micropulse laser treatments of postkeratoplasty eyes were retrospectively reviewed. IOP was assessed with applanation tonometry. Keratoplasty survival was calculated with Kaplan–Meier survival analysis.

Results: Sixty-one eyes in 57 patients received laser treatment; 31 eyes received 1, 21 received 2, 8 received 3, and 1 received 4 treatments. The median follow-up was 21 months (range, 2–35 months). At baseline, the mean IOP was 28 ± 11 mm Hg. At 1, 3, 6, and 12 months after the last treatment, respectively, the numbers of eyes with IOP data were 58, 50, 46, and 38; the mean IOP was 17 ± 7, 17 ± 8, 18 ± 9, and 15 ± 5 mm Hg; the proportions of eyes with IOP ≤ 15 mm Hg were 40%, 51%, 48%, and 55%; and the proportions with IOP ≤ 12 mm Hg were 21%, 29%, 20% and 29%. Six eyes (10%) received subsequent glaucoma filtration surgery. The mean number of antiglaucoma medications used before the initial treatment was 2.7 (range, 0–4) versus 2.2 (range, 0–4) at last follow-up. At baseline, 7 grafts were decompensated and 5 of 54 clear grafts (9%) had endothelial cell density < 700 cells/mm^2. Graft survival was 94% at 1 year and 81% at 2 years after the initial laser treatment.

Conclusions: Micropulse transscleral cyclophotocoagulation is a noninvasive alternative to glaucoma filtration surgery for IOP reduction in keratoplasty eyes.

Key Words: glaucoma, micropulse laser, cyclophotocoagulation, penetrating keratoplasty, endothelial keratoplasty, DSEK, DMEK, ALK, DALK

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Glaucoma has long been recognized as an important factor influencing corneal graft survival.[1–5] High intraocular pressure (IOP) not only is detrimental to optic nerve function, but can also lead to corneal endothelial cell attrition. Glaucoma filtration surgery is sometimes necessary for the preservation of visual function, but it adversely affects corneal graft survival and is the most significant risk factor for endothelial keratoplasty failure.[6–8] Keratoplasty survival is particularly poor in the presence of aqueous shunt devices, which disrupt the blood–aqueous barrier and are associated with a dramatic alteration of the protein content of the anterior chamber.[9] Because of the increased rate of graft failures with plastic filtration tubes, we are continually looking for more safe and effective ways to manage medically uncontrolled IOP in eyes with corneal grafts.

Pulsed transscleral cyclophotocoagulation (TSCPC) is a tissue-sparing technology that can be used in simple and complex glaucoma cases.[10] Standard cyclophotocoagulation (CPC) involves ciliary body destruction by targeting the ciliary epithelium and stroma, resulting in a reduction in aqueous secretion and IOP. Unlike conventional CPC, which delivers continuous, high intensity energy to the ciliary body, pulsed TSCPC administers a series of repetitive, short pulses of laser energy separated by rest periods.[11] Traditional CPC is more effective than medical therapy at lowering IOP in patients with recalcitrant glaucoma, but it is associated with complications, including hypotony, hyphema, phthisis bulbi, and macular edema.[12] By comparison, pulsed TSCPC seems to have a better safety profile.[11] To our knowledge, no one has assessed the outcomes of pulsed TSCPC in keratoplasty eyes. The purpose of this study is to address this knowledge gap.

METHODS

This was a retrospective analysis of eyes treated with pulsed TSCPC by 5 surgeons in a single center (Price Vision Group, Indianapolis, IN). The study inclusion criteria were eyes that received prior keratoplasty and that were treated for uncontrolled IOP with micropulse TSCPC between September 2015 and February 2018. The study was approved by an independent review board (IRBCo, Inc, Buena Park, CA), adhered to the tenets of the Declaration of Helsinki, and complied with the Health Insurance Privacy and Portability Act. The subjects provided written informed consent.

Micropulse Laser Treatment (TSCPC-GP3)

The patients received monitored intravenous sedation using propofol. After application of topical proparacaine, the micropulse laser (Cyclo G6 MicroPulse P3; IRIDEX, Mountain View, CA) was applied to the sclera posterior to the

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limbus using a 31.3% duty cycle and 2000 mW power for 80 or 90 seconds per hemisphere, but sparing 3 and 9 o'clock as well as any quadrant with a bleb. After the TSCPC treatment, prednisolone acetate 1% was prescribed 4 times daily for 1 week and then tapered by 1 drop per week. Subsequent steroid use was at the treating physician's discretion, taking into consideration the type of keratoplasty and patient's history of rejection episodes.

Outcome Measures and Statistical Analysis

The main outcome measure was IOP, assessed with Goldmann applanation tonometry at baseline, 1 week, and 1, 3, 6, and 12 months after treatment. Efficacy criteria were defined as IOP reduction to ≤15 mm Hg, IOP reduction to ≤12 mm Hg, and IOP reduction of >20% from baseline. Eight eyes underwent a subsequent glaucoma procedure; 3 were within 6 months, 1 was at 1 year, and 4 were more than 1 year after the last TSCPC treatment. The IOP data were truncated after a subsequent glaucoma procedure.

Secondary outcome measures were graft failure, rate of immunologic rejection episodes, and graft endothelial cell loss. Graft failure was defined as the occurrence of a regraft for any reason or, in the absence of a regraft, a cornea that became cloudy for 3 months or longer. A graft rejection episode was defined as either the presence of an endothelial rejection line or inflammation (keratic precipitates or cells in the stroma) in a previously clear graft. Central graft endothelial cell density (ECD) was assessed with specular microscopy (Noncon Robo; Konan Medical Inc, Hyogo, Japan), using the center method and the manufacturers' calibration and software.

The cumulative probability of graft survival after the initial TSCPC treatment was estimated with Kaplan–Meier survival analysis, which took length of follow-up into consideration. The probability of experiencing an immunologic rejection episode after each TSCPC treatment or retreatment was assessed with Kaplan–Meier survival analysis; each time retreatment was performed, the follow-up for the prior treatment was truncated. The statistical analyses were 2-sided with a 5% significance level and were performed with SAS version 9.4 (SAS Inc, Cary, NC).

TABLE 1. Baseline Ocular Characteristics, Number of Micropulse Laser Treatments, Vision Status, Glaucoma Medications and Glaucoma Types

	No. of Eyes
No. of prior keratoplasties per eye	
1	33
2	14
3	9
4	2
5	2
6	1
Types of prior keratoplasty (some had more than 1 type)	
Penetrating keratoplasty	38
Endothelial keratoplasty	31
Anterior lamellar keratoplasty	3
Keratoprosthesis	4
Type of glaucoma	
Open angle	50
Angle closure	11
Prior glaucoma surgeries	
Trabeculectomy	15
Single aqueous shunt	14
More than 1 aqueous shunt	3
Selective laser trabeculoplasty	13
No prior glaucoma surgery	23
Vision status	
Monocular	11
≤20/400 in both eyes	12
No. of glaucoma medications at baseline	
0	5
1	5
2	7
3	28
4	16
No. of micropulse laser treatments	
1	31
2	21
3	8
4	1

RESULTS

A total of 61 postkeratoplasty eyes in 57 patients received pulsed TSCPC; 34 patients (62%) were male and 23 (38%) were female. The median patient age was 65 years (range, 25–91 years) at the time of treatment. Table 1 describes the keratoplasty and glaucoma procedures previously performed in these eyes, vision status, and the number of glaucoma medications used at baseline. Thirty-one eyes underwent single TSCPC treatment, 21 received 2, 8 received 3, and 1 eye received 4 treatments. The median length of follow-up after the initial treatment was 21 months (range, 2–35 months).

IOP

The mean IOP at baseline was 28 ± 11 mm Hg (range, 17–39 mm Hg). Table 2 summarizes the IOP outcomes following the laser treatments, and Figure 1 shows the IOP at 1, 3, 6, and 12 months after the last TSCPC treatment.

Eight eyes underwent subsequent glaucoma surgical procedures. Three received a Xen gel stent (Allergan, Dublin, Ireland), 3 received implantation of an aqueous shunt, 1 received goniosynechiolysis, and 1 underwent a tube revision.

At baseline before TSCPC, the study eyes were being treated with a mean of 2.7 antihypertensive medications (range, 0–4). At last follow-up, the treated eyes were on a mean of 2.2 antihypertensive medications (range, 0–4).

Graft Survival and Endothelial Cell Loss

Graft failure was noted in 7 eyes before TSCPC. Among the 54 eyes with clear grafts that received TSCPC-GP3, 10 grafts failed during subsequent follow-up. Five of the 10 grafts that subsequently failed had a baseline ECD < 700

TABLE 2. IOP Outcomes After Micropulse TSCPC Treatments in Postkeratoplasty Eyes

	No. of Eyes	IOP mm Hg; Mean ± SD (range)	Percentage IOP Change From Baseline, Mean ± SD	Proportion of Eyes With ≥20% IOP Reduction	Proportion of Eyes With IOP ≤15 mm Hg (%)	Proportion of Eyes With IOP ≤12 mm Hg (%)
Baseline IOP	61	28 ± 11 (17–39)				
Efficacy after last laser treatment, mo						
1	58	17 ± 7 (6–52)	30 ± 42	72	40	21
3	50	17 ± 8 (4–52)	30 ± 40	71	51	29
6	46	18 ± 9 (7–48)	31 ± 28	61	48	20
12	38	15 ± 5 (3–27)	34 ± 26	71	55	29
Efficacy 1 wk after						
First treatment	61	15 ± 7 (3–37)	38 ± 41	72	64	39
Second treatment	30	16 ± 9 (5–45)	30 ± 33	63	53	30
Third treatment	9	15 ± 7 (3–25)	38 ± 27	89	56	22

cells/mm^2. The graft failure rate was 6% at 1 year and 19% at 2 years after TSCPC.

Thirty-seven eyes had ECD measurements taken within 18 months before TSCPC treatment and the median ECD was 1215 cells/mm^2 (range, 469–2632). Twenty-two eyes had ECD measurements taken within 18 months after the last laser treatment; the median posttreatment ECD was 1097 cells/mm^2 (range, 551–2564). The median cell loss was 9% in 15 eyes that had not undergone previous glaucoma filtration surgery (aqueous shunt or trabeculectomy) and 10% in 8 eyes that had.

Immunologic Rejection Episodes

Seven of the 54 grafts that were clear at the time of the initial TSCPC procedure subsequently experienced an immunologic rejection episode. The rejection episode rate was 0% within 2 months, 1% within 3 months, 3% within 6 months, and 5% within 1 year of undergoing TSCPC treatment or retreatment.

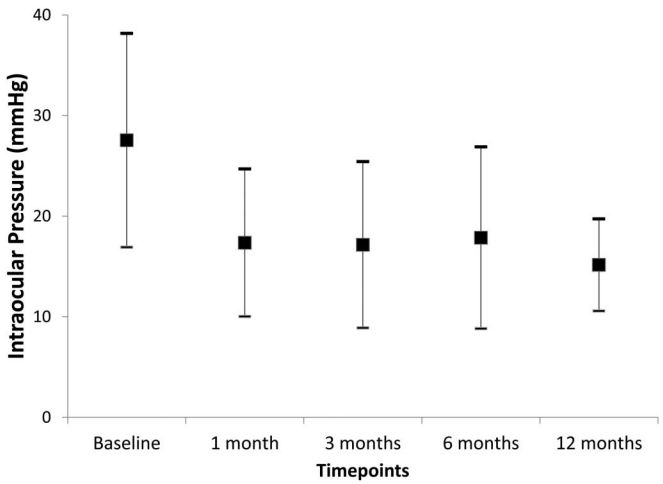

FIGURE 1. Mean and SD of IOP at baseline (before micropulse laser treatment) and at 1, 3, 6, and 12 months after the last micropulse laser treatment in keratoplasty eyes.

Complications

One patient underwent enucleation for a painful blind eye, and another patient had a Gunderson flap for severe band keratopathy. Six eyes (10%) had subsequent glaucoma filtration surgical procedures, as described above. One eye that had undergone multiple anterior segment and retinal surgeries developed hypotony.

DISCUSSION

This study found that pulsed TSCPC was generally an effective noninvasive alternative to glaucoma filtration surgery in keratoplasty eyes; it reduced IOP by a mean of 35% at 12 months and was well-tolerated by most treated subjects. Management of postkeratoplasty glaucoma is crucial because high IOP is detrimental to both optic nerve fibers and endothelial cells of the corneal graft. IOP control is often more complicated in postkeratoplasty eyes because the long-term use of topical corticosteroids to prevent transplant rejection causes IOP elevation. Many eyes in this study had already undergone glaucoma filtration surgery, which is a major risk factor for graft failure.[13]

We considered the rates of graft failure, rejection episodes, and endothelial cell loss after TSCPC to be unremarkable, given the baseline status of the eyes. Many of the study eyes had both end-stage glaucoma and end-stage degenerative changes in the cornea and anterior segment from multiple surgeries and scarring.

Micropulse TSCPC breaks a continuous-wave laser into a series of repetitive pulses separated by pauses that prevent thermal build-up in the tissue. It is a noninvasive procedure, in which the system's probe is placed directly on the sclera. The mechanism of action in the treatment of glaucoma is not completely understood; some effect on the ciliary body is suspected but no gross destruction to the ciliary body has been detected with ultrasonic biomicroscopy, in contrast to other cyclodestructive procedures such as cyclocryotherapy or laser cyclodestruction.[10] The TSCPC procedure is easily undertaken and well-tolerated, with transscleral application eliminating bleeding and postoperative infection risks.

Postoperative inflammation and pain are insignificant, and hospital admission is not required. However, intraoperative pain can be intense and intravenous sedation is required for the short duration of the treatment.

Our IOP reduction rates in keratoplasty eyes (Table 2) were similar to the rates that have been reported with TSCPC in eyes without prior keratoplasty. Gavris et al[14] reported a mean IOP decrease of 60% at 1 week (range, 35%–72% reduction from baseline) and 33% at 1 month after the procedure (range, 0%–61% from baseline). Williams et al[15] performed TSCPC treatments on 79 eyes with refractory glaucoma and achieved an IOP reduction of at least 20% in 75% of the treated eyes at 3 months and 66% at 6 months. Similarly, Lee et al[16] reported that among 27 adult eyes with at least 12 months of follow-up after TSCPC, 72% had an IOP reduction of at least 20%. Emanuel et al[17] found that 5 of 84 treated eyes (6%) needed a further laser or surgical intervention at a mean follow-up duration of 4 months, and the mean number of glaucoma medications was reduced from 3.3 at baseline to 2.0 at 6 months after TSCPC. Tan et al[18] reported that 73% of the treated eyes achieved an IOP reduction of at least 20% after a mean of 1.3 treatment sessions. Kuchar et al[19] found that mean IOP decreased from 38 mm Hg preoperatively to 23 mm Hg at last follow-up, representing a 40% decrease, and 74% achieved an IOP reduction of at least 20% after the initial treatment (n = 14). Aquino et al[11] randomized eyes to TSCPC or continuous-wave CPC and reported an overall success rate (IOP between 6 and 21 mm Hg and at least a 30% reduction with or without antiglaucoma medications) of 75% with TSCPC versus 29% with continuous-wave CPC at 12 months.

Pulsed TSCPC can be titrated to hopefully minimize the occurrence of hypotony. It is not known how often the treatment can be repeated if the IOP is not sufficiently reduced. To some degree, the laser is being applied blindly and may be treating either the ciliary body and/or the trabecular meshwork, and where the treatment is actually being applied could influence the effect of subsequent treatments.

Further studies are warranted to determine whether breakdown of the blood–aqueous barrier is less intense with TSCPC than it is with a trabeculectomy or aqueous shunt and to further assess graft survival and endothelial cell loss in eyes that are not as severely compromised as many of the eyes were in our study. Interestingly, the TSCPC treatment reduced IOP in our eyes with total angle closure, indicating that either the iris tissue covering the trabecular meshwork becomes more porous to fluid transfer across it or production of aqueous fluid by the ciliary body decreased. There is also evidence that uveoscleral outflow is increased by micropulse TSCPC.[20]

In conclusion, we found that TSCPC reduced IOP by a mean of 35% at 12 months in keratoplasty eyes. The rate of successful IOP reduction matched that achieved in previous studies with nonkeratoplasty eyes. The procedure was generally well-tolerated and subsequent rates of immunologic rejection episodes, endothelial cell loss, and graft failure were unremarkable given the baseline status of the treated eyes.

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