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Transscleral red laser cyclophotocoagulation for the treatment of therapy-resistant inflammatory glaucoma

P.M. PUSKA, A.H.A. TARKKANEN

Helsinki University Eye Hospital, Helsinki - Finland

PURPOSE. *To evaluate in a retrospective study the long-term usefulness of red 647 nm krypton and 670 nm diode laser for transscleral contact cyclophotocoagulation (CPC) in the treatment of therapy-resistant inflammatory glaucoma.*
METHODS. *The authors treated 48 eyes of 38 consecutive patients (mean age 36.8 years, range 6-81 years) with therapy-resistant inflammatory glaucoma secondary to chronic uveitis (45/48), chronic scleritis (1/48), or combined scleritis with keratouveitis (2/48) using transscleral red 647 nm Krypton or 670 nm Diode laser. All eyes had failed maximum tolerated medical therapy and 19/48 (40%) eyes also previous antiglaucoma surgery. Laser power at the scleral surface was 0.35 to 0.45 W and the application time 10 seconds each. The follow-up was 42.8± 40.0 (range 2-145) months.*
RESULTS. *The mean preoperative intraocular pressure (IOP) of 35.6±8.1 mmHg fell to 6-21 mmHg level in 75% after one or repeated CPC. Among adult patients this was achieved in 85%, among children in 54%. More than one treatment was needed in 52%. No cases of hypotony, phthisis bulbi, or other devastating complications occurred.*
CONCLUSIONS. *Transscleral CPC using red 647 nm krypton or 670 nm diode laser is an effective and well-tolerated procedure for the treatment of therapy-resistant inflammatory glaucoma in adults. CPC can be considered before incisional antiglaucoma surgery with a shunt or antimetabolites is undertaken (Eur J Ophthalmol 2007; 17: 550-6)*

KEY WORDS. *Cyclophotocoagulation, Inflammatory glaucoma, Laser surgery, Secondary glaucoma*

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INTRODUCTION

Glaucoma caused by chronic inflammatory eye disease may present a difficult clinical problem. Intraocular pressure (IOP) reducing medications may create problems and traditional incisional operations are doomed to failure (1). Since the 1960s, cyclocryocoagulation has been commonly used. However, it may cause a number of severe complications, such as intense postoperative pain lasting for several days, transient marked elevations of IOP, hyphema, persistent hypotony, and even phthisis (2). Therefore, this technique was abandoned at our hospital more than 15 years ago. The introduction of neodymium:yttrium-aluminium-garnet (Nd:YAG) lasers have markedly increased the popularity of cyclophotocoagulation (CPC). However, the complications of transscleral Nd:YAG laser CPC resemble those seen after cyclocryotherapy, but are less severe (3). Still there are reports of occasional sympathetic ophthalmia after Nd:YAG CPC (4, 5). Infrared diode lasers operate within 780 to 850 nm spectrum, in contrast to the 1064 nm wavelength delivered by the Nd:YAG laser. The near infrared light has an excellent scleral penetrance (6) and better melanin absorption than the longer wavelength by Nd:YAG (7). By treating 22 eyes

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of 20 patients with inflammatory, medically refractive glaucoma with 810 nm diode laser CPC, the IOP was controlled in 77.3% (1).

Red 647 nm krypton and 670 nm diode lasers show superior melanin absorption when compared with 1064 nm Nd:YAG lasers or even with the 810 nm diode laser (7). Lesions in the pars plicata of the rabbit eye similar to those obtained using contact Nd:YAG laser can be produced by using only half of the energy (8). Poorer transit of the krypton laser energy through the sclera can be overcome by pressing the contact probe against the sclera (6, 9). With red lasers the power at the scleral surface amounts 0.35 to 0.45 W only, whereas with the 810 nm diode laser it is 1.5 to 2 W (10). The red laser's duration of each application is 10 seconds, whereas with 810 nm diode laser it is 1.5 to 2 seconds. Hence long duration of the applications of the low-power red lasers allow gentle tissue effects. Explosive reactions or "puffs" can be avoided and the complications minimized. Our aim is to report long-term results of treating patients with treatment-resistant inflammatory glaucoma with red 647 nm krypton or 670 nm diode laser CPC.

PATIENTS AND METHODS

Twenty-five adults with a mean age of 50.4±13.3 years and 13 children with a mean age of 10.8±3.1 years with therapy-resistant inflammatory glaucoma treated at the Department of Ophthalmology of Helsinki University Eye Hospital from December 1991 to March 2004 were included in this retrospective study. The study protocol was reviewed by the ethics committee of the Helsinki University Ear and Eye Hospital and the study was conducted according to the guidelines set by the Declaration of Helsinki. All patients were consecutive referrals by eye departments or private ophthalmologists in Finland. Two patients were excluded from the study, one with retinal ablation and another with neovascular glaucoma. Follow-up data were retrieved from the patient files of Helsinki University Eye Hospital and of the referring centers. The follow-up was 42.8±40.0 (range 2–145) months.

The main underlying inflammatory disease was chronic uveitis (Tab. I). Maximum tolerated medical therapy had been given. Nineteen eyes of the 48 had failed glaucoma surgery (trabeculectomy, cyclocryocoagulation, implant surgery); this figure among 34 adult eyes is 16 (47%) and among 14 children's eyes is 3 (21%). Also, other modes of surgery had been performed (Tab. II).

All patients had a thorough clinical and ocular evaluation before treatment. The number of antiglaucoma medications used was recorded, and Snellen visual acuity, slit-lamp biomicroscopy, IOP with Goldmann applanation tonometer, ophthalmoscopy after pupillary dilatation, and, when needed, Goldmann or Octopus perimetry were performed.

All adult operations were performed by the senior author,

TABLE I - CHARACTERISTICS OF PATIENTS

	All patients	Adults	Children
No. of patients	38	25	13
No. of eyes	48	34	14
Mean (SD) age, yr	36.8 (21.9)	50.4 (13.3)	10.8 (3.1)
Underlying inflammatory eye disease, no. patients (eyes)			
Chronic uveitis	36 (45)	23 (31)	13 (14)
Chronic scleritis	1	1	0
Chronic scleritis with keratouveitis	1 (2)	1 (2)	0

TABLE II - PREVIOUSLY PERFORMED OCULAR PROCEDURES

	All patients	Adults	Children
Previous failed glaucoma surgery			
Trabeculectomy, 1–3 times	12	10	2
Implant surgery, 1–2 times	3	1	2
Cyclocryocoagulation, 1–3 times	5	5	0
Laser trabeculoplasty	8	7	1
Previous other surgery			
Cataract extraction/phaco	10	7	3
With IOL implantation	16	4	2
Secondary IOL implantation	1	1	0
Suturing of a sclerocorneal wound	1	1	0
Vitreoretinal surgery	2	2	0
Nd:YAG laser capsulotomy	7	6	1
Nd:YAG laser iridotomy	3	1	2
Refractive surgery	2	0	2

Values are number of eyes.
IOL = Intraocular lens; Nd:YAG = Neodymium: yttrium-aluminum- garnet

P.P., with a personal experience of more than 2000 CPCs, in an outpatient ward of the hospital. To avoid postoperative IOP rise, a drop of 1% apraclonidine or 250 mg oral acetazolamide or both were given.

Patients were placed in a supine position and a few drops of oxybuprocaine hydrochloride drops were instilled. Peribulbar anesthesia using 1% lidocaine hydrochloride was given. No oral or intravenous sedation was given. The children were treated under general anesthesia. Conjunctival peritomy was not performed.

The room was darkened and the shadow of the pars plicata on the scleral surface was identified using transscleral illumination. The 647 nm krypton laser was delivered from a Lasertek 41 AKTrKr krypton laser unit, and the 670 nm diode laser from a prototype 670 nm diode laser unit (Dual Laser Oy, Helsinki, Finland) via a fiberoptic tip (Laser Peripherals, Inc., Minnetonka, MN/Dual Laser Oy). At the tip of the probe, the power was 0.35 to 0.5 W (krypton group) and 0.40 to 0.45 W (670 nm diode group) (Scientec Calorimeter, Bolden, CO). The probe was held perpendicular to the scleral surface and pressed at the site of the pars plicata shadow. Each application was for 10 seconds. At the first session lower 180º, two inferior quadrants, 10 applications per quadrant were treated.

After treatment a topical corticosteroid and antibiotic was instilled and the eye was given a bandage until the evening of the day of the operation. The patients were discharged without any systemic analgesics. Previous antiglaucoma and/or anti-inflammatory medication was continued but with the follow-up it was tapered off according to the therapeutic response. In case the procedure had to be repeated, the temporal 180º was usually treated, i.e., the lower temporal quadrant was retreated. If a third treatment became necessary, the inferior nasal 90º and the superior temporal 90º received a retreatment. One quadrant was saved. Treatment was defined as a success if IOP was reduced to a 6 to 21 mmHg level with or without medication. A special aim was to reduce systemic carbonic anhydrase inhibitor use in all patients.

Statistical methods

Pre- and postoperative IOP levels and pre- and postoperative glaucoma medications were compared using the Wilcoxon signed rank test. The nonparametric Quantile (Sign) test was used to compare pre- and postoperative visual acuity. Data were calculated with the NCSS 2000 statistical soft ware program (NCSS Statistical Software, Kaysville, UT), $p<0.05$ denoting statistical significance of differences. Missing data were not substituted by any method.

RESULTS

After one or repeated CPC the mean baseline IOP of the adults, 36.4±8.9 mmHg, fell immediately, and in 21 eyes it was still 15.8±5.6 mmHg after 2 years. Among children the corresponding figures are 33.8±5.5 mmHg at baseline and 22.0±9.6 mmHg at the last follow-up (Tab. III).

TABLE III - INTRAOCULAR PRESSURE (IOP) AFTER ONE OR MORE CYCLOPHOTOCOAGULATIONS BUT NO OTHER GLAUCOMA PROCEDURES

	All patients	p value	Adults	p value	Children	p value
Baseline	35.6±8.1		36.4±8.9		33.8±5.5	
No. of eyes	48		34		14	
1 month	18.1±6.9	<0.0001	18.1±7.1	<0.0001	18.2±6.7	<0.01
No. of eyes	44		31		13	
3 months	17.3±5.8	<0.0001	16.4±5.0	<0.0001	19.5±7.1	<0.01
No. of eyes	41		29		12	
6 months	16.5±5.4	<0.0001	16.0±4.4	<0.0001	18.0±7.7	<0.05
No. of eyes	35		26		9	
1 year	16.3±6.1	<0.0001	14.8±4.6	<0.0001	21.3±8.4	
No. of eyes	30		23		7	
2 years	16.6±6.7	<0.0001	15.8±5.6	<0.0001	24.5±14.8	
No. of eyes	23		21		2	
Last follow-up	17.9±8.2	<0.0001	16.4±7.2	<0.0001	22.0±9.6	<0.01
No. of eyes	47		34		13	

Values are mean ± SD IOP, in mmHg

TABLE IV - INTRAOCULAR PRESSURE (IOP) AFTER ONE OR MORE CYCLOPHOTOCOAGULATIONS BUT NO OTHER GLAUCOMA PROCEDURES

	Adults	Children
Baseline	1/34 (2.9)	0
1 mo	27/34 (79.4)	12/13 (92.3)
3 mo	24/31 (77.4)	9/14 (64.2)
6 m	25/29 (86.2)	7/13 (53.8)
1 yr	21/26 (80.8)	3/11 (27.3)
2 yr	19/24 (79.2)	1/7 (14.3)
Last follow-up	29/34 (85.3)	7/13 (53.8)

Number (%) of eyes achieving an IOP of 6–21 mmHg. The total number of eyes at each time point gives the number of eyes deemed as successes at the given time point plus the number of eyes regarded as failures at the given time point or at any previous time point. The number excludes eyes lost to follow-up. The IOP data of two adult patients were missing at 3 months, three adults at 6 months and 1 year, and four adults at 2 years. Last follow-up = the last follow-up visit for which IOP data are available. Of eyes that received other glaucoma procedures, the last available IOP before such an operation was used

An IOP of 6–21 mmHg was achieved in 85.3% of the adult eyes. This IOP level was present already at 1 month postoperatively. Among children 92.3% were successes at 1 month, but then the effect started to taper off. After 2 years only 14.3% were still controlled according to our criteria (Tab. IV). Of the adults, 59% needed a repeated treatment (Tab. V).

After treatment 73% of the adults could be maintained with topical glaucoma medication only and preoperative 68% using oral carbonic anhydrase inhibitors fell to 26%. Among children similar alterations in the glaucoma medication was not noted (Tab. VI). At the endpoint 23% of the adult eyes and 43% of the children's eyes needed incisional glaucoma surgery (Tab. VII). The baseline visual acuity was not reduced after CPC (Tab. VIII). A decline in visual acuity of >2 Snellen lines was noted in 15 eyes, but 9 eyes showed improvement of >2 Snellen lines (5 eyes after cataract operation and one after laser capsulotomy) (Tab. VIII). The main causes for the decline of visual acuity were progression of cataract and development of cystic macular edema due to uveitis (Tab. IX). The operative complications are listed in Table X. No "pop" effects were noted. Marked ciliary injection occurred seldom and no cases of persistent hypotony or phthisis were obtained. The patients did not complain of pain and if needed, they were willing to have the repeated CPC. No systemic analgesics were prescribed.

TABLE V - NUMBER OF TREATMENT SESSIONS IN A SERIES OF 48 EYES WITH THERAPY RESISTANT GLAUCOMA AFTER INFLAMMATORY EYE DISEASE

	All patients	Adults	Children
1 session	23 (48)	14 (41)	9 (64)
2 sessions	15 (31)	12 (35)	3 (21)
3 sessions	6 (13)	5 (15)	1 (7)
4 sessions	3 (6)	2 (6)	1 (7)
5 sessions	1 (2)	1 (3)	

Values are n (%) of eyes

TABLE VI - GLAUCOMA MEDICATION PREOPERATIVELY AND POSTOPERATIVELY AT THE LAST FOLLOW-UP (study endpoint or before additional glaucoma surgery)

Type of medication	Preoperatively	Postoperatively
None	1 (2)	1 (2)
Topical only	27 (56)	35 (73)
Adults	16 (47)	25 (74)
Children	11 (8)	11 (8)
Carbonic anhydrase inhibitors	20 (53)	12 (34)
Adults	17 (68)	9 (26)
Children	3 (23)	3 (23)

Values are n (%) of eyes

DISCUSSION

There are only a few reports on the treatment of inflammatory glaucoma with contact transscleral CPC. Our series of 48 eyes of 38 consecutive patients appears to be the largest one so far reported. In the interesting article of Schlote et al (1), 18 eyes with chronic uveitis/trabeculitis were treated with transscleral 810 nm diode laser. Their success rate of 72.2% is similar to our study. Also, 63% needing more than one treatment agrees well with our figure of 59%. In two smaller studies similar success rates were achieved (11, 12). In both, nine eyes with inflammatory glaucoma were treated.

In all of these studies 810 nm diode laser has been used. In the study of Schlote et al (1) no serious complications occurred. Nearly half of the patients had mild anterior

uveitis on the first postoperative day. In two eyes "pop" effects during the operation were encountered as well as conjunctival burn in one. In another study using the 810 nm laser for all types of refractory glaucoma 37% of the patients complained of pain and burning sensation during the operation. In one case the pain symptoms persisted for 14 days (13). It has to be emphasized that red 647 nm krypton and 670 nm diode laser in our study allow a slow release of low-dose laser energy, which may explain the almost total absence of complications. Even visual acuity remained closely in the preoperative level. The main causes for slight deterioration were cataract progression and the development of cystic macular edema.

The qualities of the red (647 nm krypton and 670 nm diode) lasers differ from those of the 810 nm diode and the1064 nm Nd:YAG lasers. Although the red lasers traverse the sclera less efficiently than the infrared diode and the Nd:YAG lasers, scleral transmission is increased when they are applied with pressure on the sclera, especially at shorter wavelengths (6, 9). The wavelengths of the red lasers are near to that maximally absorbed by the melanin granules in the pigment epithelium. It has been shown that melanin granules absorb 670 nm laser twice as effectively as 810 nm laser, and six times more effectively than 1064 nm laser (7). The red lasers have also been shown to require less energy than Nd:YAG laser to produce comparable lesions in the pars plicata of the rabbit eye (8, 14). The poorer scleral transmission and better absorption by melanin of the red lasers indicate that less energy enters the eye, the vitreous humor, and the retina of the contralateral wall of the eye, which may be of practical importance. Also, long duration of laser exposure (10 seconds) allows for a lower power of laser. Thus explosive tissue reactions in the ciliary body are avoided and complications are minimized.

In proposing a better outcome for CPC the use of transs-

TABLE VII - ADDITIONAL GLAUCOMA PROCEDURES AT THE ENDPOINT OF FOLLOW-UP PERIOD

Procedure	Eyes	Time after the initial (last) cyclophotocoagulation
Adults (n=8)		
Trabeculectomy	2	1) 5 yr 7mo (1 yr 5 mo); 2) 5 yr 8 mo (3 yr)
Mitomycin trabeculectomy	3	1) 2 mo; 2) 9 (3) mo; 3) 9 mo
Implant surgery	2	1) 5 yr 7 mo (2 mo); 2) 4 yr (3 yr)
Phaco + mitomycin trabeculectomy	1	1) 4 yr 2 mo (3 yr 11 mo)
Children (n=6)		
Trabeculectomy	1	1) 3 mo (later M-Tre)
Mitomycin trabeculectomy	3	1) 2 yr; 2) 3 (1) mo; 3) 13 (1) mo (later implant surgery)
Deep sclerectomy	1	1) 3 mo
Viscocanalostomy	1	1) 4 mo (later M-Tre)

M-Tre = Mitomycin trabeculectomy

TABLE VIII - VISUAL ACUITY BEFORE CYCLOPHOTOCOAGULATION (N=48) AND AT THE LAST FOLLOW-UP (N=46)

Visual acuity	All eyes		Adults		Children	
	Before	Last	Before	Last	Before	Last ≥
0.8	9	8	6	6	3	2
0.5–0.7	15	9	12	4	3	5
0.2–0.4	19	14	12	10	7	4
0.05–0.1	3	6*	2	5*	1	1
CF	2	8†/‡	2	6‡	0	2†
HM	0	1	0	1	0	0
Missing	0	2	0	0	0	2

All eyes, before/last p=0.152; adults, before/last p=0.077; children, before/last p=1.000.
*After cataract operation visual acuity was 1.0 in one eye.
†After cataract operation visual acuities were 0.7 and 0.4 in these two eyes.
‡After cataract operation visual acuities were between 0.4 and 0.5 in three eyes.
CF = Counting fingers; HM = Hand movements

TABLE IX - EYES WITH A DECLINE IN VISUAL ACUITY OF >2 SNELLEN LINES

Cause of decline in visual acuity	Adults	Children
Within 12 mo postoperatively		
Cataract progression	1 (2.9)*	2 (14.3)*
Dry eye	1 (2.9)	
Progression of cyclitic membrane		1 (7.1)
Progression of cataract and glaucoma	1 (2.9)	
Unknown reason	1 (2.9)	
1.5–3 yr postoperatively		
Cataract progression	2 (5.9)*	
Progression of secondary cataract	1 (2.9)	
Progression of corneal decompensation	1 (2.9)	
Cataract and CME after active uveitis	2 (5.9)	
Progression of glaucoma and active uveitis	1 (2.9)	
Progression of cataract, corneal guttata, and glaucoma (active uveitis)	1 (2.9)	

Values are n (%) of eyes.
*After cataract operation visual acuity was better than before cyclophotocoagulation.
CME = Cystoid macular edema

TABLE X - COMPLICATIONS AND EVENTS AFTER ONE OR MORE CYCLOPHOTOCOAGULATIONS IN 48 EYES WITH INFLAMMATORY GLAUCOMA (a total of 88 treatment sessions)

Complication/event	All	Adults	Children
During operation			
Pop effects	0	0	0
Conjunctival burns	0	0	0
Next days postoperatively			
Marked ciliary injection	2 (4.2)	2 (5.9)	0
Anterior uveitis, moderate	5 (10.4)	2 (5.9)	3 (21.4)
Dry eye (persistent)	2 (4.2)	2 (5.9)	0
Within 1 mo postoperatively			
Anterior vitreitis	1 (2.1)	1 (2.9)	0
Preretinal hemorrhage	1 (2.1)	1 (2.9)	0
Within 12 mo postoperatively			
Decrease in vision >2			
Snellen lines	7 (14.6)	4 (11.8)	3 (21.4)
Hypotonia (<6 mmHg)	0	0	0
Phthisis	0	0	0
1.5–3 yr postoperatively			
Decrease in vision >2			
Snellen lines	8 (16.7)	8 (23.5)	0

Values are n (%) of eyes

cleral transillumination has been emphasized (15). We share this opinion. We have been using transscleral illumination routinely for the identification of pars plicata for the past 20 years. In our histopathologic experience in studying enucleated globes after cyclocryocoagulation for neovascular glaucoma, it was noted that the treatment site had been too posterior as a rule. Our experience confirms the individual anatomic variations of the pars plicata in relation to the limbus. Another important point is the perpendicular alignment of the probe against the sclera.

The mechanism of IOP reduction after CPC has been debated. An eye with therapy-resistant chamber angle recession glaucoma was successfully treated with transscleral CPC. When the eye was examined at autopsy 10 months later it was found that effective ablation of the ciliary processes had been achieved. Only a slight chronic inflammatory reaction was present (16). The findings support the view that nonconventional outflow routes including uveoscleral outflow are increased after CPC (17).

Transscleral CPC using red 647 nm krypton or 670 nm diode lasers is effective and safe in treatment-resistant inflammatory glaucoma. It does not impair corneal innervation (18). Low-dose energy with slow release is equally effective to the 810 nm diode laser with higher energy pulses delivered in 1.5 to 2 seconds. The absence of severe side effects and postoperative pain makes this simple outpatient procedure a useful choice in the management of treatment-resistant inflammatory glaucoma before incisional surgery with shunts or antimetabolites is considered.

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Reprint requests to:
Päivi Puska, MD
Helsinki University Eye Hospital
P.O.B. 220, 00029 HUS
Helsinki, Finland
Paivi.Puska@hus.fi

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