Therapy-resistant Inflammatory Glaucoma – 647nm Krypton and 670nm Diode Lasers for Transscleral Contact Cyclophotocoagulation

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Abstract

Only a few reports exist on the treatment of therapy-resistant inflammatory glaucoma with contact transscleral cyclophotocoagulation (CPC), and only one in which the red 647nm krypton or 670nm diode lasers are used. The lasers most frequently employed in clinical practice are the 810nm diode and the 1,064nm neodynium:yttrium–aluminium–garnet (Nd:YAG) lasers. Although transmission through the sclera is lower with the red 647nm krypton and 670nm diode lasers than with the infrared 810nm diode and Nd:YAG lasers, this is compensated for by using contact application and compressing the sclera with the probe. Also, the red lasers have a higher affinity for the pigment epithelium of the pars plicata. Transscleral red laser CPC has proved to be an effective, simple and well tolerated procedure for the treatment of therapy-resistant inflammatory glaucoma, particularly in adults.

Keywords

Secondary glaucoma, inflammatory glaucoma, cyclophotocoagulation, laser surgery

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Laser Transmission and Absorption

The choice of laser type for transscleral cyclophotocoagulation (CPC) has been based on scleral transmission rather than on efficacy at the target tissue. Since scleral transmission increases at longer wavelengths, the lasers most frequently employed in clinical practice have been the 810nm diode and the 1,064nm neodynium:yttrium–aluminium–garnet (Nd:YAG). However, the contact application with pressure on the sclera increases scleral transmission, especially at shorter wavelengths.[1] This increase is 2.5-fold for the krypton laser compared with 1.5-fold for the Nd:YAG laser. Moreover, the wavelength of red 647nm krypton and 670nm diode lasers is near to that maximally absorbed by melanin granules (600nm) in the retinal pigment epithelium. Melanin granules absorb 670nm laser twice as effectively as 810nm diode laser and six times more effectively than 1,064nm Nd:YAG laser.[2] Lesions in the pars plicata of the rabbit eye, similar to those obtained using contact Nd:YAG lasers, can be produced by red lasers using only half the energy.[3] The poorer scleral transmission and better absorption by melanin of the red lasers indicate that less energy enters the eye, the vitreous humour and the retina of the contralateral wall of the eye, which may be of practical importance.

Possible Cellular Effects and Mechanisms of Intraocular Pressure Reduction

The low power (0.4W) and the long duration of application (10 seconds) may result in parts of the ciliary body lesions being warmed to levels above 43°C but not being coagulated. Such hyperthermic effects may induce apoptosis in the cellular components of the ciliary body[4] instead of necrosis, which occurs after coagulative lesions. It is known that, compared with necrotic cell death, the inflammatory reaction following apoptosis is minimal.[4,5] The hyperthermia produced in the lesions by the low-power, slow-burn laser may partly explain the mild post-operative uveitis observed after this treatment modality.[6–13]

The mechanism of intraocular pressure (IOP) reduction after CPC has been debated. In addition to destroying the epithelium and capillaries of the ciliary processes,[14] the findings support the view that non-conventional outflow routes, including uveoscleral outflow, are increased after CPC.[7,15]

Morphological Changes After Red Laser Cyclophotocoagulation

A histopathological study of an eye after long-term successful krypton laser CPC showed that effective ablation of the ciliary processes was achieved and only a slight chronic inflammatory reaction was present. Also, the sclera, iris, lens and zonules were intact.[7] The histological changes observed after 670nm diode laser CPC are essentially identical.[8] With the use of *in vivo* confocal microscopy, no changes were noted in the corneal layers or sub-basal nerves after krypton laser CPC. In addition, corneal sensitivity, tested with the Cochet-Bonnet esthesiometer, was normal, as was tear fluid secretion.[16]

Cyclophotocoagulation in the Treatment of Therapy-resistant Inflammatory Glaucoma

There are only a few reports on the treatment of inflammatory glaucoma with contact transscleral CPC.[17–22] In most studies 810nm diode lasers were used; in only one study were red 647nm krypton and 670nm diode lasers used.[9]

Table 1: Patient Characteristics – Previously Performed Ocular Procedures

	Number of Eyes		
	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	
Laser trabeculoplasty	8	7	1
Previous Other Surgery			
Cataract extraction/phaco	10	7	3
With IOL implantation	16	14	2
Secondary IOL implantation	1	1	
Suturing of a sclerocorneal wound	1	1	
Vitreoretinal surgery	2	2	
Nd:YAG laser capsulotomy	7	6	1
Nd:YAG laser iridotomy	3	1	2
Refractive surgery	2	2	

IOL = intraocular lens; Nd:YAG = neodymium:yttrium-aluminum-garnet.

Table 2: Intraocular Pressure (mmHg) 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	

Table 3: Visual Acuity Before Cyclophotocoagulation (n=48) and at the Last Follow-up (n=46)

Visual Acuity	All Eyes		Adults		Children	
	Before	Last (p=0.152)	Before	Last (p=0.077)	Before	Last (p=1.000)
≥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

CF = counting fingers; HM = hand movements.
**After cataract operation, visual acuity was 0.4–0.5 in three eyes.*
***After cataract operation, visual acuity was 0.7 and 0.4 in these two eyes.*
****After cataract operation, visual acuity was 1.0 in one eye.*

Red Laser Cyclophotocoagulation in the Treatment of Therapy-resistant Inflammatory Glaucoma Patients

We retrospectively reviewed the charts of 38 consecutive patients (25 adults, mean age 50.4±13.3 years, and 13 children, mean age 10.8±3.1 years) treated with the 647nm krypton or 670nm diode laser for therapy-resistant inflammatory glaucoma at Helsinki University Eye Hospital from December 1991 to March 2004.[9] Two patients were excluded (one with chronic uveitis and retinal ablation and another with chronic uveitis and neovascular glaucoma). Follow-up data were retrieved from the patient files of Helsinki University Eye Hospital and of the referring centres. The follow-up was 42.8±40.0 (range two to 145) months. The main underlying inflammatory disease was chronic uveitis (31 out of 34 adult eyes and 14 out of 14 children's eyes), but one adult eye had scleritis and two adult eyes had scleritis with keratouveitis. Maximal tolerated medication had been given. Nineteen of the 48 eyes had failed glaucoma surgery (trabeculectomy, cyclocryocoagulation, implant surgery): 16 of 34 adult eyes (47%) and three of 14 children's eyes (21%). Also, other modes of surgery had been performed (see *Table 1*).

Methods

The CPC was performed under periocular anaesthesia in adults; children were treated under general anaesthesia. With the patient in a supine position, the pars plicata region of the ciliary body was identified using transscleral illumination. The 647nm krypton laser was delivered from a Lasertek 41 AKTrKr krypton laser unit, and the 670nm diode laser from a prototype 670nm diode laser unit (Dual Laser Oy, Helsinki, Finland) via a fibre optic tip (Laser Peripherals, Inc., Minnetonka, MN, US/Dual Laser Oy, Helsinki, Finland). At the tip of the probe, the power was 0.35–0.5W in the krypton group and 0.40–0.45W in the 670nm diode group (Scientec Calorimeter, Bolden, CO, US). The probe was held perpendicular to the scleral surface and pressed at the site of the pars plicata shadow. Each application lasted for 10 seconds. At the first session the inferior 180º of the ciliary body was treated. If needed, a second treatment was given to the temporal 180º, a third treatment to the inferior nasal 90º and superior temporal 90º and a fourth again to the inferior 180º. One quadrant was always left intact in an attempt to avoid hypotonia. To avoid post-operative IOP rises, a drop of 1% apraclonidine or 250mg oral acetazolamide, or both, was given before treatment. After treatment, the patients used antibiotic steroid drops four to five times a day for three to four weeks. Previous antiglaucoma and/or anti-inflammatory medication was continued, but with the follow-up it was tapered off according to the therapeutic response.

Statistical Methods

Pre- and post-operative IOP levels and pre- and post-operative glaucoma medications were compared using the Wilcoxon signed rank test. The non-parametric Quantile (Sign) test was used to compare pre- and post-operative visual acuity. $p<0.05$ denoted statistical significance of differences. Missing data were not substituted by any method.

Results

Treatment was defined as a success if IOP was reduced to 6–21mmHg with or without medication. After one or repeated CPCs, the mean IOP of the adults fell from a baseline of 36.4±8.9mmHg to 16.4±7.2mmHg at the last follow-up; among children the corresponding figures were 33.8±5.5 and 22.0±9.6mmHg, respectively (see *Table 2*). At the last follow-up, after one or more CPCs but no other glaucoma procedures, an IOP of 6–21mmHg was achieved in 85.3% of the adult eyes. Among children, 92.3% were successes at one month, but then the effect

started to taper off. After two years only 14.3% were still controlled according to our criteria. Fifty-nine per cent of the adult eyes and 36% of the children's eyes needed a repeat treatment: 31% were treated twice, 31% three times, 6% four times and 2% five times. At the end-point, 23% of the adult eyes and 43% of the children's eyes needed incisional glaucoma surgery combined with a topical antimetabolite or a shunt.

After treatment, 73% of the adults could be maintained with topical glaucoma medication only. Pre-operatively, 68% of the adults were on oral carbonic anhydrase inhibitors (CAIs), but only 36% needed them post-operatively. Among children, similar alterations in glaucoma medication were not noted: 23% used oral CAIs both pre- and post-operatively. The baseline visual acuity was not reduced after CPC (see *Table 3*). Decline in visual acuity of >2 Snellen lines was noted in 15 eyes, but nine eyes showed improvement of >2 Snellen lines – five after cataract operation, one after laser capsulotomy and three for some other reason. The main causes of the decline of visual acuity were progression of cataract or development of cystic macular oedema (CME) due to uveitis (see *Table 4*). No 'pop' effects were noted. Marked ciliary injection occurred seldom and no cases of persistent hypotonia or phthisis were seen (see *Table 5*).

Comparison of Red Laser with 810nm Laser Cyclophotocoagulation in Inflammatory Glaucoma

With red lasers the power at the scleral surface is only 0.35–0.45W, whereas with the 810nm diode laser it is 1.5–2W. With the red lasers the duration of each application is 10 seconds, whereas with the 810nm diode laser it is 1.5–2 seconds. Red lasers allow a slow release of low-dose, short-wavelength laser energy and may thus induce less trauma to the eye, which explains the low rate of complications. No explosive pop effects, severe anterior uveitis or hypotonia were encountered in our study. Also, visual acuity remained close to the pre-operative level.[9]

In a prospective study by Schlote et al.,[21] 18 eyes with chronic uveitis/trabeculitis were treated with transscleral 810nm diode laser CPC. Their success rate of 72% is very similar to that seen in our study. Also, the figure of 63% needing more than one treatment corresponds well to our figure of 56%. No serious complications occurred in their study. Nearly half of the patients had mild anterior uveitis on the first post-operative day, and no marked activation of the underlying inflammatory disease was seen. In two eyes pop effects during the operation were encountered, and conjunctival burn in one. Visual acuity decreased in 38%.

In a retrospective study by Heinz et al.,[19] 21 eyes of 12 paediatric patients with juvenile idiopathic arthritis (JIA)-associated uveitis and secondary glaucoma were treated with transscleral 810nm diode CPC as a primary surgical treatment. An IOP ≤21mmHg was achieved in only 32% of the eyes. Pop effects occurred in six of 41 treatments (14.6%) and a change in pupil configuration in four eyes (21%). No hypotonia or severe increase in inflammatory activity was seen in their study.

In the study by Bloom et al.,[17] 210 eyes of heterogenous glaucoma patients were treated using 810nm diode laser CPC. Nine eyes with inflammatory glaucoma were included. In eyes with inflammatory glaucoma, IOP fell from a pre-operative level of 33.3mmHg to 18.0mmHg at the last follow-up. No phthisis or hypotonia occurred in these eyes, but macular pucker was seen in one eye. In contrast, in the study by Murphy et al.[20] 16 out of 263 eyes had uveitic glaucoma. Maximum hypotonia and phthisis occurred in 18.8 and 12.5% of eyes with uveitic glaucoma, respectively, after treatment with 810nm diode CPC. In eyes with uveitic glaucoma the success rate was high (75%) and the re-treatment rate was low (38%). The authors suggested reduction of laser energy – in particular in patients with high pre-operative IOP, and especially if associated with neovascular or uveitic glaucoma – to limit the hypotonia rate.

Table 4: Eyes with a Decline in Visual Acuity of >2 Snellen Lines

Cause of Decline in Visual Acuity	Number of Eyes (%)	
	Adults	Children
Cataract progression	3 (8.8)*	2 (14.3)*
Dry eye (temporary)	1 (2.9)	
Progression of cyclitic membrane		1 (7.1)
Progression of cataract and glaucoma	1 (2.9)	
Progression of secondary cataract	1 (2.9)	
Cataract and CME after active uveitis	2 (5.9)	
Progression of cataract, corneal guttata and glaucoma (active uveitis)	1 (2.9)	
Progression of glaucoma and active uveitis	1 (2.9)	
Progression of corneal decompensation	1 (2.9)	
Unknown reason	1 (2.9)	

**After cataract operation, visual acuity was better than before cyclophotocoagulation. CME = cystic macular oedema.*

Table 5: Complications and Events After One or More Cyclophotocoagulation in 48 Eyes with Inflammatory Glaucoma (Total of 88 Treatment Sessions)

Complication/Event	Number of Eyes (%)		
	All Patients	Adults	Children
Pop effects	0	0	0
Conjunctival burns	0	0	0
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
Anterior vitreitis	1 (2.1)	1 (2.9)	0
Preretinal haemmorhage	1 (2.1)	1 (2.9)	0
Decrease in vision >2 Snellen lines	15 (31.3)	12 (35.3)	3 (21.4)
Hypotonia (<6mmHg)	0	0	0
Phthisis	0	0	0

Conclusion

Low-dose energy with slow release is equally effective as the 810nm diode laser with higher energy pulses delivered in 1.5–2 seconds. The absence of severe side effects and post-operative pain makes this simple outpatient procedure a useful alternative in the management of treatment-resistant inflammatory glaucoma in adults before incisional surgery with shunts or antimetabolites is considered. ■

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Editor's Recommendations

Optic Nerve Head Topography in Nonglaucomatous, Normotensive Patients with Unilateral Exfoliation Syndrome

Puska P, Harju M, *Graefes Arch Clin Exp Ophthalmol*, 2009;247(8):1111–17.

Optic nerve head damage may result from high intraocular pressure (IOP) associated with the exfoliation syndrome (EXS). At equal IOP levels, eyes with EXS may suffer damage more easily than eyes without EXS. Opinion differs as to whether EXS alone, without the contributory effect of a raised IOP, is a risk factor for optic nerve head damage. Thirty-six non-glaucomatous, normotensive patients (mean age 68.4±7.1 years) with unilateral EXS were examined for optic disc topography with confocal scanning laser ophthalmoscopy (the Heidelberg Retina Tomograph). The only patients included were those with an IOP difference of ≤3 mmHg between fellow eyes and with IOP fluctuation ≤5 mmHg in diurnal curves.

The results showed that mean IOP was higher in the EXS than in the fellow non-EXS eyes (15.0±2.8 versus 14.1±2.7mmHg; p<0.001). According to the multivariate analysis of variance, no differences existed in the global parameters between EXS and non-EXS eyes (p=0.778). Nor did differences appear in sectoral parameters between fellow eyes in the temporal (p=0.634), temporal superior (p=0.236), temporal inferior (p=0.330), nasal (p=0.711), nasal superior (p=0.307) and nasal inferior (p=0.434) sectors. In conclusion, EXS may not in itself be a risk factor for optic disc damage when IOP is not elevated from its base level and when its variation is normal. ■

Transscleral Red Laser Cyclophotocoagulation for the Treatment of Therapy-resistant Inflammatory Glaucoma

Puska PM, Tarkkanen AH, *Eur J Ophthalmol,* 2007;17(4):550–56.

The purpose was to evaluate in a retrospective study the long-term usefulness of red 647nm krypton and 670nm diode laser for transscleral contact cyclophotocoagulation (CPC) in the treatment of therapy-resistant inflammatory glaucoma. The authors treated 48 eyes of 38 consecutive patients (mean age 36.8 years, range six to 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 647nm krypton or 670nm diode laser. All eyes had failed maximum tolerated medical therapy and 19/48 eyes (40%) also previous antiglaucoma surgery. Laser power at the scleral surface was 0.35–0.45W and the application time was 10 seconds each. The follow-up was 42.8±40.0 (range two to 145) months. Results showed that the mean pre-operative intraocular pressure (IOP) of 35.6±8.1mmHg fell to 6–21mmHg 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. In conclusion, transscleral CPC using red 647nm krypton or 670nm 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 treatment with antimetabolites is undertaken. ■