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Another Look on Cyclodestructive Procedures

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1. Introduction

Cycloablation is a destructive procedure used to decrease the intra-ocular pressure (IOP) through the ablation of the ciliary body that produces aqueous humour. Many destructive techniques, including diathermy, cryotherapy, ultrasounds, beta irradiation, and laser photocoagulation have been employed with a wide range of results and side effects. Although all above techniques can effectively destroy the ciliary body, only few of them have been used widely enough to convincingly demonstrate their clinical usefulness and gain general acceptance. The ideal method of cyclodestruction should produce clinically useful and predictable reduction of intraocular pressure (IOP), with minimal complications and side effects. (Bartamian & Higginbotham, 2001). Ideally it should have a wide therapeutic window between insufficient and too aggressive treatment intensity, that can result in either insufficient IOP reduction or hypotony/phtisis. Cyclodestructive procedures are usually reserved for cases of glaucoma in eyes with little or no visual potential that proved refractory to medical treatment and outflow surgeries. (Lin, 2008) As an exception to this long established indication, cyclodestructive procedures performed with the 810 nm infrared diode laser transscleral cyclophotocoagulation have been successfully applied also in eyes with refractory glaucoma and good visual potential (Rotchford et al., 2010; Wilensky & Kammer, 2004) supporting an emerging notion that the indications for transscleral laser cyclophotocoagulation should not be limited to eyes with poor visual acuity or potential.

2. Background

Coagulation or destruction of the ciliary body to reduce aqueous production has been advocated in the treatment of glaucoma since the 1930s with the introduction of penetrating cyclo-diathermy (Voght et al., 1936). In the 1950s, cyclocryotherapy was proven reasonably safe and effective to reduce IOP with less tissue destruction and better predictability compared to cyclo-diathermy (Bietti, 1950). Problems still existed, however, including intense postoperative pain, intraocular pressure (IOP) rise, marked inflammation, hemorrhage, and a significant incidence of hypotony and visual loss. Ciliary ablation with ultrasounds was also briefly utilized, but it was eventually abandoned because of marked scleral thinning and ectasia at the treatment site (Coleman et al., 1985).

2.1 Laser cyclophotocoagulation

Laser cyclophotocoagulation has become the principal surgical method for reducing aqueous production. The first laser transscleral cyclophotocoagulation (TSCPC) was described by Beckam and Sugar in the early 1970s. Initially, they used the 694 nm ruby laser, but later reported that the 1064 nm infrared Neodymium : Yttrium-Aluminium-Garnet laser (Nd : YAG) was more effective due to its superior transmission through the sclera and absorption by the ciliary epithelium. The delivery of laser energy to the ciliary processes through the sclera may be performed either with an indenting contact probe or a noncontact projected beam. The development of the compact, portable 810 nm I.R. ophthalmic diode laser has made it more convenient to perform contact TSCPC. The same 810 nm I.R. diode laser beam can also be delivered inside the eye through an endoscope to directly photocoagulate the ciliary body under endoscopic guidance. This technique, named endoscopic cyclophotocoagulation (ECP), has become an increasingly important weapon in the glaucoma surgeon's armamentarium for the treatment of refractory glaucoma at the time of ocular surgery and may have some distinct advantages over the transscleral approach in eyes with visual potential. In 1976, Merritt described his method of transpupillary cyclophotocoagulation of the ciliary processes under indirect visualization via a gonioscopic laser lens. This interesting approach, potentially safer than the more invasive ECP, did not become popular because of the difficulty in visualizing and treating the ciliary processes through the gonio-lens, but it may still represent a good option for aniridic eyes.

Laser cyclo-destructive procedures can be divided as follows:

- Transpupillary CPC
- Transvitreal endophotocoagulation
- Transscleral CPC
 - Noncontact and contact 1064 nm Nd:YAG laser
 - Contact 810 nm diode laser
- Endoscopic 810 nm diode laser CPC

In the United States, CPC is used predominantly for refractory glaucoma difficult to control with conventional glaucoma filtration, such as neovascular glaucoma, traumatic glaucoma, glaucoma in aphakic eyes, advanced developmental glaucoma, inflammatory glaucoma, glaucoma associated with corneal transplantation, silicone oil-induced glaucoma, and glaucoma in eyes with conjunctival scarring from previous surgery. Cyclophotocoagulation is also used in eyes with limited visual potential, in urgent situations with dangerously elevated IOP, or for pain relief in eyes with no visual potential. It has uncommonly been used in patients who are not candidates for conventional glaucoma therapy due to poor compliance with care or poor postoperative follow-up. Cyclophotocoagulation has also been evaluated for use as primary surgical treatment in developing countries where conventional glaucoma therapy is not available (Egbert 2001).

3. Description of the various CPC procedures

3.1 Transpupillary cyclophotocoagulation

Direct transpupillary treatment of the ciliary processes with the argon laser (488/514 nm) is rarely used, because a clear visual axis and a well-dilated pupil are required to enable photocoagulation of the entire length of the ciliary processes. Clinical results have been poor when treatment was limited to the anterior most portions of the ciliary processes. Transpupillary CPC of the ciliary processes, exposed through peripheral iridectomy or a

widely dilated pupil, can be effective. The mechanism may be related to a laser-induced retraction of the ciliary body.

3.2 Transvitreal endophotocoagulation

Transvitreal endophotocoagulation using a visible or infrared laser beam (514 nm argon, 532 nm solid-state or 810 nm diode) delivered through a vitreo-retinal endoprobe has been used with some success when performed in conjunction with a vitrectomy in the operating room. It requires clear media, aphakia or pseudophakia to directly treat the ciliary processes visible in the field of the operating microscope with scleral indentation. The laser power is titrated to produce a visible burn using continuous wave exposure durations that favour some thermal spread in the deeper layers of the ciliary processes.

3.3 Transscleral cyclophotocoagulation (TSCPC)

Due to the optical properties of the human sclera, TSCPC is performed with infrared emitting lasers, most commonly with the 810 nm Diode Laser delivered via a contact probe or with the 1064 nm Nd:YAG laser, delivered either with a non-contact projected beam or with a contact probe.

3.4 1064 nm Nd:Yag Laser Non-Contact TSCPC

Transscleral ciliary body ablation utilizing the Nd:YAG laser at 1064 nm wavelength has the theoretical advantage of better transmission through the sclera with less back scatter than shorter wavelengths, such as 514 nm argon and 810 nm diode lasers. Non-contact TSCPC was performed using the Nd:YAG laser in the free-running thermal mode (Microruptor III Lasag, Thun, Switzerland, no longer commercially available) for a duration of 20 msec, and the defocus setting number, which offsets the focal point of the 1064 nm infrared treating beam 3.6 mm posteriorly to the focal point of the red aiming beam. In this way, when the red aiming beam is focused on the conjunctiva, the infrared treatment beam is focused 3.6 mm below, supposedly within the ciliary processes. The laser energy is adjusted from 5 to 8 Joules (J) per application. Retrobulbar or peribulbar anaesthesia is given, and the patient is seated at the laser slit lamp. The treatment is directed parallel to the visual axis, focusing the aiming beam on the sclera, 1.5 mm posterior to the limbus, superiorly and inferiorly, and 1.0 mm posterior to the limbus nasally and temporally. A contact lens with 1.0 mm markings parallel to the limbus can be used to facilitate the placing of the applications, to hold the eyelids open and to bleach the conjunctiva. Alternatively, a lid speculum can be used to open the eyelids, and the red aiming beam can be focused on the centre of a 3 mm slit beam. Approximately eight to ten applications per quadrant are placed from 270 to 360 degrees. Treatment may be reduced to 180 degrees in patients judged to be clinically at risk for hypotony (Pastor et al., 2001).

3.5 1064 nm Nd:Yag Laser Contact TSCPC

Retrobulbar or peribulbar anaesthesia is given, the patient lies supine, and a eyelid speculum is placed. The anterior edge of the 2.2 mm sapphire tip of the delivery fibre optic handpiece (Surgical Laser Technologies, Inc., Malvern, PA) is placed 0.5 to 1.0 mm posterior to the limbus (the probe is centred 1.5 to 2.0 mm posterior to the limbus). Gentle pressure is applied with the probe, which is oriented perpendicular to the sclera. The laser energy setting is 5 to 9 Joules, for a duration of 0.7 seconds, with approximately eight spots per

quadrant placed from 270 to 360 degrees. After the procedure, atropine and dexamethasone ointments are applied and the eye is patched. The patch may be removed in the evening and anti-glaucoma drops should be reinstituted. Prostaglandin analogues may be excluded in the short term if cystoid macular edema (CME) is a concern, and cholinergics should be temporarily discontinued to avoid increased anterior segment inflammation. Postoperative prednisolone acetate 1% is applied 4 times daily for 10 to 14 days and tapered according to inflammation (Lin, 2008).

3.6 810 nm Diode Laser Contact TSCPC

It is performed using a semiconductor diode laser system (IRIS Oculight SLx, IRIDEX Corp., Mountain View, CA), its 810 nm wavelength exhibits lower scleral transmission (35%) but considerably greater absorption by melanin than the 1064 nm wavelength. The laser energy is transmitted through a 600 µm diameter quartz fiber with a spherical protruding tip oriented by the footplate of the hand-piece called "G-Probe". Positioning the G-Probe parallel to the optical visual axis with the shorter edge of the footplate next to the anterior border of the limbus will centre the fibre optic tip 1.0-1.2 mm posterior to the corneoscleral limbus and direct the energy toward the ciliary processes. The tip protrudes 0.7 mm beyond the footplate contact surface, which indents the conjunctiva and sclera to enhance the transmission of the laser energy. The probe footplate is curved spherically to match the scleral curvature. Maximum settings from the system are 3.0 watts power and 9.9 seconds duration. Retrobulbar or peribulbar anesthesia is given and a lid speculum is placed. Duration is set at 2000 ms (2 seconds), and the initial power setting is 1750 mW. The power is increased in 250 mW increments to a maximum of 2500mW until an audible "pop" (caused by tissue explosion of the ciliary process, the iris root anteriorly or the retina posteriorly) is heard, then the power is reduced by 250 mW and treatment is completed at this power. Some surgeons recommend lower power and longer burn duration, for example 1250 mW at 4 seconds (5.0 Joules) in heavily pigmented eyes and 1500 mW at 3.5 seconds in lightly pigmented eyes (5.25 Joules). Six applications per quadrant are typically placed over 270 degrees involving the inferior, nasal and superior quadrants for a total of 18 applications per treatment. This is based on burns spaced half the width of the G-Probe footplate (2 mm), but various reports have used from 18 to 40 spots, with 180 to 360 degrees for the initial treatment (Pastor et al., 2001). Generally, the incidence of retreatment increases when a lower energy and/or a lower number of spots are applied. With all non-contact or contact TSCPC procedures, the outcome predictability is limited by the inability to visualize treated tissue. In lieu of direct visualization, trans-illumination may be used to identify the location of the ciliary body, especially in eyes with abnormal anatomy or in enlarged eyes (congenital glaucoma). An ocular trans-illuminator is placed against the posterior globe and directed towards the ciliary sulcus. In a darkened room, the diffuse illumination will demarcate the ciliary body, which can be marked externally (Sharkey & Murray, 1994).

3.7 810 nm diode laser endoscopic cyclophotocoagulation (ECP)

The laser unit for ECP (Endo Optiks, Little Silver, NJ) incorporates 1) a diode laser that emits 810 nm continuous-wave energy, 2) a 175W Xenon light source, 3) a Helium-Neon laser aiming beam, and 4) a video imaging and recording camera. All 4 optical elements are transmitted through a 18-gauge or 20-gauge fibre-optic probe, which is inserted into the eye. The optimal focus for the laser is 0.75 mm from the probe tip, and the endoscope provides a 70-degree field of view. The main unit is compact and portable with a maximum power

output of 2.0 W. The laser power and the exposure duration (up to 9.99 seconds) are adjustable with the controls in the console. The foot pedal controls the laser firing, with the actual duration of each application determined by the exposure duration setting or by the pedal depression, whichever ends first. The 2 main approaches to reach the ciliary processes are via a limbal or a pars plana entry. The limbal approach is preferred to avoid the anterior vitrectomy and the associated risks for choroidal and retinal detachment. However, certain cases are more safely treated through the pars plana, for example, aphakic eyes with posterior synechiae limiting the access to the ciliary sulcus. In both situations, a retrobulbar block with lidocaine and bupivacaine is performed or general anaesthesia can be considered in selective cases. In the limbal approach, after dilation of the pupil with cyclopentolate 1% and phenylephrine 2.5%, a paracentesis is created and the anterior chamber is filled with viscoelastic agent, which is further used to expand the nasal posterior sulcus. This viscoelastic expansion of the posterior chamber allows for easier approach to the pars plicata with the ECP probe. A 2.2-mm keratome is then used to enter into the anterior chamber at the temporal limbus. After orientation of the probe image outside of the eye, the 18-gauge or 20-gauge endoprobe is inserted through the incision into the posterior sulcus. At this time, the ciliary processes are viewed on the monitor and treatment can begin. The laser is set at continuous-wave and power settings are 300 to 900 mW. Approximately a 180-degree span of ciliary processes is photocoagulated (more area can be treated if a curved probe is used). Laser energy is applied to each process until shrinkage and whitening occur. The ciliary processes are treated individually or in a "painting" fashion across multiple processes. If excessive energy is used, the process explodes with a "pop" sound due to bubble formation, leading to excessive inflammation and breakdown of the blood-aqueous barrier. After the nasal 180 degrees of ciliary processes are treated, a separate incision is created at the nasal limbus in a similar fashion as above. The temporal processes are then photocoagulated for a total of up to 360 degrees, if desired. Typically, 180 to 360 degrees are treated. Before closure of the wounds, the viscoelastic material is removed from the anterior chamber with irrigation and aspiration. In the pars plana approach, an infusion port is inserted through the inferior pars plana and 2 superior entries are created for vitrectomy and illumination. Only a limited anterior vitrectomy is performed to allow adequate and safe access to all of the ciliary processes. The ECP probe can be inserted through each superior entry for treatment of the opposite 180 degrees of processes. There may be a few superior processes that cannot be accessed because the entry ports are not exactly 180 degrees opposite to each other. Laser CPC is carried out with the same parameters and end points as described for the limbal approach. If the anterior segment surgeon has not had extensive experience in posterior segment surgery, assistance from a retinal surgeon should be sought for the establishment of the pars plana entry ports and the limited anterior vitrectomy. Risk of inadvertent choroidal and/or retinal detachment is a serious concern and should be minimized. In all patients, whether under local or general anaesthesia, retrobulbar bupivacaine is administered before or at end of the surgery to minimize postoperative pain. Sub-Tenon's injection of 1mL of triamcinolone (40 mg/mL) is also given for inflammation. On postoperative day 1, patients are placed on a regimen of topical antibiotics, steroids, nonsteroidal anti-inflammatory agents, cycloplegics, and their preoperative glaucoma medications except for miotics and prostaglandin analogues because these may exacerbate intraocular inflammation or its sequelae. Antibiotics are discontinued after 1 week, and the steroids, nonsteroidal anti-inflammatory agents, and cycloplegics are tapered as inflammation subsides. Glaucoma medications are removed according to the intraocular pressure (IOP) requirements. Administration of acetazolamide during the evening of

surgery may be used to prevent a spike in IOP from underlying glaucoma, inflammation, or possible retained viscoelastic (Lin, 2008).

4. Published results

It is difficult if not impossible to compare studies that have different entry criteria and definitions of success. In fact, "success" in cyclophotocoagulation procedures has been defined as achieving IOP < 21 or 22 mmHg, and/or an IOP reduction of 20% or 30%; some study considered IOP < 5 mmHg as hypotony and, thus, a failure. Most studies allow the postoperative use of medications to achieve this definition of success.

4.1 Transscleral cyclophotocoagulation

4.1.1 1064 nm Nd:Yag Laser Non-Contact TSCPC

In a retrospective study, Youn et al. (Youn et al., 1996) reviewed 479 patients in a follow-up period of 3-75 months (mean 22 months). The range of laser energy settings was 4 to 8 J. Postoperative IOP was between 5 and 20 mmHg in 52% of the patients. Forty percent of the patients lost two or more Snellen visual acuity lines. Visual deterioration was significantly associated with neovascular glaucoma, African descent, post-treatment hypotony, and more than 6 months of follow-up. Phthisis was encountered in 14% of treated patients. Noncontact Nd:YAG cyclophotocoagulation enhances the risk of graft failure in patients with previous penetrating keratoplasty. In a prospective, unmasked randomized trial, Shields et al. (Shields et al., 1993) assigned two groups of 89 patients to two energy settings, 4 J (range 3.7 to 4.5 J) for the Group A and 8 J (range 7 to 8.5 J) for the Group B, with 30 applications utilizing a contact lens. Among the patients who did not require further surgery, better success (75% versus 60%) and fewer retreatments (25% versus 40%) were observed in the higher energy. Among those patients who received no further surgery, vision loss was 56% of patients in Group A (4 J) versus 42% of patients in group B (8 J). There was no significant difference between the two groups. Mean follow-up was 12.6 months, ranging from 5 to 20 months. Delgado et al. (2003) studied the results of Nd:YAG laser non-contact TSCPC on neovascular glaucoma. Mean follow-up was 27 months (range 1 - 148), 115 eyes were evaluated using 7.8 J energy setting (20 to 40 application over 270 degrees) and the success rate was 65%, 49.8% and 34.8% after 1, 3 and 6 years respectively. There were 11.5% phtisis and 39.1% eyes had a loss of two or more Snellen visual acuity lines. An interesting retrospective study (Ayyala et al., 1998) attempted to compare mitomycin C trabeculectomy, glaucoma drainage device (GDD) and Nd:YAG non-contact TSCPC in the glaucoma management after penetrating keratoplasty. This was a non-comparative case series with fewer than 20 patients in each group. Mean follow-up was 12.9 months. There was no statistically significant difference in successful IOP control between mitomycin C trabeculectomy (77% success), GDD (80% success), or non-contact TSCPC (63%). There was no significant difference in the rate of failure of the corneal graft following trabeculectomy (15%), GDD (0%), or TSCPC (17%) that compared fairly with the 11% to 65% failure rate of the corneal graft following glaucoma surgery reported in the literature. (Pastor et al., 2001). As the criteria for success varied in the different studies, it is not surprising that the rate of success spanned from 35% to 83%. The most common complications included the loss of two or more Snellen visual acuity lines in up to 40% of patients, phthisis in 0 to 14%, hyphema in 0 to 4%, and corneal oedema in 0 to 6% of patients. Sympathetic ophthalmia has also been reported as an extremely rare complication. (Bechrakis et al., 1994).

STUDY	LASER TYPE	GLAUCOMA	F-UP (mo)	N (eyes)	VA LOSS (%)	N. TREAT	POWER	DEGREES	N.
Delgado et al., 2003	nc YAG	neovascular	27	115	39	1,4	7,8 (J)	270	1
Youn et al., 1998	nc YAG	all	10,4	46	0	1,13	5,21 to 7,5 (J)	360	
Shields et al., 1993	nc YAG	all	12	45	26	1	4 (J)	360	
Shields et al., 1993	nc YAG	all	12	44	36	1	8 (J)	360	
Youn et al., 1996	nc YAG	all	22	479	40	1	6 (J)	N/A	
Lin et al., 2004	c YAG	all	67	68	16	1,4	7 to 9 (W)	360	3
Schuman et al., 1992	c YAG	all	19	116	31	1,27	7 to 9 (W)	N/A	3

Table 1. Nd: YAG Laser

4.1.2 1064 nm Nd:Yag laser contact TSCPC

There are fewer studies (see Table 1) reporting the use of Nd:YAG laser contact TSCPC than there are reporting non-contact TSCPC. Schuman et al. (Schuman et al., 1992) reported retrospectively on a series of 116 eyes of 114 patients with a mean follow-up of 1 year (range 6-19 months). Treatment consisted of 32 to 40 applications, for a total of 7 to 9 W of power delivered for 0.7 seconds. IOP control of 3 to 22 mmHg was achieved in 65% of eyes. Twenty-seven percent were retreated. Hypotony with less than 3 mmHg occurred in nine eyes, six of which were phthisical. Nineteen eyes (16%) lost light perception, and 47% of eyes with V.A. of 20/200 or better lost two or more Snellen visual acuity lines (17 of 36 eyes). Lin et al (Lin et al., 2004) in 2004 reported similar results about a series of 68 eyes with a mean follow-up of 5.58 years (range 0.1 - 10 years). Treatment consisted of 32 to 40 applications, for a total of 7 to 9 watts of power delivered for 0.7 seconds. Intraocular pressure control of 3 to 25 mmHg was achieved in 60 % of eyes after one year and in 48% after ten years with only one treatment. 40% of patient where retreated, and this has been considered a failure. Hypotony less than 3 mmHg was seen in 3 eyes, none of which were phthisical. Eleven eyes worsened their visual acuity.

4.1.3 810 Nm diode laser contact TSCPC

For a variety of reasons, mainly clinical effectiveness and practicality, 810 nm diode laser contact TSCPC has been universally adopted to the point to become the standard of care for specific conditions. As a result, there are more publications in the literature on 810nm diode TSCPC (see Table 2) than on any other CPC modality, although many of them are only retrospective. As indicated in Table 2, the mean number of eyes reported in the studies was 55.82 (SD =+/- 58.26) (Standard Deviation) eyes with a variety of diagnoses and of laser treatment parameters. Laser power ranged from 1.25 to 3 watts (mean 1.94 W) for a mean exposure time of 2.16 seconds, for a mean number of applications of 22.10 (SD=+/- 7.02) over 180 to 360 degrees, sometimes adjusting the power for pops and sometimes not. Mean follow-up was 19.86 months (SD=+/- 12.71). Mean success rate was 67.26% (SD=+/- 15.70), but this cannot be a good indicator, because the definition of success was heterogeneous (see Table 2). Mean number of medication was 2.52 (SD=+/- 0.63) pre-operatively and 1.62 (SD=+/- 0.71) post-operatively. Mean loss of visual acuity was 24.74% (SD=+/- 16.78). Retreatment rate was 1.48 (SD=+/- 0.45). Complications were, hypotony (0 to 25%), phthisis (0 to 11%), AS inflammation (0 to 27%), choroidal detachment (0 to 10%), cataract progression (0 to 40%), atonic pupil (0 to 70%) and hyphema (0 to 13%). Rarely reported complications were endophthalmitis, failure of corneal graft, CMO, bullous keratopathy, band keratopathy, persistent ocular pain. Rarely reported complications included necrotizing scleritis (Ganesh et al., 2006), scleral perforation (Kwong at al., 2005), iris retraction and retroflexion (Sony et al., 2003) and malignant glaucoma (Azuara-Blanco et al., 1999). Table 2 stratifies the outcomes among various types of glaucoma. In Neovascular Glaucoma success rate ranges from 40% to 64% with a mean follow up from 9 to 60 months; in Silicon Oil Glaucoma success rate ranges from 44% to 82% with a mean follow up from 4 to 22 months; in Pediatric Glaucoma success rate ranges from 67% to 72% with a mean follow up from 20 to 21 months; in Chronic Angle Closure Glaucoma (CACG) success rate ranges from 86% to 92% with a mean follow up from 12 to 26 months; and in Keratoprosthesis Glaucoma success rate is 66% with a mean follow up of 26.6 months. 810 nm Diode Laser Contact TSCPC has also been used in 49 eyes with a good visual acuity (20/60 or better).

STUDY	GLAUCOMA	F-UP (mo)	N (eyes)	N. TREAT	POWER (W)	TIME (s)	DEGREES	N. SPOTS
Spencer et al., 1999	all	21,5	58	1,6	2,00	2	270	14
Yildirim et al., 2009	nv	24	33	1	1,50	2	270	17
Ghosh et al., 2010	nv	9	14	1	2,00	2	180-270	25
Preussner et al., 2010	africans	6	75	N/ A	5,00	0,2	360	20
Malik et al., 2006	all	35	28	2	2,12	2	360	24
Semchyshyn et al., 2002	all	26,9	21	1,38	2,00	2	270	21,9
Schlote et al., 2000	inflammatory	12	22	2	2,00	2	270	12,5
Rotchford et al., 2010	good vision	60	49	1,73	2,00	2	N/ A	14,4
Sood et al., 2009	pediatric	19,8	9	1	1,25	3,5	180-270	17,4
Kirwan et al., 2009	pediatric	21	77	2,3	1,50	1,5	300	40
Lai et al., 2002	CACG	12	14	1,14	2,00	2	270	16,3
Lai et al., 2005	CACG	26,5	13	1,15	2,00	2	270	17,5
Han et al., 1999	silicon oil	12	11	1,18	2,00	2	360	23,5
Agarwal et al., 2004	all types	15,8	30	1,2	1,50	2	360	40
Rivier et al., 2009	keratoprotesis	26,6	18	1,3	1,87	2	270	17,5
Noureddin et al., 2006	all	13,69	36	1,25	2,25	2	360	28
Sivagnanavel et al., 2005	silicone oil glaucoma	21,8	18	1,5	2,00	1,5	180	25
Egbert et al., 2001	all	13,2	40	1,22	1,50	1,5	360	20
Egbert et al., 2001	all	13,2	39	1,22	1,25	2,5	360	20

Table 2. (continues on next page) 810 nm diode laser contact TSCPC

STUDY	GLAUCOMA	F-UP (mo)	N (eyes)	N. TREAT	POWER (W)	TIME (s)	DEGREES	N. SPOTS
Ansari et al., 2007	all	12,5	74	1,01	2,00	2	360	30
Kaushik et al., 2008	all	14,3	66	1,16	2,00	2	270	18
Nabili et al., 2004	diabetic neovascular glaucoma	N/A	20	1,45	2,00	2	270	15
Kramp et al., 2002	all	13,9	193	1,3	1,60	2	360	27
Grueb et al., 2006	all	24	90	1,3	2,00	2	180	17,5
Iliev et al., 2007	all	30,1	131	1,54	2,00	2	270	22
Schlote et al., 2007	aphakic and posttraumatic	42	46	2,58	2,00	2	180	20
Heinz et al., 2006	juvenile idiopathic arthritis	10,1	21	2,15	2,00	2	180	25
Ocakoglu et al., 2005	all	11,4	32	1,68	2,50	2	270-300	22
Murphy et al., 2003	all	17	263	1,5	N/A	N/A	N/A	N/A
Walland, 1998	all	10,1	22	1	1,50	1,5	360	40
Walland, 1998	all	11,4	8	1	1,50	1,5	180	20
Frezzotti et al., 2010	all	17	124	1,26	2,00	2	180-270	15
Leszczynski et al., 2009	neovascular	60	30	2,4	1,75	N/A	270	17,5
Raivio et al., 2008	all	26	60	1,4	0,43	10	180	20
Gangwani et al., 2010	silicon oil	4	9	2,34	1,87	2	270	30
Youn et al., 1998	all	10,4	49	1,2	2,37	2	360	24,63
Brancato et al., 1995	all	20,7	68	N/A	2,60	2	360	18

Table 2. (continued) 810 nm diode laser contact TSCPC

The success rate on pressure reduction (IOP <21) was 90%, but 60% of eyes lost 1 Snellen visual acuity line and 30% of the eyes lost more than 2 Snellen visual acuity lines. 810 nm Diode Laser Contact TSCPC has been compared to Ahmed Valve implantation by Yildirim et al. (Yildirim et al., 2009) who found a success rate of 61% for TSCPC vs. 59% for Ahmed Valve with a mean follow up of 24 months. In a similar study Sood et al (Sood et al., 2009) compared 810 nm Diode TSCPC to Ahmed Valve implantation in Pediatric Glaucoma and found a success rate of 66.7% for TSCPC vs 62.5% for Ahmed Valve with a mean follow up of 19.8 and 26.3 months respectively. Malik et al (Malik et al., 2006) compared 810 nm Diode TSCPC to Molteno tube shunt and found a success rate of 64% for TSCPC vs 81% for Molteno tube shunt with a mean follow up of 35 months. Youn et al (Youn et al., 1998) compared non-contact TSCPC with 1064 nm Nd:YAG and 810 nm diode lasers in a prospective, randomized, unmasked trial. Mean follow-up was 10.4 months. Success was 83% and 71% of the YAG and diode patients, respectively, (no statistically significant difference). Retreatment in the YAG group was lower (8.7%; 4/46) than the diode group (18%; 6/49). Although not statistically significant, the Nd:YAG group had a slightly higher success. In clinical practice the 1064 nm Nd:YAG laser in the free-running thermal mode is not commercially available anymore and most clinicians have elected to use the more compact and user-friendly 810 nm diode laser with the contact G-Probe. Agarwal et al (Agarwal et al., 2004) compared the 830 nm Diode Laser contact TSCPC to the 830 nm Diode Laser non-contact TSCPC 830 and found a success rate of 94% for Contact vs. 90% for Non-Contact after a mean follow up of 15.8 months. Although there is not a general agreement, most studies have found that the amount of energy used for 810 nm diode laser contact TSCPC seems to correlate with treatment success rate, without implying a higher complication or vision loss rate.

4.2 Endoscopic cyclophotocoagulation

4.2.1 810 Nm diode laser endoscopic cyclophotocoagulation (ECP)

810 nm diode laser ECP is a relatively new method for CPC, and this is reflected in the relatively smaller number of publications (see Table 3). It's very difficult to compare such studies because laser parameters are different or not well specified. In Table 3 we summarized six studies that evaluated a 33.3 mean number of patients (SD=+/- 18.3) range 12 - 68, with various types of glaucoma, including pediatric glaucoma, for a mean follow-up of 11.9 months (SD=+/- 5.5) range 4.5-21.3 and with different definition of success. Mean success rate was 59.1% (SD=+/- 23.7) range 17-82.9%. Mean pre- and post-operative number of medication was 2.2 (SD=+/- 0.5) and 1.5 (SD=+/- 0.5) respectively. Mean visual acuity loss of two or more Snellen lines was 9% (SD=+/- 8) range 0-22% and retreatment rate was 1.16 (SD=+/- 0.2). Complications were hypotony (0 to 8%), phthisis (0 to 3%), anterior segment inflammation (0 to 6%), hyphema (0 to 9%), and RD (0 to 8%). In pediatric glaucoma (refractory glaucoma with corneal opacities) the success rate (IOP <21mmHg without complication and further surgery) was 17% at 13 months of follow up. (Al-Haddad et al., 2007). The authors attributed the poor results to the surgical difficulties of refractory pediatric glaucoma. Lima et al (Lima et al., 2004) compared ECP to Ahmed Valve implantation in 6\8 patients and found a success rate of 73.5% vs 70.6% (p = 0.7) respectively (mean follow up of 21.3 and 19.8 months respectively). Complications were different: ECP reported more cases of hypotony, phthisis, anterior segment inflammation, while Ahmed valve reported more cases of endophthalmitis, choroidal detachment and

STUDY	GLAUCOMA	F-UP (mo)	N (eyes)	VA LOSS (%)	N. TREAT	DEGREES	SUCCESS (%)	
Lima et al., 2004	all	21,3	68	9	1	210	73,5	
Yip et al., 2009	all	15,9	29	17	1	270	48,3	
Kahook et al., 2007 (1 site)	all	4,5	15	0	1	240-300	47	IOP re
Kahook et al., 2007 (2 sites)	all	4,5	25	0	1	240-300	92	IOP re
Al-Haddad et al., 2007	pediatric	13,0	12	8	1,17	270	17	IOP<=
Carter et al., 2007	aphakic and pseudophakic children	12	34	N/A	1,8	180-270	53	IOP<
Murty et al., 2009	all	12,3	50	22	N/A	270-360	82,9	

Table 3. 810 nm diode laser ECP

retinal detachment. Kahook et al (Kahook et al., 2007) compared 2-incision ECP to 1-incision ECP, finding a success rate of 92% for 2-incision vs. 47% for 1-incision. No major complications have been reported.

5. Personal considerations and role of anti-VEGF and panphotocoagulation

We personally have experience with cyclocryotherapy, contact diode TSCP and ciliary ablation with ultrasound. We long ago abandoned the US ciliary ablation due to the difficulties of the treatment and some serious adverse events related to the difficulty of centering the ultrasound beam exactly on the ciliary body. We are not using anymore cyclocryotherapy mainly because of the inflammatory processes related to this method. Inflammatory processes might be present with diode laser TSCP as well if the treatment is not titrated. We are very concerned of possible adverse events related to cyclodestruction and with the diode laser we prefer to stay on the safe side at the eventual price of retreatment rather than risk serious complications. Our current protocol with the diode laser is to treat 180 degrees using the G-probe. The time is pre-set at 2 seconds and we generally start with a 1800 mW power. We increase the power until a bob can be appreciated and then we decrease the power by 100 mW and we continue the treatment. We pay a lot of attention to keep the probe strongly pressed on the globe in order to achieve a better conduction through the sclera. The number of applications is titrated on the basis of the IOP level and on the type of glaucoma. We generally give more applications if the IOP is elevated with the exception of uveitic and neovascular glaucoma where we never apply as first treatment more than 14 applications, because we fear that in this forms of secondary glaucoma there might coexist a lower aqueous production. Concerning the use of anti-VEGF, Although there are several reports that claim a resolution of IOP elevation, we cannot confirm these findings. Probably the patients that come to our Department present long standing forms of iris neovascularisation. Although some of our patients did not present a complete angle occlusion at gonioscopy, we never had a complete normalization of IOP by using intravitreal injections. In a few cases intravitreal ant-VEGF injection, nevertheless, allowed for a partial recovery of the glaucoma with some clearing of the cornea, which allowed us for starting a pan-retinal photocoagulation. Retinal cryotherapy is always added whenever the panretinal photocoagulation is impossible due to corneal decompensation, cataract or vitreous hemorrhage.

6. Summary

Both 810 nm diode laser TSCPC and ECP are effective procedures for the treatment of refractory glaucoma. TSCPC is an extra-ocular procedure that has mainly been used in eyes that had received prior filtration surgeries or that had very limited visual potential. However, more recently, there has been a trend toward using 810 nm diode laser TSCPC as the primary surgery in eyes with relatively good vision. ECP is an intra-ocular surgery that has also been used as a primary procedure, often combined with phacoemulsification cataract extraction, but should probably be considered almost exclusively in eyes that have good potential vision. These relative indications for each type of CPC are guided by the possible complications of each procedure. TSCPC is a “blind” procedure that has significant rates of success, but also hypotony and/or phthisis, which may relate to its external approach. Greater energy is generally required to penetrate the sclera as compared with the

STUDY	PROCEDURE	GLAUCOMA	F-UP (mo)	N (eyes)	VA LOSS (%)	N. TREAT	POWER (J)	DEGREE
Yildirim et al., 2009	TCP diode vs	neovascular	24	33	18	1	>1,5	270
Yildirim et al., 2009	ahmed valve	neovascular	24	33	27	N/A	N/A	N/A
Malik et al., 2006	TCP diode vs	all	35	28	46	2	1,75 - 2,5	360
Malik et al., 2006	molteno tube	all	35	26	54	N/A	N/A	N/A
Sood et al., 2009	TCP diode vs	pediatric	19,8	9	20	1	1 - 1,5	180-270
Sood et al., 2009	ahmed valve	pediatric	26,3	8	75	N/A	N/A	N/A
Agarwal et al., 2004	C TCP diode 830 nm vs.	all	15,8	30	6	1,2	1,5	360
Agarwal et al., 2004	NC TCPdiode 830 nm	all	15,8	30	6	1,6	1,5	360
Youn et al., 1998	TCP YAG vs.	all	10,4	46	0	1,13	5,21 - 7,5	360
Youn et al., 1998	TCP diode	all	10,4	49	8	1,2	1,75 - 3	360

Table 4. Comparing procedures

endoscopic approach. EPC allows the photocoagulation of the ciliary processes under direct visualization, but can also lead to the overtreatment of the ciliary tissues and surrounded structures, including the vascular structure of ciliary process, the pars plana, and the iris root, all of which may potentially predispose to phthisis or hypotony. The major disadvantage of ECP is that it is an intra-ocular procedure. Endophthalmitis, choroidal haemorrhage, and retinal detachment are rare, but remain potential serious complications. New transscleral 810 nm laser applications over the pars plana with a new micropulse laser emission mode, have been reported to result in effective IOP lowering, while avoiding most collateral problems of 810 nm continuous wave diode laser TSCPC and EPC (Tan et al., 2010).

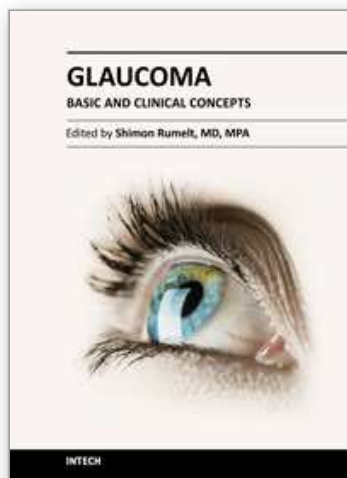
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