·Review·

Endoscopic cyclophotocoagulation: an overview and Asian perspective

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Abstract

• Surgical treatment of glaucoma has been classified as cyclodestructive (reducing inflow) or filtering (increasing outflow). Cyclodestructive procedures have traditionally been reserved for eyes with poor visual prognoses and refractory glaucomas including post-trauma, aphakia, congenital and developmental glaucoma. Since Uram described the first use of endoscopic cyclophotocoagulation (ECP) in 1992, short and long-term outcomes for ECP have been promising. In the present article, we conduct a Pubmed search and review of published English literature on endoscopic cyclophotocoagulation and comparison with limited results in a single Singapore ophthalmic tertiary hospital. Safety and efficacy of ECP and combined phacoemulsification-ECP procedures in treatment of pediatric and adult glaucomas of various etiologies and severities is reported. Local short-term unpublished results from a single Singapore tertiary ophthalmic service is reported and concurs with previously published results.Published reports and current experience with ECP has demonstrated that ECP with direct visualization of the target tissues avoids the complications associated with blind trans-scleral cyclophotocoagulation by applying optimum energy to target tissue ciliary epithelium with endoscopic visualization and infrared laser wavelength application. Significant financial barriers exist to introducing this service. It is safe and effective in controlling IOP and reducing reliance on anti-glaucoma medications. Widespread acceptance and use of this technique awaits large-scale randomized controlled studies.

• KEYWORDS: glaucoma; endoscopic cyclophotocoagulation; cyclodestructive procedures

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INTRODUCTION

The heterogeneous group of conditions resulting in glaucomatous optic neuropathy have been treated with a combination of medical and surgical therapies. The advent of anti-glaucoma medications has reduced the requirement for surgical procedures in glaucoma.

Surgical treatment of glaucoma has traditionally been classified as cyclodestructive (reducing inflow) or filtering (increasing outflow).

Filtering procedures have been the procedure of choice, and in an Asian context are increasingly performed with the use of adjunctive anti-metabolites including mitomycin-C and 5-fluorouracil due to the increased propensity for scarring as well as early and late bleb-failure in individuals of pigmented races [1]. Trabeculectomy performed alone or in combination with small-incision cataract surgery is the most commonly performed surgical procedure for glaucoma in Singapore. This is due to its efficacy and relative predictability [1]. However, trabeculectomy surgery is not without its own problems, as it requires frequent post-operative clinic visits and multiple interventions to ensure long-term bleb survivability. In addition, early/late bleb failure and bleb-related complications, ocular hypertension or hypotony, may further complicate the post-surgical course of trabeculectomy [2].

Cyclodestructive procedures have traditionally been reserved for eyes with poor visual prognoses and refractory glaucomas including post-trauma [3,4], aphakia [5], congenital/ developmental glaucoma [5,6], and glaucoma associated with previous penetrating keratoplasties [7], as well as eyes with scarred conjunctiva not suitable for filtering procedures [3]. The reticence with the use of cyclodestructive procedures is related to the blind nature of trans-scleral procedures, and the high incidence of post-procedure inflammation, hypotony, cataract formation and treatment failure [8]. The earliest cyclodestruction methods were performed by surgical excision, diathermy, cryotherapy, light coagulation and eventually laser [4]. Laser cyclophotocoagulation may be performed with an Argon laser through a contact lens via the

transpupillary route for aphakic eyes. More commonly, trans-scleral cyclodestruction is performed through a non-contact or contact probe. Initial experience using the ruby laser was subsequently superceded by the Neodymium: Yttrium-Aluminium-Garnet (Nd:YAG) laser which demonstrated improved scleral penetration [4]. Further developments in laser technology led to the employment of the compact and portable 810nm wavelength semi-conductor diode laser which offers improved melanin absorption and hence selectivity, over the Nd:YAG.

The principles of trans-scleral cyclophotocoagulation remain identical, regardless of method of delivery. Laser delivery is blind, and requires transmission of laser energy through the sclera, ciliary body and ciliary vessels, before final absorption by the target tissues of ciliary epithelium[9]. Histopathological changes of different modalities of trans-scleral cyclophotocoagulation are identical, demonstrating moderate to severe disorganization of ciliary processes with fibrosis and atrophy of stroma, as well as non-pigmented and pigmented ciliary epithelium [10,11].

Trans-scleral cyclophotocoagulation has been demonstrated to be effective for treating severe end stage glaucoma in which other surgeries have failed or potential vision is limited. Within the limitations of varying definitions of success for this procedure, overall success rates vary between 34%-81% of patients achieving target intraocular pressure (IOP) with or without concomitant use of anti-glaucoma medications, over a mean follow-up period of 30 months [12-15]. This procedure is also associated with a significant incidence of serious complications and post-operative discomfort [15]. In addition, due to the blind nature of treatment delivery, the use of trans-scleral cyclophotocoagulation is conventionally limited in eyes with disorganized anterior segments.

Uram [4] initially developed and described a novel method to directly photocoagulate the ciliary body under endoscopic guidance, termed endoscopic cyclophotocoagulation (ECP). He was the first to incorporate a diode laser emitting pulsed continuous wave energy at 810nm wavelength, coupled with a 175W xenon light source, helium-neon laser aiming beam and a video camera for imaging while recording. These functions were housed in a 0.88mm (20-gauge) probe which offered a 70° field of view (Endo Optiks, Little Silver, NJ, USA). All elements of the probe are transmitted via fibreoptics. Initial descriptions of the endoprobe were performed in vitreous surgery [16], although the applications to anterior segment cataract and glaucoma surgery followed. ECP has been gaining increasing popularity, but concerns still linger about the inherently ablative nature of this therapy, as well as the requirement for intraocular access to perform this procedure.

PERFORMING ECP

Endoscopic cycloablation is performed through an 18-gauge (1.2mm diameter probe with viewing angle of 110°) or 20-gauge (0.88mm diameter probe with viewing angle of 70°) probe inserted intraocularly. Depth of focus varies from 1mm-30mm for the 18 gauge probe, and 0.5mm-15mm for the 20-gauge probe [3,4]. Laser power (maximum of 1.2W) and duration are adjusted on the console. The actual duration of each treatment is determined by the period of pedal depression.

ECP may be performed in any patients including those of phakic, pseudophakic or aphakes. Due to the requirement for intraocular access in order to perform ECP, this procedure is frequently performed in conjunction with other intraocular procedures, most commonly with phacoemulsification cataract surgery.

Anterior segment and glaucoma surgeons routinely perform endocycloablation through their choice of preferred clear cornea/scleral tunnel incision. If combined with cataract extraction, the preference is for extracapsular phacoemulsification and posterior chamber lens implantation. Following placement of the intraocular lens (IOL) into an intracapsular position, the posterior chamber between the posterior surface of the iris and the anterior leaf of the anterior capsule is insufflated with ophthalmic viscoelastic device (OVD). The straight or curved tip endoprobe is oriented outside of the eye, and inserted through the incision and directed toward the posterior chamber. The ciliary processes are photocoagulated under direct visualisation with energy settings commencing between 40mW-60mW and adjusted accordingly to achieve shrinkage and whitening of the ciliary processes while avoiding an audible "pop" (with bubble formation) indicating excess energy is administered. Energy delivered is minimized to avoid significant breakdown of the blood-aqueous barrier and excessive inflammation. Initial photocoagulation is directed at the raised processes without affecting the "valleys" of non-displaced ciliary epithelium. A minimum of 270° to a maximum of 360° is treated. A single incision is adequate to perform 180° of photocoagulation with a straight probe,

while a similar incision is adequate to perform treatment over 270° for a curved probe. At the conclusion of the procedure, remaining OVD is removed from the anterior chamber by irrigation with balanced salt solution, and the wound is closed in the usual manner.

A posterior approach may be indicated in certain clinical conditions including aphakia or severe posterior synechiae limiting ciliary sulcus access. This is performed via standard 3-port pars plana vitrectomy with limited anterior vitrectomy. This would allow safe and adequate access to all ciliary processes. Treatment parameters and end points are identical to the anterior segment approach. Wound closure is in the usual manner for posterior segment surgery.

At the conclusion of surgery, an appropriate anti-inflammatory and antibiotic regime is administered as per routine cataract surgery. Cycloplegics, non-steroidal anti-inflammatory drugs (NSAID) and routine glaucoma medications are administered. The exceptions include miotics and prostaglandin analogues which may theoretically exacerbate intraocular inflammation and its attendant sequelae. Oral acetazolamide is administered post-procedure in patients with advanced glaucomatous damage for prophylaxis against intraocular pressure spikes due to inflammation, or retained OVD. Glaucoma medications are expected to be continued for 2-4 weeks until the clinical effects of ECP suggest tapering of glaucoma medications are appropriate. Hollander and Lin [7] described an isolated case of delayed-ECP effect 3 months following treatment for penetrating keratoplasty-associated ocular hypertension. This suggests that delaying ECP retreatments in medically controlled glaucoma for patients with good visual potential may result in late treatment benefit, whilst offering the benefit of avoiding over-treatment. Topical antibiotics are administered for a minimum of 1 week, whilst steroids, NSAIDS and cycloplegics are tapered as inflammation subsides. Glaucoma medications are removed as clinically dictated.

CLINICAL RESULTS OF ECP

Clinical experience with ECP has been expanding rapidly. Literature review was performed using a Pubmed search with the key words "endoscopic" and "cyclophotocoagulation" This returned a total of 15 published reports in the English language, between the years 1992 and 2007.

The first description of ECP was reported by Uram [4] in 1992. The initial reports for ECP included a retrospective case series of 10 eyes with recalcitrant neovascular glaucoma treated with ECP for treatment areas between 90°-180°. After a mean follow-up of 8.8 months, the eyes demonstrated a mean reduction of 28.3% and a significant reduction in requirement for systemic and topical anti-glaucoma medications. Subsequently, Uram described a larger case series of 143 patients with intractable neovascular glaucoma, which demonstrated a dramatic IOP reduction of 67.6% from baseline, with a similar reduction in requirement for systemic and topical anti-glaucoma medications. There were no reports of serious intraoperative complications.

Following these initial descriptions of ECP, subsequent studies evaluated the safety and efficacy of ECP in the treatment of other forms of refractory glaucomas [3,5,9,17-20]. The majority of studies described retrospective case series or poorly designed prospective studies. There was a predominant problem of the lack of a uniform definition for success which makes comparison between studies difficult.

Several reports retrospectively describe case series of ECP in the treatment of recalcitrant glaucomas [3,18]. Uram [4] was the first to describe the effects of phaco-ECP against phacoemulsification alone. Chen *et al* [19] reported their series of 68 patients with diverse forms of refractory glaucoma which had failed prior treatment on maximal medical therapy and previous filtration/cyclodestructive procedures. Mean IOP reduction of 34% was reported after an average follow-up period of 12.9 months, with a corresponding decrease in requirement for anti-glaucoma medications. No significant intraoperative complications were described, with the exception of post-operative inflammation, transient choroidal detachment and a single case of malignant glaucoma.

Berke [21] was the first to report a randomized series of sufficiently large cohort and length of follow-up comparing combined phaco-ECP patients against phacoemulsification alone. He reported a series of 626 eyes with mean follow-up of 30 months of patients with moderately severe glaucoma. He compared in a randomized, non-blinded fashion patients treated by five surgeons with combined phaco-ECP against phacoemulsification alone. Treatment endpoints included mean IOP reduction and mean reduction in anti-glaucoma medications. With regards to the primary endpoints, there was no statistically significant difference for the phacoemulsification group alone, whilst the combined phaco-ECP group demonstrated mean reduction of IOP from (19.13±4.14)mmHg to (15.73±3.00)mmHg (P<4.48±10^{-72}),

and reduction in mean number of anti-glaucoma medications from(1.53±0.89)mmHg to(0.65±0.95)mmHg($P<1.23\pm10^{-85}$). Berke [21] concluded that phaco-ECP effectively lowered IOP as well as reduced the number of anti-glaucoma medications required after 2 years, which translated into effective cost-savings for the patient and the medical community. Combined phaco-ECP did not increase the potential for developing cystoid macular edema postoperatively, not was it associated with an increased risk of serious complications such as endophthalmitis and visual loss compared to phacoemulsification alone. Rates of cystoid macular edema were slightly lower in the combined phaco-ECP group (0.8% *vs* 1.2%) compared to the phacoemulsification group alone, although this difference was not statistically significant.

Gayton [22] published the only randomized controlled trial to date comparing combined cataract-glaucoma surgery (phaco-trabeculectomy) versus cataract-ECP. In his study, 58 eyes in 58 patients with combined cataract and progressive glaucoma requiring surgery were randomized into treatment arms of combined phaco-trabeculectomy versus phaco-ECP. These patients were followed up for 2 years and the main outcomes measured were postoperative inflammation and intraocular pressure (IOP). Treatment failure was defined as IOP control requiring subsequent surgical intervention. Study results showed that IOP reduction was greater immediately postoperatively in the trabeculectomy group, but both groups were equivalent at 1 month follow-up. In the immediate postoperative period, less inflammation was observed in the ECP group. In general, however, the overall IOP reduction was greater in the trabeculectomy group, and less anti-glaucoma medications were required at all time points during follow-up. Trabeculectomy patients achieved target IOP control without medications in 42% of cases, compared to 30% for ECP patients. For patients achieving IOP control with medications, this was 54% for trabeculectomy *vs* 65% for the ECP group. Overall success rates for IOP control with or without medications were identical. Most significantly, there were no cases of post-treatment hypotony in either group. ECP was demonstrated to be effective in reducing IOP, was less invasive, caused less inflammation and has potentially less complications than traditional trabeculectomy filters.

Lima *et al* [17] described 34 patients in a prospective series comparing refractory pseudophakic glaucoma versus Ahmed tube implantation. Similar to previous studies, the ECP patients demonstrated significant reductions of 66.2% (average of 27.54mmHg) and mean reduction of one anti-glaucoma medication after a mean follow-up of 21.29 months. The ECP group reported an overall higher success rate of 73.53% (IOP<21mmHg) with or without anti-glaucoma medications. Most importantly, there were no serious complications associated with ECP, and it was simpler and less time-consuming to perform than Ahmed tube implantation.

ECP efficacy in treatment of pediatric glaucomas has also been demonstrated in several retrospective case series. Neely *et al* [5,6,23] treated 36 eyes of 29 patients with childhood glaucomas of differing etiologies. Treatment strategy varied between 180° and 270° (mean of 260°). Mean follow-up period of 19 months demonstrated that 34% eyes were successfully treated with a single treatment (mean reduction of 30%), and 43% achieved target IOPs with >1 treatments (average of 1.42 procedures). The most significant complications occurred in four aphakic eyes which included two eyes with retinal detachments, one eye with chronic hypotony and one experiencing severe visual loss (hand movement vision deteriorating to no perception of light). Neely concluded that ECP was moderately effective for the management of difficult pediatric glaucomas, with aphakic patients having an increased risk of significant postoperative complications.

Published Asian experience has been limited, with initial results trending towards general agreement with previously published results in Caucasian populations. Yip *et al* reported unpublished early results of 23 eyes in 22 patients treated with ECP in a single tertiary centre in Singapore between October 2004 and April 2005. Eighteen eyes had combined phacoemulsification-ECP for moderate to severe glaucoma of various etiologies. They reported overall success rates of 78.3% of eyes achieving target IOP of 22mmHg or lower with or without anti-glaucoma medications. There was a mean reduction in IOP [from (20.96 ±4.63)mmHg to (17.83±6.19)mmHg] which was statistically significant (P= 0.003) and number of anti-glaucoma medications required from 2.0±0.8 to 1.0±1.1. Both treatment endpoints demonstrated statistical signifi-cance (P=0.003). No serious post-operative side-effects were observed. However three (13%) patients reported moderate visual loss (VA loss >10 ETDRS letters).

DISCUSSION

Published reports and current experience with ECP has demonstrated that this novel technique of treatment delivery with direct visualization of the target tissues avoids the

Table 1 Endoscopic cyclophotocoagulation: an overview and Asian perspective

Year	Author	Age Group	*n*	Glaucoma type	Procedure type	Mean reduction (mmHg)	Mean reduction topical anti-glaucoma med ication	Success rate (with or without medication)	Significant complications
1992	Uram	Adult	10	Neovascular glaucoma	ECP	28.3	Not reported	90%	Hypotony 2 with chronic RRD
1995	Uram	Adult	10	Combination cataract-uncontrolled POAG	Phaco-ECP	17.9 (57.0%)	Not reported	Unknown	Vitreous Hb 1
1995	Uram	Adult	143	Neovascular glaucoma	ECP	32.7 (67.6%)	2.8	Unknown	Transient visual loss (number unknown)
1997	Mora	Adult	8	Moderate-severe glaucoma	ECP	Unknown	Not reported	Unknown	Nil
1997	Chen	Adult	68	Refractory glaucoma	ECP 56, combined 12	10.7 (38.6%)	1	90% (IOP<22)	Fibrin 16 (24%), hyphaema 8 (12%), CMO 7 (10%), VA loss 4 (6%), choroidal 3 (4%), malignant glaucoma 1 (1%), vitreous hemorrhage 2
1999	Gayton	Adult	29	IOP>30mmHg, progressive cupping/field loss	Phaco-ECP	16 (64.5%)	Not reported	95% (IOP<19)	Chronic inflammation >1 month *n*=2
2001	Neely	Paediatric	36	Pediatric glaucomas	ECP	11.43 (32.6%)	Not reported	34% (IOP <=21)	RRD 2, chronic hypotony 1, VA loss 1
2004	Lima	Adult	34	Pseudophakic glaucoma *vs.* Ahmed	ECP	27.54 (66.2%)	1	73.52% (IOP <21)	VA loss 16%
2004	McFarland	Adult	180	Moderate glaucoma	Phaco-ECP	8.0 (44.4%)	90% reduction in use	Unknown	Nil
2005	Lin	Adult	68	Refractory glaucoma	ECP/combined	10.7 (34%)	1	90% (IOP<22)	Nil
2006	Berke	Adult	626	Moderate glaucoma	Phaco-ECP	3.4 (17.8%)	0.88	90%	Nli
2007	Carter	Paediatric	34	Childhood glaucomas	ECP	9.7 (29.8%)	Not reported	53% (IOP<23, >15% reduction)	RRD 2
Unpublished	Yip	Adult	23	Moderate glaucoma	ECP/combined	3.1 (14.9%)	Not reported	78.3% (IOP<22)	VA loss 3 (13%). All pseudo-exfoliation cases treatment failure

CMO: cystoid macular edema; ECP: endoscopic cyclophotocoagulation; IOP: intraocular pressure; POAG: primary open angle glaucoma

complications associated with blind trans-scleral cyclophotocoagulation by applying optimum energy to target tissue ciliary epithelium with endoscopic visualization and infrared laser wavelength application. Table 1 summarises the major studies in the English language examining the safety and efficacy of ECP in the management of moderate to severe glaucomas in eyes with good to poor visual prognoses. Across all etiologies, disease severity and age-groups, ECP has been demonstrated either in isolation or performed in combination with phacoemulsification, to effectively lower IOP in a sustained fashion and reduce the number of anti-glaucoma medications required to achieve target IOP in a cost-effective manner. Literature review in the previous 15 years suggests that the total reported short-term complication rates are less than 25% for severe inflammation, cataract or hyphema formation, and long-term complication rate of reduced vision for any reason is <16% in any individual study related to ECP treatment. Overall review of reported numbers for all glaucoma types and severities treated with ECP, suggest that the long-term complication rate is less than 4.6%.

The use of ECP has had strong support in certain sections of the ophthalmic community in which glaucoma management is a significant part of their practice. Its relatively low-rate of take-up in the majority of centres, especially in most parts of Asia include the prohibitive start-up costs of ECP equipment versus traditional filtering surgery equipment. As a surgical adjunct, ECP widens the choices available to glaucoma specialists in managing refracatory glaucomas, particularly in clinical situations with limited visibility of the anterior segment or failed trans-scleral endocyclophotocoagulation. It has demonstrated safety and efficacy in retrospective and small randomized trials in controlling IOP for all etiologies of glaucoma, reducing dependence on anti-glaucoma medications, as well as delaying progression to filtering trabeculectomy shunt procedures.

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