Int Ophthalmol (2019) 39:2257–2265
https://doi.org/10.1007/s10792-018-01062-9

ORIGINAL PAPER

Intermediate results of phaco-endocycloplasty in an exclusive cohort of angle closure glaucoma: potential for change

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Received: 30 July 2018 / Accepted: 21 December 2018 / Published online: 3 January 2019

Abstract

Purpose The objective of this study was to investigate the efficacy and safety of phaco-endocycloplasty in an exclusive cohort of primary angle closure disease/glaucoma.

Methods The study was interventional and non-comparative, carried out at a tertiary level eye care Institute. All adult patients (> 18 years) with angle closure disease, who had controlled or uncontrolled intra-ocular pressure (IOP) and had visually significant cataract, requiring surgery, and had undergone phaco-endocycloplasty, performed for 180°–210° simultaneously with cataract surgery, were included.

Main outcome measures Primary outcome measure includes IOP, and secondary outcome measures include best corrected logMAR visual acuity (BCVA), anti-glaucoma medication (AGM) and complications.

Results Thirty-two eyes of 28 patients were included. Median follow-up was 15 months (range 3–42 months, Q1 7.5, Q3 18, IQR 10.5). Median IOP pre-procedure (20.5 mmHg, range 11–46, Q1 16.75, Q3 31, IQR 14.25) decreased significantly post-procedure at last follow-up (IOP 16 mmHg, range 10–20, Q1 12, Q3 17.5, IQR 5.5) ($p < 0.001$). There was significant decrease in use of AGM (median 3 pre-procedure, range 1–5, Q1 2, Q3 3.25, IQR 1.25) at last follow-up (median 0) ($p < 0.001$) post-procedure. Median logMAR BCVA improved from 0.4 (Q1 0.3, Q3 0.625, IQR 0.325) to 0.05 (Q1 0, Q3 0.3, IQR 0.3) at last follow-up ($p < 0.001$). None of the patients had serious sight-threatening complications.

Conclusions This study indicates that phaco-endocycloplasty can effectively control IOP, significantly reducing need for AGM, without compromising safety, in angle closure glaucoma. When combined surgery is indicated, this conjunctiva-sparing procedure may be employed in the management of coexisting cataract and glaucoma prior to bleb-forming surgery.

Keywords Endocycloplasty · Phaco-endocycloplasty · Primary angle closure glaucoma · Endocyclophotocoagulation

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10792-018-01062-9) contains supplementary material, which is available to authorized users.

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Introduction

Glaucoma is the second leading cause of blindness, with primary open angle glaucoma (POAG) being the most common form worldwide; however, morbidity caused by primary angle closure glaucoma (PACG) is, in the least, the same as that of POAG [1].

In Asia, the prevalence of PACG can exceed that of POAG as it exists in a wide clinical spectrum [2]. Moreover, there is evidence that angle closure disease is more difficult to manage and is associated with more severe long-term visual morbidity in Asians than Caucasians [3].

Cataract and glaucoma frequently coexist, as both are diseases of advancing age; the presence of glaucomflecken, diffuse small white opacities in the anterior subcapsular region due to ischaemic necrosis of the lens epithelium, is virtually diagnostic of a past acute attack of angle closure [4, 5]. The chronic condition develops insidiously, the patient often being unaware of the ocular problem until relatively late in the disease process [6]. In either situation, laser peripheral iridotomy (LPI) is undertaken first, in an attempt to eliminate the element of relative pupillary block and deepen the anterior chamber [7]. However, occludability may not resolve post-LPI, when plateau iris syndrome (PIS) or a lens-related cause, or both are suspected.

The lens—due to its relatively anterior position, its thickness and increased lens rise [8–10]—plays an important role in the pathogenesis of PACG; its removal is thus advocated early, rather than late, even clear lens [11]. It has been shown that lens extraction alone significantly deepens the anterior chamber (AC), widens the anterior chamber angle and reduces IOP [12, 13]. However, this may be a rather simplistic view as there are multiple pathophysiological mechanisms causing angle closure and in PIS, there is evidence that the plateau may not resolve post-lens extraction alone [14]. There have been recent reports of endocycloplasty combined with lens extraction providing success in PIS [15] (Ahmed Ik, Podbielski D, Naqi A, et al. Endoscopic cycloplasty in angle closure glaucoma secondary to plateau iris. American Glaucoma Society Annual Meeting; March 5–8, 2009; San Diego, CA 2009) as well as in other aetiologies of angle closure [16].

The aim of this study was to explore the outcomes of phacoemulsification with PCIOL and endocycloplasty in all forms of primary angle closure disease, with or without synaechial angle closure.

Methods

Informed consent was obtained from all participants for the surgical procedure, and the study was approved by the ethics committee and review board (IRB) of the Institute. It was conducted in accordance with the tenets as laid down by the Declaration of Helsinki.

A review of all subjects with angle closure disease, who had coexisting visually significant cataract and had undergone phaco-ECPL at a tertiary level academic practice, was done over the study period of May 2014–December 2016. We only considered subjects who had a documented post-surgical follow-up of at least 3 months.

Subjects with previous intra-ocular surgery or who had phaco-ECPL in complex refractory glaucomas (previous filtering surgery, corneal graft, retinal surgery, etc.) were excluded.

Relevant history for all subjects was recorded, and each subject underwent a comprehensive ophthalmic examination, including best corrected visual acuity (BCVA) assessment, slit-lamp biomicroscopy, intraocular pressure (IOP) assessment with Goldmann applanation tonometry (Zeiss SL 130 slit lamp with Goldmann style applanation tonometer AT 030), gonioscopy with Sussman 4-mirror under standard dark-room conditions, dilated stereo fundoscopy with +66D Volk lens (Volk Instruments, OH, USA). Visual fields were documented by the Humphrey field analyser (HFA).

Biometrics were obtained by Lenstar (Alcon, Fort Worth, TX, USA) and included axial length (AL), lens thickness (LT), central corneal thickness (CCT) and anterior chamber depth (ACD) measurements.

Surgical procedure

Phaco-endocycloplasty (phaco-ECPL)

All surgeries were done by a single fellowship-trained surgeon and were performed in the operating room under regional anaesthesia; Inj. mannitol 20% (1–3 mg/Kg, Claris Otsuka, India) was administered pre-operatively, when indicated.

A clear corneal phaco was completed, and intraocular lens implant (IOL) was inserted in the bag, as per routine phaco surgery. Following this, a 20-gauge endoscope (Endo Optiks, Little Silver, NJ) was introduced through the phaco wound, after creating space in the sulcus with a cohesive viscoelastic and the ciliary processes (CP) were visualised. Delivery of laser was under direct vision, and it was aimed at the 'tail' of the ciliary process, in a modification of the endocyclophotocoagulation process called endocycloplasty (ECPL) [15, 16], wherein the ciliary body shrinks posteriorly, away from the iris (Fig. 1 and Electronic Supplementary Material 1—video demonstrating technique of ECPL). The end-point of whitening and shrinkage of ciliary body posteriorly determined the power of the laser delivered. Approximately 180°–210° were treated; laser energy was determined by shrinkage of CP and varied between 250 and 500 mw, with duration being constant at 2000 ms. 'Pops' were strictly avoided, and when encountered, it warranted an immediate reduction in power.

At the end of the procedure, viscoelastic was washed and sub-conjunctival steroid was administered (dexamethasone 2 mg).

Post-operatively all subjects were administered topical prednisolone acetate 1% (Predforte, Allergan, Irvine, CA, USA) for 4 weeks (in tapering dose) and moxifloxacin hydrochloride 0.5% (Vigamox, Alcon, Fort Worth, TX, USA) four times daily for 1 week, and if required, cycloplegic eye drops (homatropine hydrochloride 2%, Homide, Warren Excel, India) thrice daily were used for 1–2 weeks. All anti-glaucoma medications were discontinued and re-introduced as per indication.

Primary outcome measure was IOP with complete success being defined as an IOP > 5 and ≤ 18 mmHg without medication; qualified success was defined as meeting these criteria with medication. Failure to meet these criteria and/or requirement for reoperation (trabeculectomy or glaucoma drainage device or transscleral cyclophotocoagulation) was defined as failure of the phaco-endocycloplasty procedure.

Secondary outcome measures included logMAR best corrected visual acuity (BCVA), anti-glaucoma medications (AGM) and major complications.

Data are presented as median, quartiles and interquartile range. Pre- and post-procedure IOP, AGM and BCVA were analysed using the Wilcoxon signed-rank test.

Results

During the study period of May 2014–December 2016, 32 eyes of 28 patients underwent phaco with endocycloplasty for primary angle closure disease alone, with at least 3-month follow-up. All subjects had primary angle closure with glaucoma which mostly ranged from moderate to severe.

Median age was 62.5 years (range 47–79). Median follow-up was 15 months (range 3–42 months, Q1 7.5, Q3 18, IQR 10.5). Nineteen eyes continued to demonstrate post-LPI occludability (posterior trabecular meshwork not visible for 3 or more quadrants along with sine-wave sign) and were presumed to have plateau iris syndrome (PIS); however, not all of these

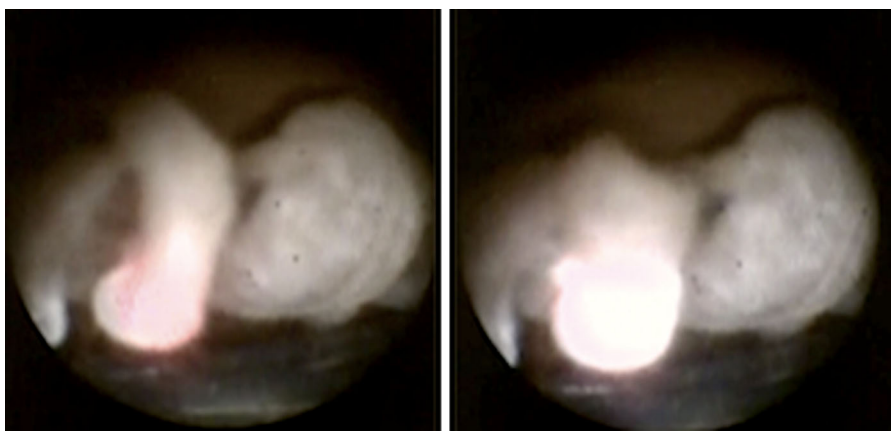

Fig. 1 Left: diode laser is aimed at the tail of the ciliary process. Right: whitening, contraction and retraction of ciliary body posteriorly post-laser, as ascertained by its height in relation to the ciliary process adjacent to it

had UBM-documented PIS. Fourteen eyes had peripheral anterior synaechiae (PAS) and synaechial angle closure ranging from less than 1 to all 4 quadrants. Glaucoma was advanced with mean MD (mean deviation) on 24-2 Humphrey visual field (Carl Zeiss, Dublin, CA) being − 17.6 SD 11.5 (range − 3.2 to − 29.32) and visual field index (VFI) of 30% SD 37%.

Table 1 lists the pre-operative characteristics, and post-operative results at last follow-up are shown in Table 2.

The median IOP pre-procedure decreased significantly post-procedure at last follow-up; there was also significant decrease in use of AGM. Mean pre- and post-operative IOP at different time intervals in phaco-ECPL is shown in Fig. 2. Median logMAR BCVA too improved significantly and none of the eyes lost vision. This was seen even when the cohort was analysed separately with respect to controlled (n = 16) and uncontrolled (n = 16) IOP (Tables 3 and 4).

Fibrinous uveitis was seen in six eyes post-operatively; all presented within 1 week, and most settled on conservative management. Only one such eye developed secondary pupillary block and had a repeat laser peripheral iridotomy. None of the eyes had cystoid macular oedema nor hypotony or any other notable complication. Subluxation or dislocation of IOL was also not seen.

Outcomes: complete success as per our definition was obtained in 75% eyes (n = 24); another 9.4% achieved qualified success (n = 3). Therefore, total success was seen in 84.4% eyes. Five eyes failed (15.6%); 2 eyes underwent trabeculectomy and have controlled IOP ever since. Two eyes had borderline IOP (22 mmHg without medication) at 3 months but were subsequently lost to follow-up.

Table 1 Pre-operative characteristics of patients undergoing phaco-endocycloplasty

Pre-op characteristics	Median (Q1, Q3; IQR)
Age	62.5 (55.75, 70.5; 14.75)
Gender (female/male ratio)	9:5
Right versus left eye ratio	17:15
Axial length in mm	22.2 (21.9, 22.8; 0.8)
Anterior chamber depth in mm	2.6 (2.3, 2.9; 0.6)
Lens thickness in mm	4.7 (4.6, 4.7; 0.2)
Corneal thickness in microns	510.5 (493, 527.25; 34.25)
Lens position	5.0 (4.5, 5.2; 0.7)
Relative lens position	0.22 (0.21, 0.23; 0.02)

Discussion

Trabeculectomy, since its first description in 1968 by Cairns [17], continues to occupy the foremost position in the surgical management of angle closure glaucoma, perhaps for lack of a suitable alternative. This is in contrast to the current day management of POAG where, with the advent of minimally invasive glaucoma surgical procedures (MIGS), several newer alternative approaches have been made available. MIGS has not only provided alternatives, but also options are available earlier on in the course of the disease, without compromising the conjunctiva [18].

Combined cataract and trabeculectomy (trab) is still the standard and preferred procedure in PACG in the presence of a visually significant cataract, especially when the IOP is uncontrolled, or the disease is progressing. Combining the two surgeries have several benefits—reduced morbidity and cost of surgery and visual rehabilitation in approximately 6–8 weeks.

However, combined phaco-trab surgery is associated with much increased inflammation [19] (a cause for failure of bleb) and a few unique vision-threatening complications like hypotony, shallowing of anterior chamber and bleb related complications, including life-long risk of bleb-associated-endophthalmitis (BAE) [20].

A single-centre retrospective review from the 1990 s showed that the 5-year risk of blebitis and that of BAE are 6.3% and 7.5%, respectively [21]. Also filtering bleb can fail at any time, from immediate post-op to as long as 20 years after surgery [22].

Thus, it becomes imperative to find newer, better and safer surgical solutions for PACG. One such modality is combining ECP with phaco, to control IOP whilst visually rehabilitating the patient. Our study has shown that phaco when combined with modified ECP, called endocycloplasty (ECPL), is successful in controlling IOP, reducing use of AGM whilst visually rehabilitating the patient in a few weeks. This effect was sustained in the intermediate term in all variants of angle closure, even those that had synaechial angle closure.

Studies with ECP hitherto have mainly been carried out in open angle or refractory glaucomas, and this

Table 2 Post-operative results at median 15 months of all patients undergoing phaco-ECPL

Parameter	Pre-phaco-ECPL	Post-phaco-ECPL	*p*
Median IOP mmHg (quartiles, IQR)	20.5 (Q1 16.75, Q3 31, IQR 14.25)	16 (Q1 12, Q3 17.5, IQR 5.5)	< 0.001
Median AGM[a] (quartiles, IQR)	3 (Q1 2, Q3 3.25, IQR 1.25)	0	< 0.001
Median logMAR BCVA[b] (quartiles, IQR)	0.4 (Q1 0.3, Q3 0.625, IQR 0.325)	0.05(Q1 0, Q3 0.3, IQR 0.3)	< 0.001

[a]*AGM* anti-glaucoma medication

[b]*BCVA* best corrected visual acuity

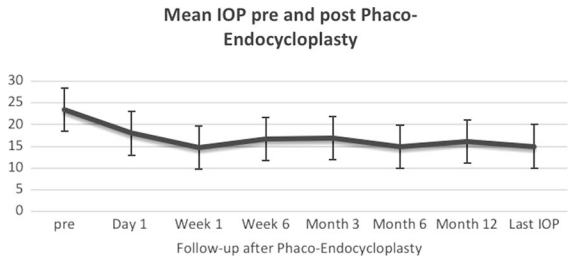

Fig. 2 Mean pre- and post-operative IOP at different time intervals in phaco-ECPL

approach has been moderately successful in POAG [23], pseudophakic and aphakic glaucoma [24], paediatric glaucomas [25] and even in refractory glaucomas [26]. Our success rate of 84.4% in angle closure glaucoma is comparable to those that are quoted in these studies; it could possibly have been higher if the two patients with borderline IOP without any anti-glaucoma medication (22 mmHg) at 3 months had not been lost to follow-up and failed as per our IOP criterion.

Delivery of laser in ECPL in angle closure and these other types of glaucomas differ in as much as the tip of the ciliary process (CP) is targeted, rather than a continuous 'painting' of the ciliary body. This results in the contraction of the entire CP away from the angle, thereby widening the angle, if it is not synaechially closed. As persistence of plateau has been reported in PIS in eyes undergoing lensectomy alone (by Tran et al. [14]), we undertook intra-operative anterior segment optical coherence tomography (ASOCT) which confirmed this finding post-phaco alone (Fig. 3, Left). The angle widened considerably at the end of combined phaco-ECPL surgery, and intra-operative ASOCT successfully demonstrated this effect (Fig. 3, Right).

Table 3 Post-operative results of patients undergoing phaco-ECPL in controlled IOP (n = 16)

Parameter	Pre-phaco-ECPL	Post-phaco-ECPL	*p*
Median IOP mmHg (quartiles, IQR)	16.5 (Q1 15, Q3 18, IQR 3)	14 (Q1 12, Q3 16, IQR 4)	0.04
Median AGM[a] (quartiles, IQR)	3 (Q1 2, Q3 3, IQR 1)	0	< 0.001
Median logMAR BCVA[b] (quartiles, IQR)	0.4 (Q1 0.3, Q3 0.6, IQR 0.3)	0.0 (Q1 0, Q3 0.3, IQR 0.3)	0.001

[a]*AGM* anti-glaucoma medication

[b]*BCVA* best corrected visual acuity

Table 4 Post-operative results of patients undergoing phaco-ECPL in uncontrolled IOP (n = 16)

Parameter	Pre-phaco-ECPL	Post-phaco-ECPL	*p*
Median IOP mmHg (quartiles, IQR)	31 (Q1 23.5, Q3 36, IQR 12.5)	16 (Q1 13 Q3 17.75, IQR 4.75)	< 0.001
Median AGM[a] (quartiles, IQR)	3 (Q1 2.5, Q3 4, IQR 1.5)	0	< 0.001
Median logMAR BCVA[b] (quartiles, IQR)	0.5 (Q1 0.3, Q3 0.85, IQR 0.55)	0.2 (Q1 0, Q3 0.45, IQR 0.45)	0.007

[a]*AGM* anti-glaucoma medication

[b]*BCVA* best corrected visual acuity

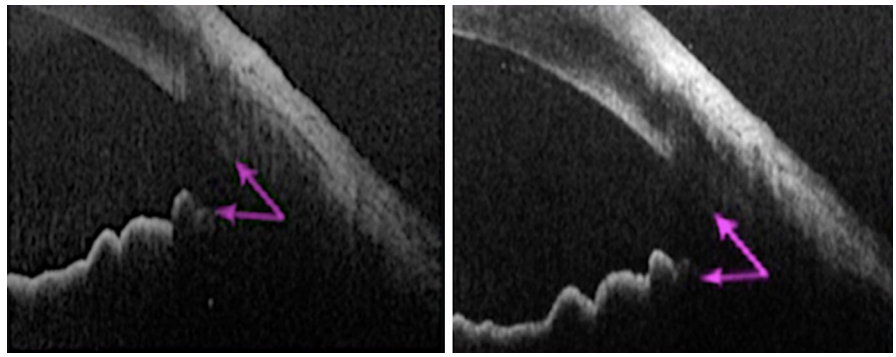

Fig. 3 Intra-operative ASOCT: left—angle recess before ECPL (after phaco) and right—after phaco-ECPL

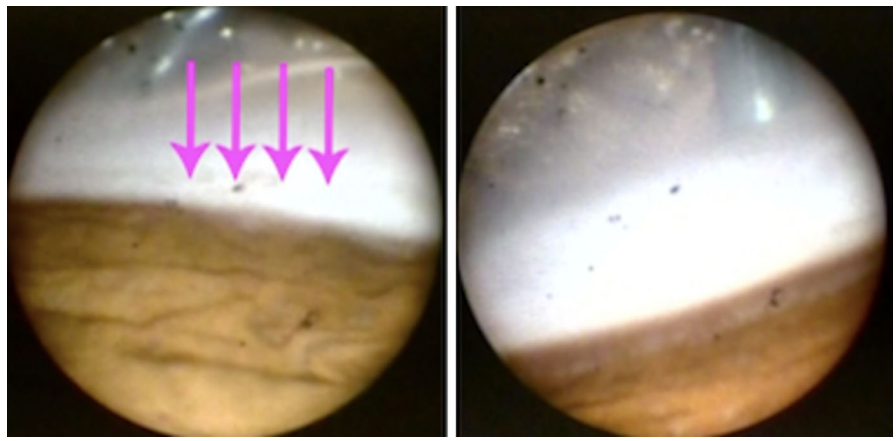

Fig. 4 Left—endoscopy pre-ECPL, post-phaco—except for 1 clock hour (arrows), the rest of the angle in the inferior 180° appears closed. Right—endoscopy post-phaco-endocycloplasty—scleral spur is visible throughout the inferior 180°

If the angle was not synaechially shut, then endoscopic appearance of the angle also supported the findings of ASOCT (Fig. 4).

However, unlike Francis et al. [15] we did not restrict phaco-ECPL to PIS alone; on the contrary, we also included patients with synaechial angle closure, with or without PIS. Therefore, it is not only the angle-widening-with-restoration-of-anatomy effect that appears to be called into play, but also the cyclophotocoagulation per se appears to be quite effective.

This technique affords extremely precise laser ablation of the ciliary body, with reduced post-operative inflammation. Nonetheless, all patients received sub-conjunctival dexamethasone and we had very few eyes with fibrinous reaction post-operatively; one such eye had to undergo a laser peripheral iridotomy for secondary pupillary block. Post-operative phaco-ECPL eyes are generally very quiet, and recovery is very swift, with much speedier visual rehabilitation; moreover, conjunctiva remains unscathed should future filtration surgery become necessary (Electronic Supplementary Material 2—Figure demonstrating quiet eye at 1-week post-phaco-ECPL with unscathed conjunctiva).

As we target only 2–3 quadrants, risk of hypotony, and sequelae, is very low. In 5824 eyes, the ECP collaborative study group (Noecker RJ. Complications of endoscopic cyclophotocoagulation: ECP Collaborative Study Group. Paper presented at: The ASCRS Symposium on Cataract, IOL and Refractive Surgery: May 1, 2007 San Diego CA 2007) had also reported very low complication rates—notably hypotony in 0.12%, choroidal haemorrhage in 0.09%.

Such a procedure also helps to avoid damage to the zonules. Although zonules are not normally visible during the procedure, in one of the study eyes, pseudoexfoliation (PXE) deposits on the zonules made them discernible and even these weakened ones did not snap during delivery of laser (Electronic Supplementary Material 1—demonstrating ECPL in PXE also). This is also corroborated by the fact that in the median 15-month follow-up, we did not encounter

any subluxation/dislocation of PCIOL, including the case with PXE. However, Wang et al. [27], aiming for emmetropia (using the Holladay 1 formula for the SN60WF IOL, Alcon), found a small myopic shift in relation to the change in effective lens position. Our eyes were shorter; we used the Hoffer Q formula for the majority of cases. However, IOL type was determined by the paying capacity of the patient and we did not aim for emmetropia. Target ametropia was between − 0.25 and − 1.0 dioptre, which we achieved for the majority of the patients.

On an average, we used only one-fourth of the total energy (500 mw), or less, when compared to transscleral cyclophotocoagulation. Hence, direct visualisation of ciliary processes for precise delivery of reduced laser energy also helps to avoid pain, excessive inflammation, hypotony, phthisis and visual loss associated with transscleral delivery of the same [28]. It is surmised that in the latter, absorption across sclera is erratic and unpredictable, leading to the stated complications.

Furthermore, there is a recent report [29] of combining endoscopy-guided goniosynaechialysis (GS) with phaco-ECPL; the authors have had success with the procedure in a small series. We have tried GS in the past (none in this cohort) with severe protracted inflammation post-operatively which was difficult to control, and, in a few cases, it proved to be counter-productive too, with increase in PAS. Therefore, we do not favour this approach in the darker irides of South Asian eyes.

Overall phaco-ECPL is a very safe and effective procedure and as opposed to phaco-trabeculectomy, adds only about 5 to 10 min to the procedure of cataract extraction. It can be easily accomplished by an anterior segment surgeon who can expect hassle-free post-operative care, akin to phaco being performed alone.

Furthermore, laser can be repeated if required, and if it is not effective, it does not preclude, or compromise, future trabeculectomy.

This technology is readily available, but expense may be a consideration, especially in low-to-middle income countries. However, it should be considered as a one-time capital expenditure, just like a phaco machine. The possibility of acquiring an endoscope alone and coupling it with a pre-existing diode laser machine, if available, can also be contemplated, driving down expenditure.

Cost notwithstanding, when seen from the perspective of the patient, this freely available, relatively new technology not only improves their quality of life, with none or fewer anti-glaucoma medications, but also faster visual rehabilitation with fewer post-operative visits.

A small sample size and relatively short follow-up are some of the limitations of the study. However, the relatively small sample size is offset by inclusion of consecutive angle closure eyes that underwent phaco-ECPL. Furthermore, performance of phaco-endocyclophlasty by one fellowship-trained glaucoma specialist ensured uniform protocol. Comparison with a cohort undergoing phaco alone is certainly desirable. However, our cohort of PACG had standard indications for combined surgery (either uncontrolled IOP, or progression in VF or IOP controlled with 3 or more medications, or non-affordability of medications) in the presence of visually significant cataract. Therefore, finding a comparable group of PACG subjects who underwent phaco alone was not possible. This, too, is a limitation of a retrospective study.

Conclusions

Phaco-endocyclophlasty can effectively control IOP, significantly reducing need for anti-glaucoma medication in primary angle closure glaucoma also. Visual rehabilitation is early, without compromising safety, in this sub-group of glaucoma patients where high morbidity is anticipated following filtration surgery. When combined surgery is indicated, this conjunctiva-sparing procedure may be employed in the management of coexisting cataract and glaucoma prior to bleb-forming surgery. Comparison with phacoemulsification alone and larger-scale studies should be conducted to explore its role as a minimally invasive procedure in all sub-types of angle closure glaucoma.

What was known:

- Endocyclophotocoagulation was hitherto moderately successful in POAG and refractory glaucomas.
- A slight modification in technique (endocyclophlasty) combined with phaco has been recently described in plateau iris syndrome.
- Recent evidence suggests phaco-endocyclophlasty is effective and safe in plateau iris syndrome.

What this paper adds:

- Phaco-endocycloplasty appears to be effective and safe in all variants of primary angle closure glaucoma, including those with synaechial closure.

Acknowledgement Author thanks IIK Ahmed, MD, University of Toronto, Department of Glaucoma, Credit Valley Eye Care, 3200 Erin Mills Parkway, Mississauga, Ontario, Canada L5L 1W8.

Funding None.

Compliance with ethical standards

Conflict of interest None relevant (Novartis, Allergan).

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