• Clinical Research •

Outcomes of chronic angle-closure glaucoma treated by phacoemulsification and endocyclophotocoagulation with or without endoscopically goniosynechialysis

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Abstract

● **AIM:** To investigate the surgical outcomes of patients with chronic angle-closure glaucoma (CACG) treated with phacoemulsification (phaco)/endocyclophotocoagulation (ECP) with and without endoscopic goniosynechialysis (E-GSL).

● **METHODS:** A retrospective, nonrandomized, comparative case series was conducted. Patients with CACG who underwent phaco in combination with either ECP alone (ECP group) or GSL with ECP (E-GSL group) from 2018 to 2019 were followed for 12mo and reviewed. Clinical features and outcomes were identified and analyzed. The ECP and E-GSL groups were matched in age and baseline intraocular pressure (IOP). Changes in IOP, mean of visual acuity (VA), peripheral anterior synechiae (PAS) formation, and the number of glaucoma medications was examined.

● **RESULTS:** The ECP group included 32 eyes of 27 patients, and the E-GSL group included 32 eyes of 26 patients. The preoperative baseline IOP was 22.18±6.48 mm Hg in the ECP group and 22.95±6.71 mm Hg in the E-GSL group (*P*=0.644). The mean IOP reduction was 26.2% in the ECP group and 41.6% in the E-GSL group at 12mo. The mean postoperative VA (logMAR units) at 12mo was 0.47 in the ECP group and 0.36 in the E-GSL group. The reduction in PAS formation and the number of glaucoma medications was also higher in the ECP group than E-GSL group at 12mo.

● **CONCLUSION:** The phaco/ECP and phaco/E-GSL groups both achieve a significant reduction in IOP without complications associated with traditional glaucoma filtration surgeries.

● **KEYWORDS:** chronic angle-closure glaucoma; endocyclophotocoagulation; goniosynechialysis; phacoemulsification

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INTRODUCTION

Glaucoma is the second leading cause of blindness worldwide. It is predicted that about one-fourth of all glaucoma cases will be angle closure in the following years. Ethnic Asians, females, and the aged are risk factors. Additional factors include shallow anterior chamber, shorter axial length, abnormal lens position, and thicker lenses. Choroidal thickness and iris volume may play vital roles in angle-closure mechanisms[1-2]. Chronic angle-closure glaucoma (CACG), caused by the closure of the angle secondary to extensive peripheral anterior synechiae (PAS), is the leading cause of irreversible blindness worldwide. Further, the Asian population is prone to developing CACG with a high prevalence and increased intraocular pressure (IOP). The treatment for CACG includes lens extraction, goniosynechialysis (GSL), laser peripheral iridotomy (LPI), argon laser peripheral iridoplasty (ALPI), filtering surgery, drainage implants, and

cyclodestruction. There is no consensus on the subsequent treatment steps in patients with CACG. CACG frequently coexists with cataracts in older patients. Trabeculectomy alone or combined with phacoemulsification (phaco) is often used to treat patients with CACG. Still, it is associated with more complications, such as the shallow anterior chamber, choroidal detachment, thin-walled bleb, hypotony, aqueous misdirection, and endophthalmitis. Other treatments with fewer complications and visual impairment could be used before filtering surgery have been investigated. The advent of phaco brought about an IOP reduction of 30% in CACG, increased anterior chamber width with fewer complications, and visual improvement in patient outcomes[3-4]. A study has also reported that primary lens extraction controlled IOP and reduced the need for future glaucoma drainage surgery in primary angle-closure glaucoma (PACG)[5]. The PAS of CACG persists, with limited aqueous outflow, after phaco or filtering procedures. Synechialysis is conventionally performed using direct goniolens, but can also be carried out endoscopically. The procedure can separate the PAS from the angle under direct visualization, exposing the functional trabecular meshwork and restoring its filtering function. This procedure, combined with phaco under an endoscope for CACG, effectively lowers IOP and minimizes the postoperative complications of the filtering procedures[6-8].

Endocyclophotocoagulation (ECP; Endo Optiks, Little Silver, NJ, USA) was first reported by Uram in 1992 and delivers laser energy *via* an ab interno approach under direct visualization of ciliary processes[6]. Because the procedure allows the laser to be precise and efficient during the procedure, its indications have been expanded to patients with better visual potential[9-10]. The procedure was used to lower IOP effectively and safely alone or combined with phaco; the maximal effect was observed about one month after the procedure[11].

Patients with glaucoma and cataracts have been increasingly treated with phaco/ECP[12-13]. ECP combined with phaco or GSL alone provides a safe alternative solution to CACG patients compared to traditional filtering procedures[14-15]. There is no consensus on the subsequent treatment steps in CACG. In this study, we compared the outcomes of patients with CACG after phaco/ECP versus phaco/E-GSL.

SUBJECTS AND METHODS

Ethical Approval The medical records of all CACG patients who underwent phaco/ECP alone (ECP group) or phaco/GSL with ECP (E-GSL group) at the ophthalmology unit of Chinese PLA General Hospital from 2018 to 2019 were reviewed. Written informed consent was obtained from the subjects, and participants did not receive a stipend. The study was approved by the PLA General Hospital Ethics Committee and adhered to the tenets of the Declaration of Helsinki.

We diagnosed the patients with CACG based on the International Society of Geographic and Epidemiologic Ophthalmology criteria. Patients with cataracts and PAS of more than 180 degrees were included. Those who had accepted anti-glaucoma surgeries other than LPI were excluded[16]. Glaucoma severity was determined by the 2010 American Academy of Ophthalmology Preferred Practice Pattern guidelines. The patients with mild to moderate glaucoma underwent the phaco/ECP procedure, whereas patients with severe glaucoma underwent the phaco/GSL with ECP. Mild-to-moderate glaucoma was defined as a normal visual field or only a visual field defect in one hemifield. Severe glaucoma was defined as a visual field defect in both hemifields[17].

All of the patients were followed up for at least one year after the surgery. We focused on changes in best-corrected visual acuity (VA), IOP, and the number of antiglaucoma drugs. All of the patients underwent gonioscopy six to twelve months after surgery. Final gonioscopy conducted at one year was used uniformly for analysis of all subjects. Any postoperative complications were recorded. In this study, there was no washout period for an antiglaucoma medication.

The ECP was performed using the URAM E2 laser endoscopic system (Endo Optiks, NJ, USA). The same doctor conducted the ECP and GSL aided by an endoscope. Some viscoelastic agents were injected to press down the peripheral iris foot. A curved 23G endoscope probe was inserted through the main corneal incision in all cases. To blanch the ciliary processes, the ECP was performed, leaving 60 degrees untreated, with a power ranging from 250 to 350 mW. Endoscopic GSL with the same range as the ECP was performed using an iris repositor, which was used to press on the foot of the iris with PAS. The site incision was expanded to help separate the residual PAS when necessary. After applying pressure, the trabecular meshwork of the PAS points was opened, with occasional bleeding. When all the PAS were separated, the scleral spur became visible using the probe in all cases[6,18]. In the E-GSL group, a miotic agent was injected into the anterior chamber at the end of the surgery. A subconjunctival injection of dexamethasone was given to both groups. All surgeries were completed by the same surgeon (Wang DJ). All patients received the same postoperative medications (tobramycin and dexamethasone eye drops), tapered over one month in the ECP group, and tapered over six to eight weeks in the E-GSL group.

Statistical Analysis Continuous variables were expressed as mean±standard deviation (SD) and compared using Student's *t*-test. Longitudinal data at serial time points were compared with the preoperative values using a paired two-tailed *t*-test or Wilcoxon rank-sum test. Categorical variables were expressed as frequencies and percentages and analyzed with Chi-square test where appropriate. Data analyses were generated using

the IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 20. Two-tailed *P* values <0.05 were considered statistically significant.

RESULTS

Patient Characteristics Fifty-three patients with CACG who accepted phaco with ECP alone (ECP group) or with ECP and GSL (E-GSL group) from 2018 to 2019 were reviewed (Table 1). The ECP group (32 eyes of 27 patients, mean±SD age 67.5±7.1y) and the E-GSL group (32 eyes of 26 patients, mean±SD age 69.9±7.4y) were followed for at least one year.

PAS Formation and the Number of Medications in the ECP and E-GSL Groups at 12mo The reduction in PAS formation and the number of medications was significantly different in the ECP group and E-GSL group at 12mo (PAS: from the baseline 248.75°±74.43° to 195.94°±76.57°, *P*<0.001; 296.25°±71.79° to 47.81°±38.75°, *P*<0.001, respectively; numbers of medications reduction: from the baseline 2.22±0.75 to 0.94±0.62, *P*<0.001; from the baseline 2.56±0.62 to 0.66±0.55, *P*<0.001, respectively). The E-GSL group showed a significantly lower formation of PAS at 12mo than the ECP group (*P*<0.001; Table 2).

Intraocular Pressure Outcomes of the ECP Group and E-GSL Group up to 12mo The IOP for both groups is shown in Table 3 and Figure 1. The preoperative baseline IOP was 22.18±6.48 and 22.95±6.71 mm Hg in the ECP group and E-GSL group, respectively (*P*=0.644). The IOP declined significantly in both groups (14.16±2.45 and 18.25±5.20 mm Hg) on day seven after surgery (*P*<0.001 and *P*=0.007 compared with the baseline). The IOP of the ECP group was 14.16±2.45, 14.62±1.18, 15.33±2.04, and 16.36±2.45 mm Hg at 1, 3, 6, and 12mo, respectively. The IOP of the E-GSL group dropped from 14.13±2.47 mm Hg at one month to 12.41±1.26, 13.48±1.68, 13.41±1.46 mm Hg at 3, 6, and 12mo, respectively. An earlier IOP reduction during the first month after surgery was observed in the ECP group compared with the E-GSL group. From 3 to 12mo, the IOPs of the E-GSL group were lower than those of the ECP group (*P*<0.001). Moreover, the mean IOP reduction was 26.2% in the ECP group and 41.6% in the E-GSL group at 12mo.

VA Outcomes of the ECP Group and E-GSL Group up to 12mo The VA (logMAR units) for both groups are shown in Table 4 and Figure 2. Compared to the mean baseline of VA (0.33), the mean VA was 0.40 (*P*=0.015), 0.50 (*P*<0.001), 0.50 (*P*<0.001), 0.50 (*P*<0.001), 0.49 (*P*<0.001), 0.47 (*P*<0.001) in the ECP group, respectively, and 0.28 (*P*=0.093), 0.33 (*P*=0.931), 0.38 (*P*=0.036), 0.38 (*P*=0.032), 0.38 (*P*=0.036), 0.36 (*P*=0.241) in E-GSL group, respectively. The two groups showed a significantly difference in VA at seven days (*P*=0.038).

Other Complications Hyphema was observed in two eyes on the first day after E-GSL surgery, which was absorbed spontaneously in two or three days. We did not observe any serious intraoperative or postoperative adverse complications of hypotony, macular edema, or consistent uveitis within 12mo of follow-up.

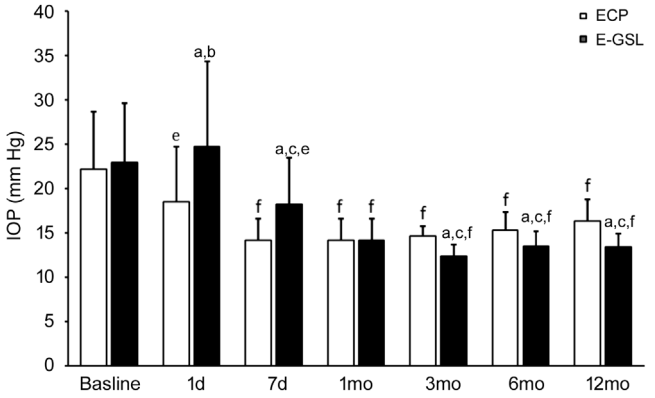

Figure 1 Change in IOP postoperatively [a]*P*<0.05, [b]*P*<0.01, [c]*P*<0.001 *vs* ECP; [e]*P*<0.01, [f]*P*<0.001 *vs* baseline. ECP: Endocyclophotocoagulation; E-GSL: Endoscopic goniosynechialysis.

Table 1 Patient characteristics

Characteristic	ECP (*n*=27)	E-GSL (*n*=26)	*P*
Age at surgery, y	67.5±7.1	69.9±7.4	0.644
No. of eyes	32	32	
Gender, *n* (%)			0.779
Men	11 (40.7)	9 (34.6)	
Women	16 (59.3)	17 (63.4)	

ECP: Endocyclophotocoagulation; E-GSL: Endoscopic goniosynechialysis.

Table 2 Comparison of medications and PAS at 12mo

Variable	ECP (*n*=32)	E-GSL (*n*=32)	*P*
No. of medications			
Preop.	2.22±0.75	2.56±0.62	0.050
Postop. (12mo)	0.94±0.62	0.66±0.55	0.068
PAS (degree)			
Preop.	248.75±74.43	296.25±71.79	0.02
Postop. (12mo)	195.94±76.57	47.81±38.75	<0.001

ECP: Endocyclophotocoagulation; E-GSL: Endoscopic goniosynechialysis; PAS: Peripheral anterior synechiae.

Table 3 Preoperative IOP and postoperative IOP of ECP group versus E-GSL group up to 12mo

IOP (mm Hg)	ECP	E-GSL	P^a	P^b
Baseline	22.18±6.48	22.95±6.71	0.644	-
1d	18.52±6.25	24.70±9.64	0.003	0.009, 0.410
7d	14.16±2.45	18.25±5.20	<0.001	<0.001, 0.007
1mo	14.16±2.45	14.13±2.47	0.981	<0.001, <0.001
3mo	14.62±1.18	12.41±1.26	<0.001	<0.001, <0.001
6mo	15.33±2.04	13.48±1.68	<0.001	<0.001, <0.001
12mo	16.36±2.45	13.41±1.46	<0.001	<0.001, <0.001

[a]ECP *vs* E-GSL; [b]Timaports vs baseline of ECP, E-GSL. ECP: Endocyclophotocoagulation; E-GSL: Endoscopic goniosynechialysis; IOP: Inoraocular pressure.

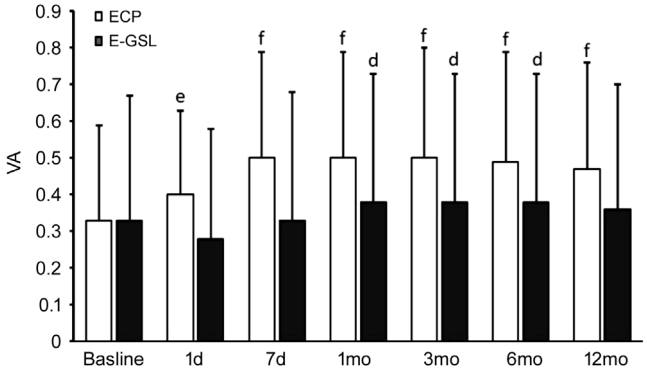

Figure 2 Change in VA (logMAR) preoperatively and postoperatively

$^{d}P<0.05$, $^{e}P<0.01$, $^{f}P<0.001$ *vs* baseline.

Table 4 Preoperative VA and postoperative VA of ECP group versus E-GSL group up to 12mo

VA	ECP (*n*=32)	E-GSL (*n*=32)	P^a	P^b
Baseline	0.33±0.26	0.33±0.34	0.964	
1d	0.40±0.23	0.28±0.30	0.069	0.015, 0.093
7d	0.50±0.29	0.33±0.35	0.038	<0.001, 0.931
1mo	0.50±0.29	0.38±0.35	0.127	<0.001, 0.036
3mo	0.50±0.30	0.38±0.35	0.143	<0.001, 0.032
6mo	0.49±0.30	0.38±0.35	0.161	<0.001, 0.036
12mo	0.47±0.29	0.36±0.34	0.058	<0.001, 0.241

[a]ECP *vs* E-GSL; [b]Timaports *vs* baseline of ECP, E-GSL. ECP: Endocyclophotocoagulation; E-GSL: Endoscopic goniosynechialysis; VA: Visual acuity.

DISCUSSION

Because of the high incidence of complications and reduced vision, the cyclodestruction procedure has typically been performed for end-stage resistant glaucoma. Recently, ECP, through a limbal approach or through the pars plana, has offered direct visualization of ciliary spurs during surgery[19]. The limbal approach is used in pseudophakic, phakic, or aphakic eyes through corneal or scleral incisions. ECP through the pars plana was initially reported in the treatment of refractory glaucoma. Both approaches obtained favorable effects. In the follow-up, transscleral cyclophotocoagulation (TCP) treated ciliary processes remained nonperfused at one-month post-treatment. In a rabbit model, the burned shrunk ciliary processes showed reperfusion at one week. In a rabbit model study, ECP was safer and had fewer complications than diode TCP after one week of follow-up[20]. ECP has been improved to avoid overtreatment and reduce postoperative complications, such as hypotony, inflammation, and phthisis.

ECP combined surgery has been reported in plateau iris syndrome (PIS). ECP represents an alternative method for patients with PIS, that addresses the underlying mechanism. The ciliary processes of at least 180° were suggested to be shrunk with ECP based on the development of PAS in the patients with PIS in the report. The preoperative mean IOP was 25.2 mm Hg, and the postoperative mean IOP was 17.1 mm Hg (32.1% reduction rate). In Hollander *et al*'s[21] research, retained viscoelastic agent and inflammation in the anterior chamber were correlated with the elevated IOP in the first postoperative week. It was noted that in eyes with less than 360 degrees of ECP treatment, new PAS developed in areas untreated by ECP. Phaco/ECP is also effective in open angle glaucoma[22-24]. There is evidence that phaco/ECP allows effective IOP reduction, avoids severe complications, and is suitable for mild and moderate glaucoma candidates[25-26]. A three-year clinical study of phaco/360-degree ECP showed in a modest IOP reduction without previous drainage surgery[27].

The position and thickness of the lens are essential for the depth of the anterior chamber, especially if it is anteriorly positioned and thickened with aging. The forward lens accounts for 0.65 mm of anterior chamber shallowing; increased lens thickness on average accounts for 0.35 mm of shallowing. Together, they cause a 1 mm difference in the anterior chamber depth of the primary angle-closure eyes compared with the normal eye[28]. The patients with CACG were more responsive to ECP in IOP than those with primary open angle glaucoma; this was due to ciliary process atrophy and the opening of the previously closed drainage angle, similar to the cases with PIS[29]. Higher preoperative IOP showed a more significant postoperative IOP reduction[27].

GSL is a surgical method for treating CACG by stripping the PAS from the iris foot to restore the original trabecular function. It is traditionally performed using a gonioscope under an operating microscope. However, the procedure requires either a microscope or an eyeball to be tilted, and the quality of the image is often affected by corneal opacities or edema. The endoscope conveniently provides the surgeon with direct visualization of the anterior chamber, which can help to achieve complete PAS separation. The combined GSL procedure can open the PAS and has become an effective surgical treatment for patients with CACG and coexisting cataracts. In Lin *et al*'s[29] study, GSL with the ophthalmic endoscope lowered the IOP for cases with previous failed trabeculectomy surgeries in PACG with cataracts. The total success rate at one year increased to 96%. A larger pupil diameter and younger age were significantly related to the failure of E-GSL[30]. In the previous study, GSL only with viscoelastic agents could eliminate only the PAS from 274.8°±81.5° to 239.8°±86.4°. About 80% of the PACG cases needed further mechanical GSL to obtain a complete open-angle[6,30]. There has been no report comparing the effect of an endoscope with a gonioscope in GSL. However, our consensus is that GSL could be performed easily with an endoscope regardless of corneal edema or opacity, promising accuracy, and safety[31-32].

Phaco/E-GSL is a combination of the three treatments described above. This treatment was demonstrated at a meeting in London in 2016, and only three papers on this combination treatment were published. It was first reported as phaco with IOL, ECP, and endoscopic goniosynechialysis (PIECES) for PACG patients with extensive PAS >270°. Following PIECES, IOP was decreased (≥30% IOP reduction), but only three patients were included[15]. In Izquierdo Villavicencio *et al*'s[31] study, mean IOP (preoperation: 18.2±6.6 mm Hg) was reduced to 12.8±3.0 mm Hg after PIECES at six months in the patients with CACG. In Panse *et al*'s[17] study, the mean IOP was reduced from 23.5±11.2 to 14.2±2.4 mm Hg in the GSL group (six eyes) and from 24.4±8.2 to 14.5±2.7 mm Hg in E-GSL (11 eyes). In the first six months, there was an earlier IOP reduction in the E-GSL group. However, both groups presented comparable IOP levels after one year. The results indicate that, compared to the GSL group, the additional IOP reduction in the E-GSL in the first six months may be due to ECP[32]. The E-GSL group in our study demonstrated a significant reduction in long-term IOP compared to the ECP group. The results demonstrated that effective GSL is essential for maintaining continuous IOP reduction.

The IOP response or final IOP is due to the comparatively lower treatment power (*i.e.*, 250 to 350 mW) used at our institution relative to the higher levels (*i.e.*, 500 to 900 mW) used in earlier iterations of ECP. In contrast to Panse *et al*'s[17] study, the phaco/E-GSL group in our study showed a later IOP lowering effect than the phaco/ECP group. The patients showed more obvious inflammation of the anterior segment in the phaco/E-GSL group at an early stage. In our study, the E-GSL group required prolonged steroid medication compared to the ECP group. VA did not improve in the E-GSL group compared to the baseline at 12mo (P=0.241), whereas VA improved at all follow-ups in the ECP group. This may be attributed to the inflammation and severity of glaucoma in the E-GSL group. About 34% of the cases in the phaco/E-GSL group experienced IOP elevation in the first week after surgery, and 6% of the cases in the phaco/ECP group experienced IOP elevation within two days post-surgery. The primary mechanisms of increased IOP spikes may be drainage obstruction of the aqueous humor, hemorrhage, debris in the trabecular meshwork, tissue edema, or the newly opened anterior chamber angle that did not regain its ability to drain aqueous humor.

There were some limitations to our study. Because it was a retrospective study, the follow-up time was relatively short. The progression of PAS during follow-up was not documented. A prospective study with an additional control group of phaco/GSL is helping to understand the effects of various surgical methods better.

In conclusion, phaco/ECP and phaco/E-GSL both achieved a significant IOP reduction, without complications associated with traditional glaucoma filtration surgeries. With additional time, phaco/E-GSL had the advantage of lowering IOP in the study. More prospective and extended studies are essential to study the effects of each treatment.

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