• Clinical Research •

Combined phacoemulsification and goniosynechialysis with or without endoscopic cyclophotocoagulation in the treatment of PACG with cataract

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Abstract

● **AIM:** To investigate the efficacy and safety of combined phacoemulsification and goniosynechialysis with or without endoscopic cyclophotocoagulation (PGE group and PG group) for the treatment of patients with coexisting primary angle-closure glaucoma (PACG) and cataracts.

● **METHODS:** The clinical data of patients with PACG and cataract were retrospectively reviewed. There was a total of 88 eyes in the study and were divided into two groups, 42 eyes in PGE group and 46 eyes in PG group. Surgery success cumulative survival, preoperative and postoperative intraocular pressure (IOP), number of IOP-lowering medications, best corrected visual acuity (BCVA) in the two groups were observed for more than 12mo and compared within each group and between two groups.

● **RESULTS:** The mean IOP in PGE group declined from 24.9 mm Hg preoperatively to 14.1 mm Hg at the first month after operation (P<0.001) and at the last visit 16.2 mm Hg (P<0.001). Meanwhile PG group also showed significant decrease, from 24.1 mm Hg preoperatively to 13.0 mm Hg at 1mo after operation (P<0.001) and 15.3 mm Hg at the last visit (P=0.004). The mean medications reliance reduced in both groups, in PGE group was reduced from 1.62 preoperatively to 0.13 at the last visit (P<0.001), in PG group from 0.87 to 0.10 (P<0.001). At the last visit, BCVA increased from 0.21 to 0.60 in PGE group (P<0.001) and from 0.24 to 0.67 in PG group (P<0.001). The success rate of PGE group at 1mo was 95.2%, then decreased to 70.7% at the last visit, whereas in PG group, the success rate at 1mo was 100%, at the last visit was 73.4%.

● **CONCLUSION:** PGE shows promise for PACG patients with cataracts to reduce IOP, lighten the medication burden and improve visual acuity, and PG still has its value in specific patients.

● **KEYWORDS:** endoscopic cyclophotocoagulation; primary angle-closure glaucoma; cataract; combined glaucoma and cataract surgery; laser surgery

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INTRODUCTION

Primary angle-closure glaucoma (PACG) is a common type of primary glaucoma in China[1]. Increased lens thickness associated with increasing age plays an important role in the mechanism of PACG formation[2]. Wang *et al*[3] divided PACG into three subtypes according to anatomy: pupillary blocking, nonpupillary blocking and multimechanism. A smaller eyeball with a thickened and forward lens causes pupillary blockage[2,4]. Therefore, removal of the thickened lens (cataract) can deepen the anterior chamber and relieve the papillary blockage. Although the level varies from study to study, the IOP reduction after cataract extraction in PACG is significant[5-6]. Recently, a large scale, multicenter and randomized controlled trial showed the advantages of clear lens extraction for early glaucoma[7]. Therefore, both cataract surgery alone and cataract surgery combined with other operations can be used to treat PACG.

Endoscopic cyclophotocoagulation (ECP) incorporates diode laser cyclophotocoagulation and endoscopy technology that enables ophthalmologists to perform photocoagulation on the ciliary body under direct visualization. ECP combined with phacoemulsification and goniosynechialysis (PGE) lowers IOP by multiple mechanisms. First, as mentioned earlier, cataract extraction was considered to be effective in lowering IOP because of the pathogenesis of PACG. Second, endoscopy offers the operator a better view of anterior chamber angle

to improve the accuracy of goniosynechialysis[8-9] and goniosynechialysis could reduce IOP through widening a narrow or closed angle, exposing the meshwork and restoring aqueous outflow function[10-16]. The third mechanism of lowering IOP is ablating ciliary body under direct vision. ECP decreases aqueous production by destroying ciliary body epithelium with diode laser.

Compared with transscleral cyclophotocoagulation, ECP has more reliable effects on IOP control and fewer complications[17]. The efficacy and safety of ECP have been confirmed by several studies in different stages of glaucoma from mild to refractory[18-27]. However, there is a lack of observations in Chinese population regarding the effects of ECP on PACG, which has a high prevalence in Asia and usually causes severe visual impairment[28].

The aim of this research was to compare efficacy and safety of combined phacoemulsification and goniosysnechialysis and ECP (PGE) versus combined phacoemulsification and goniosysnechialysis (PG) in patients with combined PACG and cataracts.

SUBJECTS AND METHODS

Ethical Approval This study conformed to the tenets of the Declaration of Helsinki. A retrospective chart review was performed at Beijing Tongren Hospital, Capital Medical University. The clinical data of 74 patients (88 eyes) with PACG and cataract who received PGE (36 patients, 42 eyes) or PG (38 patients, 46 eyes) from December 2015 to November 2016 were retrospectively collected. Informed consent was waived due to the retrospective nature of the study.

The inclusion criteria for this study were as follows: 1) patients with chronic PACG, or patients with acute attack history but the acute symptoms were relieved; 2) patients with coexisting age-related cataract and best corrected visual acuity (BCVA) ≤0.5; 3) patients with an IOP >21 mm Hg and <30 mm Hg with IOP-lowering medicines; 4) patients with visual field mean deviation <-12 dB (early and moderate stage of Hodapp-Parrish-Anderson); and 5) patients with peripheral anterior synechia (PAS) ≥180° who underwent PGE or patients with PAS<180° who underwent PG.

The exclusion criteria were as follows: 1) previous ECP and/or cataract surgery; 2) previous ocular trauma; 3) primary open angle glaucoma or secondary glaucoma; 4) other ocular lesion; and 5) patients with incomplete documentation.

All surgeries were performed by one experienced surgeon (Wang T). Phacoemulsification was performed with an Alcon Infiniti Vision System (Alcon Inc., Fort Worth, TX, USA). HOYA iSert 251 preloaded intraocular lens (Hoya Corp., Tokyo, Japan) were implanted. ECP was performed with an E2 Laser and Endoscopy System (Endo Optiks, Little Silver, NJ, USA). All patients were treated with IOP-lowering medical therapies according to their individual circumstances, and levofloxacin drops were applied three times a day for three days preoperatively.

Briefly, the ECP procedure was performed following phacoemulsification and intraocular lens implantation *via* a temporal or nasal clear corneal incision. A cohesive sodium hyaluronate ophthalmic viscosurgical device (OVD) was injected between the iris and capsule to inflate the sulcus for ECP procedure. A straight laser endoscope was inserted through the clear corneal incision and into the sulcus to display the ciliary processes. The laser (810 nm) power level was set at 0.3 W with continuous wave duration. The distance between probe and process was adjusted until 5-7 ciliary processes were seen on the video monitor. Photocoagulation time was controlled by foot tread and the ciliary processes were fully destroyed when they became pale and shrank. We treated 180 degrees of ciliary processes (from 2 to 8 o'clock or 1 to 7 o'clock, clockwise), and overtreatment was carefully avoided. The pupil was then constricted by intracameral injection of carbachol and OVD was injected into anterior chamber angle 360 degrees peripheral and a blunt spatula was gently used to separate the anterior synechia. After the procedures, OVD was thoroughly washed out using the irrigation/aspiration setting. Dexamethasone sodium phosphate was injected subconjunctivally. The procedures for PG were the same except for the ECP step.

All patients (PGE and PG) received standardized postoperative therapy with levofloxacin and prednisolone acetate drops four times a day. The frequency and duration of prednisolone acetate use were adjusted according to the postoperative circumstances. A subconjunctival injection of dexamethasone sodium phosphate was performed if anterior chamber reaction was obvious.

Surgery success was defined as IOP below or equal to 15 mm Hg or IOP drop at least 20% without antiglaucomatous medications. Failure was defined as less than a 20% reduction in IOP at least two consecutive follow-up visits or a need for surgical intervention to lower the IOP or an IOP >21 mm Hg or <5 mm Hg at least two consecutive follow-up visits 1mo or later after surgery. The baseline demographic and preoperative IOP, BCVA, number of IOP-lowering topical medications, history of surgery, and extent of PAS were evaluated and recorded, and the postoperative IOP, BCVA, number of IOP-lowering topical medications, and complications were observed and recorded at 1d, 1, 3, 6, 12mo after surgery and at the last visit. Raised postoperative IOP was reported by previous studies[19-20], Siegel *et al*[19] defined IOP spike as an increase in IOP which was 10 mm Hg higher than baseline. To better analyze and compare, we adopted this definition for our complication recording.

Data were recorded using an Excel spreadsheet (Microsoft Corp., Redmond, WA, USA). Statistical analysis was performed using Statistical Product and Service Solutions (SPSS 22; IBM Corp., Armonk, NY, USA). Unpaired *t*-tests, Wilcoxon signed rank sun tests, Chi-square tests were used to compared baseline parameters. Kaplan-Meier survival curves were used to calculate success rate. Preoperative and postoperative IOP were evaluated for statistical significance using paired *t*-tests at each visit. Preoperative and postoperative BCVA, the number of IOP-lowering agents were evaluated using Wilcoxon signed rank sum tests. A *P*-value <0.05 was considered statistically significant.

RESULTS

Patients' demographic data are presented in Table 1. There were 74 patients (88 eyes) included in the final analysis. Forty-two eyes with PAS more than 180° in group A underwent PGE. Among group A, 15 eyes did not have a history of surgery (A1), 16 eyes experienced previous peripheral iridotomy (PI; including PI by surgery and laser; A2), and 11 eyes experienced trabeculectomy (A3). There were 46 eyes included in group B who underwent PG with PAS less than 180°. Among group B, 18 eyes did not have a history of surgery (B1), and 28 eyes experienced previous PI (B2). The average follow-up period of group A was 13.8±4.6mo, and of group B was 14.5±7.8mo. The average preoperative PAS in group A was 250°±35° and that in group B was 120°±25°. The mean baseline IOP was 24.9±5.2 mm Hg in group A and 24.1±5.4 mm Hg in group B. The mean number of glaucoma medications and BCVA before surgery were 1.62±1.1 and 0.21±0.16 respectively in group A while 0.87±0.9 and 0.24±0.16 respectively in group B.

Success Survival Both the two groups had higher success rates at 1mo but decreased over time. The success rate of group A at 1mo was 95.2%, and was 70.7% at the last visit. The success rate of group B at 1mo was 100%, and was 73.4% at the last visit. Figure 1 shows the Kaplan-Meier survival curve in two groups.

Changes in Intraocular Pressure The IOP outcomes over time and reductions in IOP in the two groups are demonstrated in Tables 2 and 3. Compared to the preoperative IOP, statistically significance existed in each group at each postoperative visit, except in group A2 at 1d. The average IOPs were highest at 1d and were the lowest at 1mo after surgery and then showed a slow increasing trend in all groups. Group A2 had the lowest reduction in IOP (7.19%) at first and then was parallel with other groups.

Changes in Medication Table 4 shows the numbers of IOP-lowering topical agents in the two groups before surgery and at each point after surgery. The mean number of preoperative medications was 1.62±1.1 in group A and was 0.87±0.9 in group B. At the last visit, the mean number of medications was 0.13±0.4 and 0.10±0.2 in group A and B respectively. Every time point had statistically significant differences compared to preoperative treatments (*P*<0.001). The medication changes over time are displayed in Figure 2.

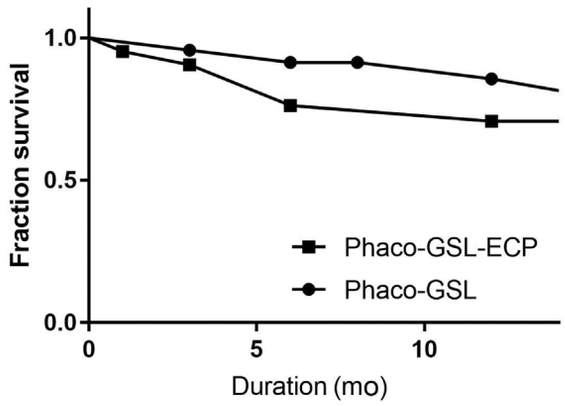

Figure 1 Kaplan-Meier survival curves for surgery success rate after PGE and PG.

Table 1 Baseline demographic characteristics

Parameters	PGE	PG
Number		
Patients	36	38
Eyes	42	46
Average age, y	69.0±7.0	69.6±5.5
Gender		
Male	8	4
Female	28	34
Prior glaucoma surgery, *n*		
None	15	18
PI	16	28
Trabeculectomy	11	0
Mean preoperative IOP, mm Hg	24.9±5.2	24.1±5.4
None	27.5±5.5	22.1±4.9
PI	22.8±5.0	25.4±5.5
Trabeculectomy	24.6±3.5	
Total	24.9±5.2	24.1±5.4
Prior mean medications, *n*	1.62±1.1	0.87±0.9
Prior mean BCVA	0.21±0.16	0.24±0.16
Mean PAS	250°±35°	120°±25°
Mean follow-up, mo	13.8±4.6	14.5±7.8

PGE: Phacoemulsification combined with endoscopic cyclophotocoagulation and goniosysnechialysis; PG: Phacoemulsification combined with goniosysnechialysis; PI: Peripheral iridotomy; IOP: Intraocular pressure; BCVA: Best corrected visual acuity; PAS: Peripheral anterior synechia.

Changes in Best Corrected Visual Acuity At the last visit, the mean BCVA in group A was 0.60±0.29, and 90.4% of patients had improved BCVA in group A, of which 57.1% had BCVA increased to better than 0.5, of which 33.3% had BCVA increased to less than 0.5 but better than baseline. Meanwhile, in group B, the mean BCVA at the last visit was 0.67±0.21, and 95.6% of patients had improved BCVA; 73.9% had BCVA that was better than 0.5; 21.7% had BCVA that was less than

Table 2 IOP from baseline to last visit mm Hg

Parameters	Baseline	1d	1mo	3mo	6mo	12mo	Last visit
Group A	24.9±5.2	19.3±9.8	14.1±3.2	14.3±3.1	15.9±4.8	16.0±3.1	16.2±4.9
t^a	-	3.333	12.469	12.469	9.281	10.427	9.803
P	-	0.002	<0.001	<0.001	<0.001	<0.001	<0.001
Group B	24.1±5.4	17.2±3.7	13.0±2.6	13.2±2.6	14.6±3.1	15.3±3.8	15.3±3.8
t^a	-	5.979	8.525	8.461	7.910	5.831	6.854
P	-	<0.001	<0.001	<0.001	<0.001	<0.001	0.004

[a]Student *t*-test for paired samples.

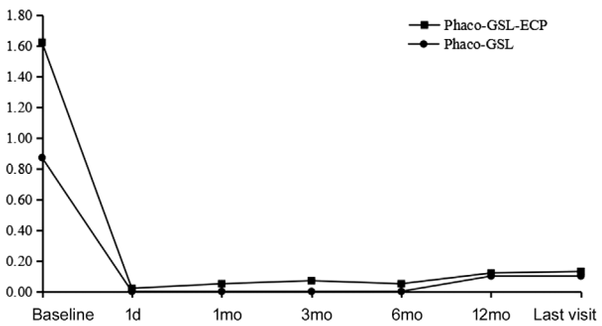

Figure 2 Numbers of IOP-lowering topical medications during observation.

Table 3 IOP reduction from baseline to last visit %

Parameters	1d	1mo	3mo	6mo	12mo	Last visit
Group A	20.57	42.46	41.35	35.28	35.95	34.89
A1	33.54	48.44	47.74	39.46	41.03	39.00
A2	7.19	40.99	39.51	32.93	33.66	31.70
A3	22.34	36.44	35.31	32.99	31.66	33.92
Group B	26.11	44.46	43.67	37.16	34.71	33.21
B1	24.58	49.13	47.03	40.14	36.07	34.55
B2	27.09	42.66	42.37	35.88	33.97	32.35

A1, B1: No history of surgery; A2, A2: Previous peripheral iridotomy; A3: Previous trabeculectomy.

0.5 but better than baseline. Compare with baseline, the mean BCVA at the last visit improved significantly in both groups (*P*<0.001 for both groups).

Complications No complications occurred during surgery. Postoperative complications included the following: IOP spikes in 3 eyes (7.1%) in group A and in 2 eyes (4.8%) in group B; fibrinous uveitis in 3 eyes (7.1%) in group A and in 4 eyes (9.5%) in group B, hyphema in 2 eyes (4.8%) in group A and in no eyes in group B, and malignant glaucoma in 1 patient in group A at 5mo after surgery. After trabeculectomy combined with vitrectomy, IOP was controlled. No cases of malignant glaucoma occurred in group B.

DISCUSSION

Our data showed that PGE was effective in treating patients with PACG and cataracts for more than 12mo. PGE also lightened the medication burden and improved the BCVA significantly. Our study is the first one to report PGE in a considerable-scale of PACG patients solely.

Some studies have reported that PE[18-24,26-27] can successfully treat mild to advanced glaucoma, but the specific results were heterogenous. The IOP reduction varied from 10.9% to 65.77%, and the changes of glaucoma medications varied from +5.1% to -88.89% (12mo postoperatively). The IOP reduction in our study (35.95%) was consistent with the findings of previous researches, and the reduction in medication (92.6%) was more significant in our study.

Previous researches focused on primary open angle glaucoma (POAG) and unspecified glaucoma, few research has been performed regarding PACG. A case report of three subjects showed that Phaco-ECP was an effective and efficient method for lowering IOP in PACG with extensive synechial[26]. In studies on unspecified glaucoma, the proportion of patients with PACG was usually small. Morales *et al*[27] reported that their PACG group (45 eyes, accounting for 43.3% of subjects) achieved lower absolute and qualified success rates than did their POAG group. Roberts *et al*[21] reported that chronic angle-closure glaucoma (12 eyes, accounting for 13.2% of subjects) achieved a higher success rate than POAG, but there was no significant difference.

Our study had large proportions of patients with a previous surgical history. Compared with patients without previous surgical history, patients with previous surgical history had less IOP reduction, although the difference was not significant. Morales *et al*[27] found that the risk of failure doubled in patients who had undergone previous surgery. Failure of treatment was defined as IOP>15 mm Hg with medications or the need for additional surgery to control IOP.

Francis *et al*[22] compared the outcomes of Phaco-ECP and Phaco alone in eyes with medically controlled POAG. Two years after Phaco-ECP surgery, IOP decreased from 18.1 mm Hg to 16.0 mm Hg, and the number of glaucoma medications used decreased from 1.5 to 0.4. However, after Phaco alone IOP decreased from 18.1 mm Hg to 17.3 mm Hg, and the number of medications used decreased from 2.4 to 2.0. The differences of two surgical methods were significant. Siegel *et al*[19] found that after 36mo there were no significant differences between patients who received ECP-Phaco or Phaco alone, but the number of medications used in the ECP-Phaco group decreased from 1.3 to 0.2 while no obvious changes were

Table 4 IOP-lowering topical agents numbers from baseline to last visit

Parameters	Baseline	1d	1mo	3mo	6mo	12mo	Last visit
Group A	1.62±1.1	0.02±0.2	0.05±0.2	0.07±0.3	0.05±0.2	0.12±0.3	0.13±0.4
A1	1.87±1.1	0	0.07±0.3	0.13±0.4	0.13±0.4	0.15±0.4	0.14±0.4
A2	1.69±1.3	0.06±0.3	0	0	0	0.08±0.29	0.13±0.5
A3	1.18±1.0	0	0.09±0.3	0.09±0.3	0	0.11±0.3	0.09±0.3
Group B	0.87±0.9	0	0	0	0	0.1±0.3	0.10±0.2
B1	0.44±0.5	0	0	0	0	0	0
B2	1.14±0.9	0	0	0	0	0.15±0.4	0.14±0.4

A1, B1: No history of surgery; A2, B2: Previous peripheral iridotomy; A3: Previous trabeculectomy.

observed in patients who underwent Phaco alone. The subjects in this study mainly were POAG (128 patients, accounting for 79.5% of subjects). Pérez Bartolomé *et al*[24] also came to the conclusion that PE is a safe and more effective way to reduce more IOP and the number of medications needed in patients with moderate to advanced POAG with cataract. Our study was inconsistent with this these researches, as group A and B both had similar positive results. Several studies have proven that the influence of cataract extraction on IOP of POAG is weak and uncertain[29-30]. The different effect of cataract surgery between the two types of glaucoma may account for the divergence in conclusions. Baseline criteria of the two groups were heterogenous with regards to degree of angle closure. Patients with PAS<180° underwent PG and patients with PAS>180° underwent PGE. The scope of PAS suggested the severity of glaucoma in some way, accounting for the different numbers of medications at baseline. The severity of glaucoma affected the outcome results and might explain the favorable outcome in PG group.

IOP spikes occurred in 7.1% of eyes in group A, and IOP was controlled with temporary topical or systemic glaucoma medications in three days. Siegel *et al*[19] defined IOP spikes as increases in IOP that were 10 mm Hg higher than baseline. The IOP spikes occurred in 7.1% of eyes in our study, which was less than the 10% reported by Siegel *et al*[19]. The higher baseline IOP in our study may account for this difference. Hyphema was observed in 4.8% of eyes in our research, which was less than the 12% reported by Chen *et al*[31], and all the affected patients had been treated successfully after taking oral hemostatic medicine. Our study showed the incidence of fibrinous uveitis was 7.1%, which corresponded with previous results (7%-24%)[20,23-24,27,31]. Anterior chamber reaction regressed after conjunctival injection of dexamethasone sodium phosphate and/or prednisolone acetate eye drops. One case of malignant glaucoma occurred at 5mo after surgery, and IOP was controlled by trabeculectomy combined with vitrectomy. There were no other complications in this study such as macular edema, choroidal detachment, hypotony or eyeball atrophy. The low incidence of complications confirms the safety of PGE.

PG has been proven by many researchers as a safe and effective way to lower IOP levels and lighten the medication burden. However, the indications for PG in previous studies varied from refractory acute angle-closure to chronic PACG, and the extent of PAS was also diverse. Our study showed that PG had good results for PACG. PG is a good option for PACG with PAS less than 180 degrees. For PACG with PAS more than 180 degrees, our results showed that PGE is an alternative approach that can avoid some of the complications of trabeculectomy, such as bleb leakage and scarring of the filtering bleb.

One of the limitations of our study was the small sample size. Another limitation was the relatively short follow-up time of 12mo. Long-term observation is needed to confirm the efficacy of treatment. Moreover, to better compare the effect of the two groups, a randomized controlled trial is needed.

In conclusion, PGE shows promise as a new method for PACG patients with PAS>180° while PG has significant effect for PACG patients with PAS<180°. PGE is an effective and safe alternative option for PACG patients with cataracts to reduce IOP, lighten the medication burden and improve visual acuity but PG still has its value in specific patients.

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