

One year Outcome of Combined phacoemulsification and Endoscopic Cyclophotocoagulation vs. phacoemulsification Alone in Patients with Primary Glaucoma: The Malaysian experience

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Background: To compare the post-operative outcomes phaco-ECP with phaco alone in patients with primary glaucoma in terms of efficacy and safety.

Methods: Retrospective comparison case series of all patients undergoing phaco and phaco-ECP were done. Inclusion criteria were all eyes with primary glaucoma and at least on 2 antiglaucoma medications who underwent phaco-ECP and phaco alone. Mean IOP and number of topical antiglaucoma medications were assessed at 1 week, 1 months, 3 months, 6 months, and 1 year post-operatively.

Results: A number of 18 eyes from each group were recruited into the study (N=36). In phaco-ECP group, mean IOP reduction were seen at 1 week ($p=0.021$), 1 month ($p=0.009$), 3 months ($p=0.034$), and 6 months ($p=0.034$), but increased at 1 year post-operation ($p=0.775$). Phaco group showed either statistically non-significant reduction or increment of mean IOP throughout the study period. For mean number of topical antiglaucoma medication used, significant reduction were seen in the phaco-ECP group at each intervals (1 week; $p=0.004$, 1 month; $p=0.001$, 3 months; $p=0.000$, 6 months; $p=0.002$, 1 year; $p=0.035$), unlike the phaco group which showed no changes.

Conclusion: Significant reduction of IOP in the first 6 months post phaco-ECP was seen, as well as elimination of 1 topical antiglaucoma medication in this group during the first year of post-operation.

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Introduction

Cataracts are common in patients with glaucoma due to aging process. Acceleration of cataract development are associated with treatment of glaucoma such as topical antiglaucoma medications, laser procedures and filtration surgery^{1,2}. As cataract causes reduced vision, compromised the aqueous outflow,

affects the acquisition of optic nerve images and interpretation of visual field, timely removal of cataract is beneficial for visual rehabilitation and glaucoma management in patients with glaucoma.

Endoscopic cyclophotocoagulation (ECP)

ECP is an emergent procedure in the management of glaucoma. It is a precise and titratable procedure which allows delivery of diode laser directly to the ciliary processes via a fibre optic viewer causing reduction of aqueous fluid production. Viewing the ciliary body directly gives the advantages of predicting

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the outcomes of the procedure and deters over-or under-treated as well as minimizing complications such as phthisis and hypotony³. Furthermore, this procedure is relatively easy to perform with great safety profile⁴ and considered as one of the minimal invasive glaucoma surgeries (MIGS).

Considering these properties, many investigators explored the efficacy of combining phacoemulsification and ECP (phaco-ECP) in cases of concurrent cataract and glaucoma to improve vision as well as lower the IOP and reduce the need for glaucoma medications in patients with glaucoma^{5,6}.

We embarked on a study to compare one year outcomes of phaco-ECP and phacoemulsification alone (phaco) in primary glaucoma patients in terms of efficacy and safety. Our centre is the only centre in Malaysia which is equipped with ECP and serves as the referral centre for the whole country.

Methods

Medical records of all stable glaucoma patients who had undergone cataract surgery for at least 1 year in Hospital Cancelor Tuanku Muhriz (HCTM), Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from 1st January 2012 until 30th September 2016 were identified through convenient sampling method. Patients who were treated with ECP alone, refractory glaucoma or data not available were excluded from this study. Patients were then divided into two groups; a) phaco-ECP group and b) phaco alone group for analysis purposes.

All ECP were performed by two different surgeons under subtenon anaesthesia. A single clear corneal incision was made with 2.75 mm keratome at 11-12 o'clock position. A high molecular weight viscoelastic (Healon GV, Advanced Medical Optics [AMO], Santa Ana, CA) was used to inflate the ciliary sulcus. Diode laser (Iridex OcuLight SL, Mountain View, California, USA) was delivered using the curved endoscopic probe (Endo Optiks, Little Silver, USA) starting at 150 mW in continuous mode. The ciliary processes and spaces between the processes were treated for at least 270 degrees. The endpoint of treatment was whitening and shrinkage of the processes. Viscoelastic was then removed using either automated or manual irrigation-aspiration (IA). At the end of the procedure, subconjunctival gentamicin 20

mg and dexamethasone 1% 2 mg was injected. All patients received standardised post-operative therapy: guttae ciprofloxacin 0.3% and guttae pred forte 1% every 2 hours tapering dose for 4-6 weeks depending on level of inflammation. Patients were also advised to continue their usual preoperative anti-glaucoma medications.

Data collected include age, race, gender, type of glaucoma, duration of glaucoma, number of topical anti-glaucoma medications, best corrected visual acuity, intraocular pressure (IOP), Mean Deviation (MD) and Pattern Standard Deviation (PSD) on Humphrey Visual Field (HVF) test and post-operative complications.

Data were collected from eyes that were operated. If both eyes in a patient met the inclusion criteria, data from both were collected.

Pre-operatively, the latest IOP measured prior to operation were taken as the baseline IOP. Similarly, nearest MD and PSD values of HVF towards the date of operation were collected.

Post-operative data were also assessed at post-operation date of 1 week, 1 months, 3 months, 6 months, and 1 year with special attention to the mean IOP and number of topical anti-glaucoma prescribed at each interval. Complications and further IOP lowering procedures or surgeries were documented as well.

However, patients who had undergone any other intraocular surgery or laser procedure of less than 6 months were excluded from the study. Additionally, performed combined operation of other than phaco-ECP or phaco alone such as penetrating keratoplasty or vitrectomy were also excluded.

Data were analysed using SPSS version 22, comparing between those two groups in terms of pre- and post-operative mean IOP and number of topical medications at each time point of assessment. Demographic data were analysed with descriptive analysis, and data comparing phaco-ECP and phaco alone group were analysed using t-test and Chi-Square. p value of less than 0.05 were considered significant.

Result

A total of 29 patients were recruited into this study, of which 5 of them having data from both eyes collected (n=34). Patients were grouped into phaco-ECP and phaco alone group, each having 17 subjects respectively.

Demographically, the mean age was 69.29 ± 18.11 and 71.94 ± 6.12 for phaco-ECP and phaco alone groups, respectively. Though female gender predominates the phaco-ECP group by 58.8%, male gender was vastly represented in the phaco alone group by 52.95%. Chinese ethnicity was the main race underwent both procedures, 52.9% for phaco-ECP group and 76.5% for phaco alone group. No statistically significant difference was found between these two groups upon comparing the subjects' demography.

The most frequent type of primary glaucoma encountered was Primary Open Angle Glaucoma (POAG), which represent 94% and 53% in phaco-ECP group and phaco alone group, respectively. The remainder of cases were Primary Angle Closure Glaucoma (PACG).

For the phaco-ECP group, significant visual improvement were seen at 6 months ($p=0.024$) and 1 year ($p=0.028$) post-operatively with best corrected visual acuity of 6/12, as compared to 6/18 pre-operatively.

Although IOP were significantly improved particularly at 1 month (IOP 12.71 ± 2.64 , $p=0.009$) as compared to pre-operation (IOP 17.59 ± 7.22), the effect was only sustainable until 6 months post-operation (IOP 13.00 ± 2.83 , $p=0.034$). IOP was found to increase back to pre-operative level at 1 year post-operation (IOP 17.46 ± 7.40 , $p=0.775$).

As for number of topical anti-glaucoma medications used in this group, patients in this group were on average 4 types of medications. A significant reduction was found during the first year of post-operation (2-3 anti-glaucoma, $p=0.00 - 0.035$), which was best at 3 months (2.41 ± 1.18 , $p=0.000$).

Meanwhile in the phaco alone group, similar improvement of visual acuity as the phaco-ECP group was shown post-operatively, with best corrected visual acuity of 6/12 at 1 year after operation (0.28 ± 0.14 , $p=0.001$).

Furthermore, mean IOP in this group was found to have been constant or minimally reduced from pre-operative value throughout the first year of post-operation (post-operative 1 week (15.56 ± 6.85 mmHg, $p=0.571$), 1 month (15.0 ± 1.84 mmHg, $p=0.309$), 3 months (13.92 ± 2.53 mmHg, $p=0.391$), 6 months (13.83 ± 2.55 mmHg, $p=0.489$), and 1 year (14 ± 1.83 mmHg, $p=0.472$)). Hence, there were no statistically significant changes seen, unlike the trend shown

in the phaco-ECP group.

In regards to number of topical anti-glaucoma medications used, patients in this group used about 3 types of eye drops pre-operatively (3.00 ± 0.71) and continue to use relatively the same amount of medications throughout each time points (post-operative 1 week (3.00 , $p=0.333$), 1 month (2.93 , $p=0.336$), 3 months (2.87 , $p=0.334$), 6 months (2.75 , $p=0.339$), and 1 year (2.92 , no changes in mean)). Thus, no statistically significant reduction in amount of eye drops used seen in this group over the period of post-operation.

The most frequent complication recorded was uncontrolled IOP (8.2%) which were documented mostly at one year post-operation. This is followed by post-operative inflammation (5.88%), which had occurred to at least one patient at each time point. There were two patients who underwent further IOP lowering procedures, one had repeated ECP at 3 months, and the other had trabeculectomy done at one year post-operation.

In summary, tremendous improvement of IOP and number of topical anti-glaucoma medications used showed by glaucoma subjects who underwent phaco-ECP procedure post-operatively, as compared to phaco alone group. These changes were significant particularly at 6 months period after operation (Table 1) (Figure 1).

Discussion

Traditionally, cycloablative procedures have been a last resort for eyes which have very poor visual potential

Attempts on lowering the IOP by acting on the ciliary body aiming to reduce the production of aqueous humour has a long history with various techniques were performed, together with their reported complications⁷. Not until the mid-nineties, when endoscopic cyclophotoncoagulation (ECP) was introduced by Martin Uram, citing a success in lowering the IOP with less adverse effects⁸. Of late, researchers were venturing to combine this cyclodestructive procedure with routine phacoemulsification in glaucoma patients with visually significant cataract⁹.

Table 1: Data comparing phaco-ECP and phaco alone group

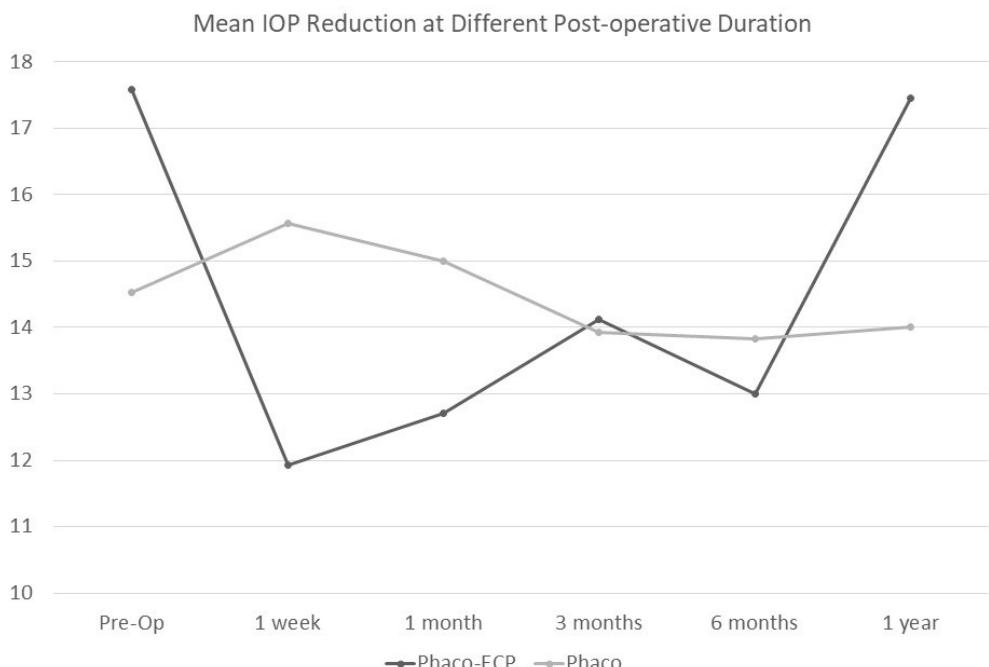
	phaco-ECP (n=17)	phaco (n=17)	<i>p</i> Value Between Groups*
Age (years)			
Mean ± SD	69.29 ± 18.11	71.94 ± 6.12	0.439
Gender (f, %)	Male 7 (41.2%) Female 10 (58.8%)	Male 9 (52.9%) Female 8 (47.1%)	0.492
Ethnicity (f, %)	Chinese 9(52.9%) Malay 8(47.1%) Indian 0(0%)	Chinese 9(52.9%) Malay 8(47.1%) Indian 0(0%)	0.135
Types of Primary Glaucoma (f, %)	POAG 16 (94%) PACG 1(6%)	POAG 9(53%) PACG 8(47%)	0.017
PreOp IOP (mm Hg)	17.59 ± 7.22	14.53 ± 1.55	0.141
Mean ± SD			
PostOp IOP at 1 week (mm Hg)	11.93 ± 2.73	15.56 ± 6.85	0.051
Mean ± SD			
PostOp IOP at 1 month (mm Hg)	12.71 ± 3.88	15.00 ± 1.84	0.071
Mean ± SD			
PostOp IOP at 3 month (mm Hg)	14.12 ± 4.20	13.93 ± 2.53	0.324
Mean ± SD			
PostOp IOP at 6 month (mm Hg)	13.00 ± 2.83	13.83 ± 2.55	0.680
Mean ± SD			
PostOp IOP at 1 year(mm Hg)	17.46 ± 7.40	14.00 ± 1.83	0.695
Mean ± SD			
PreOp Medications (n)	3.59 ± 0.71	3.00 ± 0.71	0.022
Mean ± SD			
PostOp Medications at 1 week (n)	2.36 ± 1.34	3.00 ± 0.73	0.359
Mean ± SD			
PostOp Medications at 1 month (n)	2.29 ± 1.27	2.93 ± 0.83	0.294
Mean ± SD			
PostOp Medications at 3 months (n)	2.41 ± 1.18	2.87 ± 0.83	0.243
Mean ± SD			

Table 1: Data comparing phaco-ECP and phaco alone group (Conts).

	phaco-ECP (n=17)	phaco (n=17)	<i>p</i> Value Between Groups*
PostOp Medications at 6 months (n)	2.54 ± 1.13	2.75 ± 1.14	0.396
Mean \pm SD			
PostOp Medications at 1 year (n)	2.77 ± 1.36	2.92 ± 0.76	0.223
Mean \pm SD			

*Pearson Chi-Square

Figure 1: Mean IOP Reduction at Different Post-operative Duration



A retrospective review by Siegel et. al which compare phaco-ECP group against phaco alone group in 261 eyes for a period of 3 years revealed that 61.4% of patients in the phaco-ECP group were able to have at least 20% IOP reduction with elimination of at least one anti-glaucoma medication. These findings are consistent with ours, but with a longer sustainability, possibly due to a larger area of ciliary body cycloablation. However, Siegel's analysis had few issues with data variance since case-matching was not statistically significant, hence affecting the end result of power of study¹⁰.

A prospective approach study comparing the same groups as those by Siegel's study was conducted by Francis et. al, by which it gave a statistically significant greater reduction of both IOP and number of anti-glaucoma medications in the phaco-ECP group, though the percentage of IOP reduction was 11%, lesser than Siegel's result. Furthermore, he found that phaco-ECP was superior than phaco alone in medically-controlled glaucoma patients at each time interval with regards to its IOP lowering effect as well as number of anti-glaucoma elimination. This study was able to gather larger sample size, and also

a better control-matching among both groups, though it was a non-randomized trial. Hence, our results tallied with these data, thus would hopefully contribute to a better evidence-based practice¹¹.

Major published studies in ECP including comparative analysis between phaco-ECP against phaco alone, as well as phaco-ECP versus other modalities of glaucoma surgery were being scrutinized by Cohen et. al, quoting among others important studies by Siegel and Francis in regards to our focus. Cohen further concluded that ECP should be used with caution in cases of advanced glaucoma, due to the fact that this group of patients require greater IOP reduction. He later found that corroborated evidences failed to prove success rate of IOP less than¹⁵, though 29% of patients were able to reduce the burden of medications to less than 3 eye drops. He also addressed the rare complication of ECP which was ocular hypotony, through which could lead to permanent visual impairment and phthisis, thus surgeon's prudence is necessary in using the ECP¹².

Nevertheless, this remark was argued by Lin et. al as he supported the use of ECP in refractory glaucoma cases with relatively sound vision, claiming that ECP has a favourable safety profile against other modality of procedures in lowering the IOP¹³.

Another narrative review which looked into the efficacy of phaco-ECP by Rathi et. al concluded that the IOP reduction were sustainable up until 3 years post-operation, though the effects beyond that period was unknown. He also reiterated the importance of considering phaco-ECP as a primary procedure, given the simplicity of the combined procedure and also its minimal adverse effects¹⁴.

A study published by Clement et. al revealed that greater reduction of IOP could be achieved by ECP in older patients as well as patients with higher baseline intraocular pressure. His cohort of subjects were followed-up for a period of one year, and mean IOP reduction at the end of the study was 24%, during which number of anti-glaucoma medications were also reduced by 1.2. These findings are consistent with our study, however we found out that the effect of improved IOP were only able to be sustained up until 6 months post-operation. Further study in the future need to be conducted to look at the

variability of response with regards to the IOP, which were previously postulated by Lin et. al as the theory of ciliary vessels regeneration¹⁵. Clement further explained that as a patient gets older, the aqueous drainage apparatus will be functioning suboptimally even though its production is maintained, thus leading to higher IOP and greater response towards ECP¹⁶.

Kaplowitz et. al precisely analysed previous studies which focussed on usage of ECP for severe glaucoma and suggested that in view of ample evidences regarding its safety, ECP should be incorporated in managing glaucoma at an earlier stage. This is particularly true since the ciliary processes are directly visualized, hence over- or under-treatment are able to be controlled¹⁷. Apart from reducing the IOP and number of anti-glaucoma medications, ECP also has been reported to have very minimal complications following the procedure, citing Chen et. al's study which showed the occurrence of fibrin in the anterior chamber and cystoid macular edema among the highly reported complications with incidence of 22% and 10% respectively¹⁸.

As regard to phaco alone, although level of evidence were relatively low in previous studies which looked into outcome of this surgery in patients with glaucoma, limited reduction of IOP by 20-30% were seen for both open- and closed-angle glaucoma. This effect was demonstrable by examining the anterior chamber angle, which widens after cataract extraction. While in the long run, IOP trend was noticed to increase, mostly requiring patients to take additional anti-glaucoma medications or going for glaucoma surgery at a variable period between 16 to 34 months¹⁹.

Despite that, our study has several limitations. First, the sample size was relatively small, apart from a shorter duration of retrospective analysis. We noticed the volume of patients who went for the phaco-ECP procedure in our centre were not that enormous, thus limiting the available number of subjects. In spite of this, all enrolled subjects were able to be matched with control group with a statistically significant value.

Secondly, this study recruited patients with all levels of primary glaucoma, including normal tension glaucoma and closed-angle glaucoma which have distinct pathophysiology from high-tension open-angle glaucoma. Moreover, all

stages of primary glaucoma based on the Mean Deviation of Humphrey Visual Field Analyser were also included. Having said that, results of this study may be inaccurately represented due to the different types of primary glaucoma, wide range of IOP and also severity of glaucoma pre-operatively. Hence, subgroup analysis were not done to see which group performed better.

Conclusion

Phaco-ECP is definitely a better option for medically controlled glaucoma patients going for cataract surgery, in view of its superior efficacy as compared to phaco alone, as well as its eminent safety profile. A significant reduction of IOP and anti-glaucoma medications can be seen during the first year of post-operation, thus phaco-ECP should be considered as an early option for glaucoma patients with visually significant cataract. Future studies should be undertaken to qualitatively measure how significantly phaco-ECP outcome impacts patients' quality of life, and together analyse the cost-effectiveness of this procedure, with a larger sample size of a prospective study and standardized treatment protocol.

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