Effect of Phacoemulsification on Intraocular Pressure in Healthy Subjects and Glaucoma Patients

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ABSTRACT

Background: We investigated how cataract surgery might influence long-term intraocular pressure (IOP) change in both healthy subjects and glaucoma patients.

Methods: A retrospective analysis of patients who had had clear corneal phacoemulsification with a minimum of 12 months of follow up was performed. Glaucoma patients with medically controlled open-angle glaucoma and healthy subjects with no glaucoma were included in the analysis. The change of IOP after phacoemulsification and factors associated with postoperative IOP change were investigated.

Results: In total, 754 eyes of 754 patients, specifically 106 patients with glaucoma and 648 patients with no glaucoma (i.e., healthy subjects) were enrolled. The phacoemulsification effected a reduction of IOP: 1.03 ± 3.72 mmHg in healthy subjects and 1.08 ± 3.79 mmHg in glaucoma patients at postoperative 1 year ($P = 0.656$). There were negative coefficients of IOP until 1 year of follow up (all $P < 0.001$), but the IOP change gradually showed a less steeply decreasing slope (correlation coefficient: −0.993), compared with those for 1 week and 1 month of follow up (correlation coefficients: −1.893 and −1.540, respectively). In the multivariate analysis, age and preoperative IOP showed significant associations with postoperative IOP change (regression coefficients: −0.034 and 0.419 respectively, all $P < 0.001$).

Conclusion: Phacoemulsification resulted in IOP reduction, which effect regressed in healthy subjects and glaucoma patients over the course of long-term follow up. Therefore, long-term monitoring of IOP change is needed. In cases of higher preoperative IOP and young patients, phacoemulsification alone is a reliable option for IOP control.

Keywords: Phacoemulsification; Intraocular Pressure; Healthy Subjects; Glaucoma Patients

INTRODUCTION

Cataract and glaucoma are the leading causes of blindness worldwide. The incidences of both cataract and elevated intraocular pressure (IOP), with or without glaucoma, increase with age.1 IOP, still the only known modifiable risk factor in the management of glaucoma, is well recognized as a primary risk factor for glaucoma onset, development, and progression.2 Meanwhile, cataract surgery has been suggested to be of clinical benefit for both cataract and glaucoma. It has been found to reduce IOP in eyes with or without glaucoma, though with...
variable magnitude and as influenced by factors such as anterior-chamber anatomy and angle configuration.\textsuperscript{3,7} The influence of the lens on the etiology of primary angle-closure glaucoma (PACG) is well-established. The lens can incur angle narrowing by pushing the peripheral iris anteriorly, which the effect will be more marked if the lens is also cataractous.\textsuperscript{5,8} As such, cataract surgery in cases of PACG has shown promising IOP-reduction results and can also afford less peripheral anterior synechia formation. However, questions remain as to how it might influence the clinical management of healthy subjects and other, open-angle glaucoma (OAG) patients, excluding closed-angle cases. In a previous study, OAG patients did not show as high a reduction of IOP after cataract surgery as their counterparts with closed-angle glaucoma.\textsuperscript{9,10} Additionally, some of the studies have recorded immediate IOP elevation after surgery for OAG.\textsuperscript{5,11} Other studies have reported that IOP reduction was not high when the preoperative IOP was not high.\textsuperscript{12,13} In this context, the degree of change of IOP after cataract surgery can be unpredictable and various in healthy subjects and OAG patients.

Therefore, in the present study, we investigated how cataract surgery might influence long-term IOP change in both healthy subjects and medically controlled OAG patients.

**METHODS**

**Inclusion and exclusion criteria**

The medical records of patients who had undergone cataract surgery and been followed up on for more than 1 year were reviewed. The present study included patients aged 18 years or older who had clear corneal phacoemulsification with posterior-chamber intraocular lens (IOL) implantation. Glaucoma patients with medically controlled OAG (preoperative IOP < 22 mmHg under medication) attending a glaucoma clinic and healthy subjects from the general ophthalmology clinic were enrolled. Glaucoma had been diagnosed in cases where glaucomatous visual field (VF) defect matched optic disc changes. The criteria to be eligible for the healthy subjects were a normal anterior segment on slit-lamp examination, IOP between 10 and 21 mmHg, cup-to-disc ratio of less than 0.6, no retinal nerve fiber layer (RNFL) defects in red-free RNFL photographs, and no glaucomatous VF defects.

The exclusion criteria were primary angle-closure attack, primary angle-closure suspect, PACG, ophthalmic disease (other than cataract) that could affect IOP, previous intraocular surgery, secondary glaucoma such as lens-induced glaucoma, neovascular glaucoma or uveitis, and complications during phacoemulsification. Patients were excluded also if, in the year following phacoemulsification, they underwent any additional non-glaucoma-related surgical or laser procedures such as laser capsulotomy.\textsuperscript{14}

**Study assessment**

Data on IOP were collected preoperatively and at 1 day, 1 week, 1, 3 and 6 months, and 1, 2 and 3 years postoperatively. The preoperative and postoperative IOP values were derived from the mean of IOP readings taken on two separate days on the regular visit schedule using the Goldmann applanation tonometer. Preexisting (pre-cataract-surgery) glaucoma was evaluated, and glaucomatous patients were defined as those with a glaucomatous VF defect confirmed by two reliable VF examinations and by the presence of glaucomatous optic disc cupping. Glaucomatous optic disc cupping was defined as neuroretinal rim thinning,
notching, excavation, or RNFL defect with corresponding VF deficit. All of the patients had preoperative gonioscopy showing open angles without peripheral anterior synechiae or areas of appositional closure. Visual acuity was measured using a Snellen chart. Cataract was graded using Lens Opacities Classification System III (LOCS III).

**Phacoemulsification**

The indication for surgery was reduced vision attributable to visually significant cataract. If a patient received cataract surgery on both eyes, only one eye was randomly enrolled. The operative procedures were as follows. Under topical anesthesia, a 3.0 mm clear corneal incision was made. After continuous curvilinear capsulorhexis using a bent 27-gauge needle, standard phacoemulsification was performed. A foldable IOL (Tecnis ZCB00 IOL; Abbot Medical Optics, Abbott Park, IL, USA) was inserted into the posterior chamber through the corneal incision. Irrigation-aspiration was performed for at least 30 seconds to remove as much viscoelastic material as possible from the anterior chamber. The IOL was also gently rocked to promote release of all visible viscoelastic material from behind it. The anterior chamber was reformed with balanced saline solution (BSS), and the corneal wound and side port were hydrated with BSS.

**Statistical analyses**

All of the analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Generalized estimating equations (GEE) were used to construct linear models, allowing for adjustable correlation of repetitive IOP checking in individual patients. By univariate and multivariate analyses, the associations between independent variables and the magnitude of postoperative IOP change were evaluated; these variables included gender, age, preoperative IOP, underlying disease, axial length, spherical equivalent, VF index, cataract grade, and presence of glaucoma. The variables selected for the multivariate analysis were those showing a $P$ value less than 0.2 in the univariate analysis. Additionally, multi-collinearity was examined according to the variance inflation factor (VIF), based on which, we selected a variable showing a VIF $< 4$ in the multivariate analysis. All of the statistical tests were 2-sided with a 0.05 level of significance.

**Ethics statement**

The present study protocol was reviewed and approved by the Institutional Review Board (IRB) of Hallym University Sacred Heart Hospital (IRB No. 2018-I011). The requirement to obtain written informed consent was waived by the Institutional Review Board of Hallym University Sacred Heart Hospital, because our study was retrospective research based on medical records, and also because this research presented no more than minimal risk of harm to subjects.

**RESULTS**

A total of 754 eyes of 754 patients were enrolled in the study. One hundred and six (106) were assigned to the glaucoma group and 648 to the healthy group. The mean follow-up period was $1.59 \pm 0.82$ years in the healthy group and $1.47 \pm 0.62$ years in the glaucoma group ($P = 0.128$) (Table 1). There were no differences in the baseline demographics between the two groups, except for better preoperative visual acuity in the glaucoma group ($P = 0.011$). In detail, the glaucoma group consisted of 55 normal-tension glaucoma (NTG), 39 primary open-angle glaucoma (POAG), and 12 pseudoexfoliation glaucoma (PXG) patients (Supplementary Table 1). Additionally, Supplementary Table 2 summarizes the comparison of the baseline demographics and clinical features between patients with 1 and 3 years of follow up, respectively. There were no differences in the clinical characteristics between the two groups.
Serial change of IOP

Fig. 1 plots the change in mean IOP values over time for all of the patients. The preoperative mean IOP was 14.48 ± 3.37 mmHg, which, by postoperative 1 day, had increased to 17.17 ± 6.15 mmHg. However, by postoperative 1 week, the IOP had decreased again, to 12.59 ± 3.84 mmHg. After postoperative 1 week, the mean IOP again showed an increasing tendency, as follows: 12.94 ± 3.71 mmHg at 1 month, 12.99 ± 3.21 mmHg at 3 months, 13.36 ± 3.13 mmHg at 6 months, 13.49 ± 2.97 mmHg at 1 year, 14.59 ± 3.35 mmHg at 2 years, and 14.03 ± 2.83 at 3 years.

Additionally, this study investigated the changes of mean IOP for both groups, healthy subjects and glaucoma patients, respectively (Table 2). There was no significant inter-group difference. After phacoemulsification, both groups showed immediate IOP elevation at postoperative 1 day; however, the mean IOP was decreased. In fact, from postoperative 1 week to 1 year, the mean IOP of both groups remained lower than the preoperative value. The IOP-lowering effect of phacoemulsification over the course of 1 year of follow up did not statistically differ between the healthy subjects and glaucoma patients (P > 0.05, respectively).

Table 1. Baseline demographics and clinical features of healthy subjects and glaucoma patients

| Characteristics | Healthy subjects (n = 648) | Glaucoma patients (n = 106) | P value |
|-----------------|---------------------------|---------------------------|---------|
| Mean age, yr    | 65.45 ± 13.37             | 67.55 ± 12.42             | 0.106^a |
| Gender, men:women | 241:404 (1:1.66)          | 37:69 (1:1.86)            | 0.595^a |
| Underlying disease, No. | 554                       | 88                        | 0.253^a |
| HTN             | 309                       | 61                        |         |
| DM              | 297                       | 30                        |         |
| Thyroid disease | 25                        | 4                         |         |
| Period of follow up, yr | 1.59 ± 0.82               | 1.47 ± 0.62               | 0.128^a |
| Preoperative IOP, mmHg | 14.41 ± 3.24              | 14.25 ± 3.35              | 0.184^a |
| Preoperative visual acuity (Snellen chart) | 0.40 ± 0.29               | 0.47 ± 0.29               | 0.011^a |
| Axial length, mm | 23.97 ± 2.07              | 23.85 ± 2.01              | 0.092^a |
| Spherical equivalent (diopters) | −0.71 ± 4.18              | −0.32 ± 3.63              | 0.067^a |
| LOCS III scores, median (Grade 0–5) | 1 (Arithmetic mean, 1.53) | 1 (Arithmetic mean, 1.66) | 0.151^a |

Values are presented as mean ± standard deviation.

HTN = hypertension, DM = diabetes mellitus, IOP = intraocular pressure, LOCS III = lens opacities classification system III. ^Independent samples t-test; ^χ^2 test.

Serial change of IOP

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Degree of change of IOP for total patient group

The current study investigated, at each follow-up point, the degree of change from the preoperative IOP using the GEE method (Table 3). There was a positive tendency of change between the preoperative value and postoperative 1 day ($P < 0.001$); however, each subsequent follow-up point, from postoperative 1 week to 1 year, showed a negative coefficient value (all $P < 0.001$). Note though that the change of IOP at postoperative 1 year had a less steeply decreasing slope (correlation coefficient, $-0.993$) than those at postoperative 1 week and 1 month (correlation coefficients, $-1.893$ and $-1.540$, respectively).

The present study also investigated, for the total patient group, the distribution of IOP change between the preoperative value and that of the final follow up, as plotted on a box-and-whisker graph (Fig. 2). The mean difference between the preoperative value and the final follow up was $-1.01 \pm 3.74$ mmHg (range, $-17.0$ to $10.0$ mmHg). Each IOP change showed a significant difference by Wilcoxon signed rank test ($P < 0.001$). Further, the number of antiglaucoma medications between the preoperative value and that of the final follow up also decreased, from $1.45 \pm 0.89$ to $1.27 \pm 0.82$ ($P = 0.025$) (Supplementary Table 1).

Univariate and multivariate analyses

Table 4 shows the data from univariate and multivariate analyses of the associations of baseline demographics and preoperative clinical features with postoperative IOP change at a fixed follow-up time. In the univariate analysis, age, preoperative IOP, preoperative spherical equivalent, and axial length showed significant associations with IOP change ($P < 0.001$, $< 0.001$, 0.027, and $< 0.001$, respectively) (Table 4). In the multivariate analysis employing
a backward-elimination method, only age and preoperative IOP showed significant associations with IOP change (all, \( P < 0.001 \)). Specifically, age was negatively correlated with IOP change (regression coefficient, \(-0.034\)), while preoperative IOP was positively correlated (regression coefficient, 0.419).

**DISCUSSION**

Many earlier studies on IOP change after cataract surgery in glaucoma patients have included angle-closure glaucoma.\(^4,10,15-17\) Meanwhile, the distribution of glaucoma in Korea is different from those in other countries, and the majority of glaucoma cases are composited with NTG.\(^18\) Therefore, in this study, we investigated how IOP changed in various ways after cataract surgery.

### Table 4. Univariate and multivariate analyses of baseline demographics, preoperative clinical features, and IOP at fixed follow-up time

| Variables                     | Univariate          | Multivariate       |
|-------------------------------|---------------------|--------------------|
|                               | Regression coefficient | Standard error | \( P \) value\(^a\) | Regression coefficient | Standard error | \( P \) value\(^a\) |
| Gender                        | 0.568               | 0.253             | 0.069               | \(-0.105\)            | 0.173          | 0.545               |
| Age, yr                       | \(-0.042\)          | 0.001             | \(< 0.001\)        | \(-0.034\)            | 0.008          | \(< 0.001\)        |
| Presence of underlying disease| \(-0.388\)          | 0.322             | 0.086               | 0.159                 | 0.240          | 0.506               |
| DM                            | 0.172               | 0.210             | 0.093               | 0.111                 | 0.227          | 0.470               |
| HTN                           | 0.469               | 0.199             | 0.250               | 0.047                 | 0.150          | 0.874               |
| Thyroid disease               | 0.388               | 0.322             | 0.293               | 0.222                 | 0.489          | 0.553               |
| Cerebrovascular accident      | \(-0.209\)          | 0.203             | 0.271               | 0.945                 | 0.159          | 0.506               |
| Preoperative IOP              | 0.421               | 0.045             | \(< 0.001\)        | 0.402                 | 0.175          | 0.322               |
| Preoperative spherical equivalent | 0.059             | 0.025             | \(< 0.001\)        | 0.033                 | 0.041          | 0.077               |
| Cataract density (LOCS III)   | 0.173               | 0.531             | \(< 0.001\)        | 0.312                 | 0.133          | 0.406               |
| Axial length                  | 0.105               | 0.047             | \(< 0.001\)        | \(-0.107\)            | 0.190          | 0.190               |
| Presence of glaucoma          | 0.112               | 0.227             | 0.340               | 0.020                 | 0.190          | 0.227               |
| Preoperative VF_MD, dB        | 0.005               | 0.648             | 0.922               | \(-0.007\)            | 0.458          | 0.897               |

The numbers in bold and italics denote that the association is statistically significant (\( P < 0.05 \)).

IOP = intraocular pressure, DM = diabetes mellitus, HTN = hypertension, LOCS III = lens opacities classification system III, VF = visual field, MD = mean deviation, PSD = pattern standard deviation.

\(^a\) Analysis using Generalized Estimating Equations method.
cataract surgery on open glaucoma and healthy subjects in Korea. For the total patient group, preoperatively the mean IOP was 14.48 ± 3.37 mmHg, which decreased to 13.49 ± 2.97 mmHg by postoperative 1 year, and the mean difference between the preoperative and final follow-up values was −1.01 ± 3.74 mmHg (Figs. 1 and 2). In detail, phacoemulsification showed a 1.03 ± 3.72 mmHg IOP reduction in the healthy subjects and a 1.08 ± 3.79 mmHg reduction in the glaucoma patients.

Previous studies have reported post-phacoemulsification IOP reductions from 1.1 mmHg to 3.5 mmHg in non-glaucomatous3,6,19-21 and 1.0 mmHg to 5.5 mmHg in glaucomatous eyes.5,7-9,15-17,20,22,23 Phacoemulsification in our study showed a similar pattern of IOP reduction, though the degree of reduction (1.03 mmHg and 1.08 mmHg in healthy subjects and glaucoma patients, respectively) was relatively lower than in previous studies.3,5,12,20

There are possible explanations for this. The single most-common significant factor associated with greater IOP drop after phacoemulsification is higher IOP before phacoemulsification.11-13,22,24 However, the preoperative IOP in the glaucoma group was 14.25 ± 3.35 mmHg, lower than that of the glaucoma groups in the relevant previous studies.5,12,13,24-27 Furthermore, in some of those studies,5,24,25,27 most of the enrolled glaucoma patients were high-tension glaucoma, whereas in the present study, NTG patients were a relatively high proportion (55 patients, 50.4%) of the total group, as is common in Korea,18 which fact is thought to have also contributed to the modest extent of IOP reduction achieved. Additionally, the present study excluded closed- and narrow-angle patients. Indeed, IOP reduction after cataract surgery is much higher in patients with closed-angle glaucoma than in those with OAG.10-13,22,24 Similarly, higher IOP reduction for narrow-angle patients was well demonstrated in Hayashi’s7 study on 74 eyes with ACG and 68 eyes with OAG. The ACG group’s preoperative IOP, 21.4 ± 3.9 mmHg, was reduced to 14.5 ± 2.6 mmHg, and the OAG group’s 20.7 ± 5.4 mmHg to 15.2 ± 3.8 mmHg, after 24 months of follow up. Certainly therefore, the initial exclusion of angle-closure patients in our study significantly blunted IOP-reducing effect of cataract surgery.

Among our present findings, IOP reduction was the highest at 1 week postoperatively, the degree of reduction gradually decreasing until 2 years postoperatively (Fig. 1). Accordingly, the postoperative IOP at 2 and 3 years showed no significant difference compared with the preoperative IOP (Table 3). In other words, the effect of IOP reduction regressed over time. This long-term regression phenomenon might be related to the mechanism of post-cataract-surgery IOP reduction. According to a study by Meyer et al.28, reduced trabecular outflow facility in otherwise healthy eyes can be improved by phacoemulsification. Therefore, it can be assumed that with the temporary improvement of outflow facility, the degree of IOP drop will also be lessened. However, the mechanism of IOP reduction after cataract surgery cannot be explained by a single mechanism. The present results for the healthy subjects and glaucoma patients in terms of postoperative IOP reduction strongly suggest another mechanism of IOP reduction. Our comparison of the postoperative IOP decrease in eyes with and without glaucoma at postoperative 1 year showed no statistically significant difference. If the decrease in IOP had been caused by an increase in trabecular outflow, a greater IOP reduction should have been shown in the healthy group, because the function of trabecular outflow is compromised in glaucomatous eyes. Therefore, in terms of outflow facility as it relates to IOP drop after cataract surgery, it could be assumed that the uveoscleral pathway plays a larger role than trabecular outflow in OAG. Similarly to our hypothesis, endogenous prostaglandin F2 released postoperatively is thought to enhance uveoscleral outflow.28,29 Another study has reported that expansion of the Schlemm’s canal was observed after cataract surgery.30
In the present multivariate analysis results, there was a significant association of IOP change with both preoperative IOP and age. In detail, higher preoperative IOP and younger age were associated with greater IOP reduction at a specific follow-up time point after phacoemulsification ($r = 0.419$ and $r = -0.034$, all $P < 0.001$) (Table 4). As is well known, higher preoperative IOP is a significant factor associated with greater reduction of IOP. On the other hand, prospective studies have reported that higher IOP before phacoemulsification is associated with a higher likelihood of IOP failure after phacoemulsification. In the present study, subjects with newly started or added glaucoma medications after cataract surgery had a higher preoperative IOP, $16.48 \pm 4.67$ mmHg, than did the total subjects ($14.48 \pm 3.37$ mmHg; $P < 0.001$; data not shown). Therefore, in patients with high preoperative IOP, cataract surgery can be beneficial in terms of IOP reduction, but the risk of surgery and IOP failure increase as well. Another notable finding of the present study is the correlation of younger age with a greater IOP lowering effect after surgery when controlling for time and other associated factors ($r = 0.034$). In general, we can expect that the lens of older people, due to its increased size, will have an effect on outflow and, thus, that it will affect IOP more than in younger people; therefore, greater IOP reduction is to be expected in older individuals. The exact mechanisms of this greater IOP decrease in younger patients remain unclear, but there are two possible causes. First, in contrast to previous studies, cases of angle-closure glaucoma, which occurs predominantly in old age, were intentionally excluded, which fact might have lowered the degree of IOP reduction after cataract surgery in older patients. Second, Meyer et al. reported that a reduced preoperative coefficient of aqueous outflow and biochemical or blood-aqueous barrier alterations with release of prostaglandins might improve outflow facility. Based on this study, the mechanism of higher IOP reduction in young age might be inferred to be the result of either improved postoperative outflow facility or prostaglandin-mediated inflammatory response. Further, related investigations are needed.

Overall, our results are consistent with findings in previous studies that indicate improved glaucoma control after phacoemulsification. In this respect, for a patient with cataract but mild, well-controlled glaucoma requiring few medications, phacoemulsification alone is a reliable option. However, depending on glaucoma severity, the treatment approach should be tailored to individual patients. This is especially so given the risk of complications associated with this surgery, most notably hypertensive spikes and visual-acuity loss resulting from the immediate and sharp postoperative IOP increase and fluctuations thereafter (as seen in this study, a preoperative IOP of 14.48 mmHg had increased to 17.17 mmHg by postoperative 1 day). In cases of moderate and severe glaucoma, therefore, surgeons should exercise a higher degree of attention. As noted earlier, the effect of post-phacoemulsification IOP reduction lessened over time, and postoperative IOP might regress to the baseline level. Therefore, long-term monitoring of IOP change is needed even though IOP reduction is achieved in the early phase of follow up.

There are some limitations to this study. First, the number of participants in the follow up fell significantly after 1 year. The initial total of 754 subjects had decreased to 278 at 2 years, and then again to 172 at 3 years. The minimum sample size required for regression analysis using the GEE method was calculated as 68 patients after setting the effect size at 0.15, the $\alpha$ error probability at 0.05, and the $1-\beta$ error probability at 0.8. Although the numbers of patients at postoperative 2 and 3 years satisfied the minimum sample size, there remained, due to this study’s retrospective design, a possibility of selection bias in favor of higher-IOP patients, and such bias might have played a role in the elevation of mean IOP after 2 years of follow up (Fig. 1). Second, our study enrolled only medically controlled glaucoma patients (IOP < 30
mmHg); participants who would likely be highly associated with IOP spikes and IOP failure after cataract surgery had been selectively excluded. This selection bias might have resulted in IOP-reduction overestimation.

In conclusion, phacoemulsification results in IOP reduction, which effect was lessened in healthy subjects and glaucoma patients over the course of a long-term follow up. In cases of higher preoperative IOP and young patients, phacoemulsification alone is a reliable option for IOP control. However, we also should consider the risk of early-phase IOP elevation and IOP failure. Above all, notwithstanding the fact that IOP reduction can be achieved after phacoemulsification in the early phase of follow up, long-term monitoring of IOP change is necessary, because the effect of IOP reduction cannot necessarily be maintained. We hope that our results will prove useful to physicians who are planning cataract management, especially for patients with glaucoma.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Postoperative changes of clinical characteristics in glaucoma group (n = 106)

Click here to view

Supplementary Table 2
Comparison of baseline demographics and clinical features between patients with 1 year vs. 3 years of follow up

Click here to view

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