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Prophylactic Effect of Oral Acetazolamide against Intraocular Pressure Elevation after Cataract Surgery in Eyes with Glaucoma

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Purpose: To confirm the prophylactic effect of oral acetazolamide against increased intraocular pressure (IOP) in the period immediately after cataract surgery in eyes with primary open-angle glaucoma (POAG) and to evaluate the appropriate administration time of oral acetazolamide to prevent IOP elevation.

Design: Randomized clinical study.

Participants: Ninety eyes of 90 patients with well-controlled POAG scheduled for phacoemulsification.

Methods: Eyes were assigned randomly to 1 of 3 groups: (1) oral acetazolamide (500 mg) administration 1 hour preoperatively, (2) oral acetazolamide (500 mg) administration 3 hours postoperatively, or (3) no acetazolamide administration. Intraocular pressure was measured using a rebound tonometer 1 hour preoperatively, at the conclusion of surgery (adjusted in the range between 15 and 25 mmHg), and 1, 3, 5, 7, and 24 hours postoperatively. The incidence of eyes with IOP elevation more than 100% above the preoperative IOP was compared.

Main Outcome Measures: Postoperative IOP and incidence of eyes with marked IOP elevation.

Results: Mean IOP 1 hour preoperatively and that at the conclusion of surgery did not differ significantly among groups. In all groups, mean IOP was significantly elevated from 3 to 7 hours postoperatively, and then decreased at 24 hours. At 1 and 3 hours postoperatively, mean IOP was significantly lower in the group receiving oral acetazolamide preoperatively than in the other 2 groups (postoperative administration or no administration; $P \leq 0.0031$). At 5, 7, and 24 hours postoperatively, the IOP was significantly lower in both the preoperative and postoperative administration groups than in the nonadministration group ($P \leq 0.0224$). Intraocular pressure elevation of more than 100% occurred in 1 eye (3.3%) in the preoperative administration group, 7 eyes (23.3%) in the postoperative administration group, and 8 eyes (26.6%) in the nonadministration group; the incidence was significantly lower in the preoperative administration group ($P = 0.0459$).

Conclusions: Eyes with POAG experienced short-term IOP elevation from 3 to 7 hours after phacoemulsification. Oral acetazolamide administration 1 hour preoperatively significantly reduced the IOP elevation from 1 to 24 hours, while administration 3 hours postoperatively reduced the IOP elevation at 5 hours or more after surgery. *Ophthalmology 2017;124:701-708 © 2017 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Intraocular pressure (IOP) markedly increases in a high percentage of patients with glaucoma in the immediate or early period after cataract surgery.[1–5] Short-term IOP elevation may occur within 7 hours after surgery, although in most studies, the IOP was not measured periodically.[3–7] Because marked IOP elevation may worsen glaucomatous optic nerve damage, surgeons should consider prophylaxis against a short-term IOP spike in eyes with glaucoma. According to a United Kingdom–wide consultant survey, 37.4% of ophthalmic surgeons routinely prescribe an antiglaucoma medication for eyes that are to undergo cataract surgery.[8]

Several studies have evaluated the prophylactic effects of many types of topical antiglaucoma medications, including prostaglandin $F_{2\alpha}$ analogs, topically active carbonic anhydrase inhibitor II, β-blockers, or topical α-adrenergic agonists, against immediate postoperative IOP increases, but the findings regarding their short-term effectiveness are conflicting.[4,6,9–13] In contrast, prophylactic administration of oral acetazolamide has a rapid and substantial effect against short-term IOP spikes.[14–18] Indeed, in a United Kingdom–wide consultant survey, 87% of responders who routinely prescribe prophylactic medications prefer oral acetazolamide administration to topical agents.[8] However, in most studies and in clinical situations, antiglaucoma medications, including oral acetazolamide, are used just before or after cataract surgery. Because the exact time course of short-term IOP elevation after cataract surgery remains controversial, the optimal time for administration of antiglaucoma medications to protect against postoperative IOP elevation is unclear.

The purpose of the present study was to examine the time course of short-term IOP elevation in eyes with glaucoma after cataract surgery, to assess the prophylactic effect of oral acetazolamide against IOP elevation, and to determine the optimal time for administering acetazolamide using a

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linear mixed model. Because the time course of the short-term IOP elevation may differ depending on the type of glaucoma, only patients with primary open-angle glaucoma (POAG) were recruited for this study.

Methods

Patients

This was a prospective, randomized clinical study. On September 9, 2014, a clinical research coordinator began screening all consecutive eyes with medically well-controlled POAG (IOP $\leq$21 mmHg at 2 continuous visits before surgery) that were scheduled for phacoemulsification with intraocular lens implantation at the Hayashi Eye Hospital. Exclusion criteria were eyes with any pathologic features other than cataract and POAG; eyes with pseudoexfoliation syndrome; eyes scheduled for planned extracapsular or intracapsular cataract extraction; eyes with a history of ocular surgery or inflammation; patients with contraindication for oral acetazolamide; patient declining to participate; and any anticipated difficulties with examination or follow-up. Eyes with an IOP higher than 21 mmHg at 2 prior continuous visits and included in another study also were excluded from the present study. Screening was continued until 90 patients were recruited, on May 10, 2016. This research adhered to the tenets of the Declaration of Helsinki. The Institutional Review Board/Ethics Committee of the Hayashi Eye Hospital, Fukuoka, Japan, where this study was conducted, approved the study protocol, and all patients provided written informed consent to participate. This study was registered in the University Hospital Medical Information Network (identifier, 000017556).

Randomization

All 90 enrolled patients were assigned randomly to 1 of 3 groups (n = 30/group) the day before surgery: (1) eyes that were to undergo oral acetazolamide administration 1 hour before surgery (preoperative administration group), (2) eyes that were to undergo oral acetazolamide administration 3 hours after surgery (postoperative administration group), or (3) eyes that were not to undergo administration (nonadministration group). The coordinator of this study generated a randomization code with equal numbers (1:1:1 ratio) using random number tables and assigned each patient to 1 of the 3 groups according to this code. The coordinator informed a nurse who was in charge of oral acetazolamide administration which group the patient had been assigned to. To ensure allocation concealment, the coordinator kept the assignment schedule concealed until all data were collected. The examiners, all nurses other than the nurse in charge, operating room staff, surgeon, and data analyst were unaware of the groups to which the patients had been assigned.

Oral Acetazolamide Administration

Any topical antiglaucoma hypotensive medication that was prescribed before surgery was stopped the day before surgery. The nurse in charge administered 500 mg oral acetazolamide (Diamox; Sanwa Kagaku Kenkyusho, Nagoya, Japan) to patients in the preoperative administration group 1 hour before surgery or the same dose of oral acetazolamide to patients in the postoperative administration group 3 hours after surgery. The immediate release formulation of oral acetazolamide was administered.

Surgical Techniques

One surgeon (M.Y.) performed all of the cataract surgeries. Each eye received a 2-ml injection of 2% Xylocaine (AstraZeneka, Osaka, Japan) into the sub-Tenon's capsule at the beginning of surgery. Clear corneal incision cataract surgery was performed using standardized techniques and instruments essentially as described previously.[19] After making 2 side ports with a knife, a continuous curvilinear capsulorrhexis was performed through a side port using a bent needle. A 2.2-mm single-plane clear corneal incision was made with a steel keratome from the posterior margin of the cornea. After thorough hydrodissection, phacoemulsification of the nucleus and aspiration of the residual cortex was conducted. The lens capsule was inflated with 1% sodium hyaluronate (Hyaguard; Nihon Tenganyaku Kenkyusyo, Nagoya, Japan) for implantation of a single-piece hydrophobic acrylic intraocular lens (SN60WF; Alcon Laboratories, Fort Worth, TX), after which the intraocular lens was placed into the capsular bag using a Monarch II injector with a C cartridge (Alcon). The viscoelastic material then was evacuated thoroughly. The clear corneal wound and side ports were hydrated using a balanced saline solution. At the conclusion of surgery, IOP was adjusted to range between 15 and 25 mmHg with stromal hydration using the method described previously.[20] In brief, an examiner trained to use a rebound tonometer (Icare; Tiolat, Helsinki, Finland) measured the IOP using the Icare rebound tonometer. When the IOP was not in the range between 15 and 25 mmHg, the IOP was increased to approximately 30 mmHg by injecting balanced saline solution into the anterior chamber and corneal stroma around the wound and side ports to close these incisions. After raising the IOP, it was reduced by draining the anterior chamber fluid through a side port using the cannula to obtain an IOP within the range of 15 to 25 mmHg.

Outcome Measures

All patients underwent IOP measurement and examinations of wound status and flare intensity in the immediate and early periods after cataract surgery. The IOP was measured using the Icare rebound tonometer 1 hour before surgery, at the conclusion of surgery, and 1, 3, 5, 7, and 24 hours after surgery. The details of this tonometer were described previously.[21] In brief, the Icare tonometer includes a solenoid magnetized probe and processing electronics. The probe moves toward the cornea at a speed of approximately 0.2 m/second. After the initial propulsion pulse is completed, the probe impacts the corneal surface, decelerates, and rebounds from the corneal surface. Signal processing electronics and microcontrollers register the probe's deceleration time upon corneal impact. The software is programmed for 6 measurements; the highest and lowest readings are discarded, and mean IOP is calculated from the remaining readings. The software can detect whether an incorrect measurement is obtained. In these cases, the tonometer shows an error message and does not accept the readings as correct. Additionally, the Icare tonometer considers the relationship among all measurements obtained by estimating the standard deviation to ensure a coherent final result. When the device detects the existence of any discrepancy among measurements, an error sign is displayed. In the present study, IOP was measured with the patients lying in the supine position. The same examiner performed all IOP measurements for each patient. To ensure reliability of the IOP readings, the measurements were repeated 3 times, and the mean value was used for analysis. When any type of error sign was displayed or in the event of a discrepancy between 1 IOP reading and the other 2 readings, the reading was excluded and another measurement was obtained. Many studies

have confirmed the reliability and reproducibility of data obtained using the Icare tonometer,[21–28] although Munkwitz et al[29] reported the conflicting results at a higher IOP range.

The wound architecture of the clear corneal incisions was examined approximately 5 hours after surgery using anterior segment (AS) optical coherence tomography (OCT; Tomey, Nagoya, Japan). The AS OCT scans across the AS of the eye, traversing the main incisions and side ports, and shows the incision in profile. In this study, 5 architectural wound features were used to describe the wound status according to the classification system reported by Calladine and Packard[30]: (1) wound gaping at the epithelial side, (2) wound gaping at the endothelial side, (3) misalignment of the roof and floor of the incision at the endothelial side, (4) local detachment of Descemet's membrane, and (5) loss of coaptation along the stromal tunnel. We defined wound opening as a loss of coaptation along the stromal tunnel. The incision length was measured using the AS OCT image. Flare intensity was measured 5 hours after surgery using a flare meter (FC-1000; Kowa, Tokyo, Japan). Two physicians (S.M., K.Y.) performed the Seidel test approximately 5 hours after surgery using slit-lamp microscopy.

The refractive spherical and cylindrical powers were examined using an autorefractometer (KR-7100; Topcon, Tokyo, Japan); the manifest spherical equivalent value was determined as the spherical power plus half the cylindrical power. Uncorrected and distance-corrected decimal visual acuity were recorded at all examination visits. Decimal visual acuity was converted to the logarithm of the minimum angle of resolution scale for statistical analyses. Nuclear opalescence of the lens was graded using the Lens Opacities Classification System III.[31] The duration of surgery and the total volume of irrigating solution used were recorded. Visual field sensitivity was measured with the 30-2 program of the Humphrey Visual Field Analyzer within 6 months before surgery. All examinations were performed by experienced ophthalmic technicians unaware of the purpose of the study.

Statistical Analysis

Data regarding the IOP were tested for normality of distribution using histograms. Because the IOP at some time points in the 3 groups did not follow a normal distribution, the IOP was converted to the logarithm scale for statistical analyses and was changed back to arithmetic scale for descriptions. Longitudinal changes in IOP in each of the 3 groups were examined by comparing the IOP between each interval pair using the paired *t* test. Because the IOP at the conclusion of surgery was adjusted intentionally to range between 15 and 25 mmHg, the IOP at the conclusion of surgery was excluded from the analysis.

Differences in the IOP 1, 3, 5, 7, and 24 hours after surgery among the 3 groups were compared using a linear mixed model with time points as a categorical variable and logarithm of the preoperative value as a covariate (SAS PROC MIXED with REPEATED statement and no RANDOM statement; SAS Institute Inc., Cary, NC). The IOP at the conclusion of surgery was not considered in this model because the IOP was adjusted intentionally with surgical techniques. To detect a change point after which the difference in the IOP among the groups changed, the linear mixed model included an interaction term between group and indicator variable that shows whether time beyond that point changed. Covariance structure of the linear mixed model was selected based on the Akaike information criterion index among the unstructured, compound symmetry, and autoregressive structures. The Akaike information criterion index also was used to detect the change point among 3, 5, 7, and 24 hours after surgery. Because the Akaike information criterion index selected 5 hours as the change point with an unstructured covariance structure, the linear mixed model in which intergroup difference altered 5 hours after surgery was adopted. Preoperative value-adjusted means of the IOP were calculated from this model.

The incidence of marked IOP elevation was compared among groups using the Kaplan-Meyer survival analysis with 2 criteria: (1) IOP elevation more than 100% more than preoperative IOP, and (2) IOP elevation 26 mmHg or higher. The survival curves for each pair of groups also were compared.

The flare intensity, logarithm of the minimum angle of resolution visual acuity, manifest spherical equivalent value, and other continuous variables were compared among the 3 groups using the Kruskal–Wallis test, and categorical variables were compared among the groups using the chi-square goodness-of-fit test. When a statistically significant difference was detected among groups, the difference between each group pair was compared using the Mann–Whitney *U* test for continuous variables and the chi-square or Fisher exact test for categorical variables. Any differences with a *P* value less than 0.05 were considered statistically significant.

Table 1. Comparison of Patient Characteristics at Baseline and Surgical Factors among the Eyes of Patients Taking Oral Acetazolamide 1 Hour before Surgery (Preoperative Administration Group), Eyes of Patients Taking Oral Acetazolamide 3 Hours after Surgery (Postoperative Administration Group), and Eyes of Patients Not Administered Oral Acetazolamide (Nonadministration Group)

	Preoperative Administration Group	Postoperative Administration Group	Nonadministration Group	*P* Value
Patient characteristics at baseline				
Age (yrs)	73.1±8.5	68.9±10.4	70.5±7.5	0.3213*
Gender (male/female)	12/18	12/18	20/10	0.0581*
Left eye/right eye	12/18	14/16	12/18	0.8334*
Corneal astigmatism (D)	0.76±0.5	0.92±0.78	10.02±0.73	0.3605*
MRSE (D)	−2.50±4.59	−4.08±5.20	−2.71±3.17	0.4597*
Corrected visual acuity (logMAR)	0.35±0.21	0.46±0.29	0.45±0.29	0.2817*
Surgical factors				
Nuclear opalescence	2.17±0.42	2.13±0.54	2.13±0.29	0.8676*
Surgery duration (min)	6.40±1.50	7.27±2.86	6.47±1.48	0.4397*
Infusion volume (ml)	49.0±8.5	63.3±33.3	54.3±18.6	0.2263*

D = diopter; MRSE = manifest spherical equivalent value; logMAR = logarithm of minimum angle of resolution.
*No statistically significant difference among groups.

Table 2. Comparison of the Number (Percentage) and Type of Topical Antiglaucoma Medications Prescribed before Surgery among the Eyes of Patients Taking Oral Acetazolamide 1 Hour before Surgery (Preoperative Administration Group), Eyes of Patients Taking Oral Acetazolamide 3 Hours after Surgery (Postoperative Administration Group), and Eyes of Patients Not Administered Oral Acetazolamide (Nonadministration Group)

	Preoperative Administration Group	Postoperative Administration Group	Nonadministration Group	P Value
Prostaglandin $F_{2\alpha}$ analogs	20 (66.7)	18 (60.0)	20 (66.7)	0.8237*
β-blockers	11 (36.7)	7 (23.3)	9 (30.0)	0.5300*
Carbonic anhydrase inhibitor	4 (13.3)	8 (26.7)	4 (13.3)	0.2963*
Topical brimonidine	0 (0.0)	1 (3.3)	2 (6.7)	0.3554*
Others	1 (3.3)	1 (3.3)	0 (0.0)	0.5997*
Total no. of antiglaucoma medications	1.03±0.81	1.00±0.91	1.00±0.83	0.9315*

Data in Table 2 shows number of eyes (percentage).
*No statistically significant difference among groups.

Results

All recruited patients underwent intervention and completed the scheduled examinations. Because the nurse administered acetazolamide by the prescription of the physician (data analyst) according to the study protocol, the examiners, other nurses, surgeon, operating room staff, and data analyst were not aware of the group to which each patient had been assigned. Mean ± standard deviation age of the patients was 70.9±8.9 years (range, 44–87 years); there were 44 men. Patient demographics at baseline and surgical factors of the preoperative administration group, postoperative administration group, and nonadministration group are shown in Table 1. Age, gender, ratio of left to right eyes, corneal astigmatism, manifest spherical equivalent value, nuclear opalescence, duration of surgery, and total volume of irrigating solution used did not differ significantly among the groups. The number and type of topical antiglaucoma medications prescribed before surgery was not different significantly among groups (Table 2). In the last examination using the Humphrey Visual Field Analyzer 30-2 program within 6 months before surgery, the mean values of mean deviation and pattern standard deviation were −8.80±6.68 and 9.38±4.74, respectively, in the preoperative administration group, −8.62±8.64 and 6.51±4.85, respectively, in the postoperative administration group, and −7.38±5.40 and 7.40±5.00, respectively, in the nonadministration group; the mean mean deviation ($P = 0.6640$) and pattern standard deviation ($P = 0.2684$) did not differ significantly among groups.

Examination of the longitudinal changes in IOP in each group revealed that in the nonadministration group, after adjusting the IOP at the conclusion of surgery, mean IOP 1, 3, 5, 7, and 24 hours after surgery was significantly higher than the preoperative IOP ($P < 0.0002$), and the IOP 3, 5, and 7 hours after surgery was significantly higher than the IOP 1 and 24 hours after surgery ($P \leq 0.00375$), indicating that the short-term IOP elevation occurred during 3 and 5 hours after surgery (Table 3). In the preoperative administration group, the mean IOP 3, 5, and 7 hours after surgery was significantly higher than the preoperative IOP and the IOP 1 hour after surgery ($P \leq 0.0159$), and the IOP 5 and 7 hours after surgery was higher than the IOP 24 hours after surgery ($P \leq 0.0111$). In the postoperative administration group, the IOP 1, 3, 5, and 7 hours after surgery was significantly higher than the preoperative IOP and the IOP 24 hours after surgery ($P \leq 0.0033$), and the IOP 3 hours after surgery was significantly higher than the IOP 1, 5, and 7 hours after surgery ($P \leq 0.0487$).

Mean IOP did not differ significantly among the 3 groups before surgery and at the conclusion of surgery. When comparing the IOP at 1, 3, 5, 7, and 24 hours after surgery using a linear mixed model (Fig 1), the IOP 1 and 3 hours after surgery was significantly lower in the preoperative administration group than in the postoperative administration and nonadministration groups ($P \leq 0.0031$). The IOP 5, 7, and 24 hours after surgery was significantly lower in the preoperative administration and postoperative administration groups than in the nonadministration group ($P \leq 0.0224$).

Table 3. Longitudinal Changes of Arithmetic Mean (±95% Confidence Interval) Intraocular Pressure in Eyes of Patients Taking Oral Acetazolamide 1 Hour before Surgery (Preoperative Administration Group), Eyes of Patients Taking Oral Acetazolamide 3 Hours after Surgery (Postoperative Administration Group), and Eyes of Patients Not Administered Oral Acetazolamide (Nonadministration Group)

Group	Mean Intraocular Pressure	95% Confidence Interval
Preoperative administration group		
Before surgery	13.78	12.94–14.69
At the end of surgery	19.92*	19.06–20.82
1 hr after surgery	13.99	12.70–15.42
3 hrs after surgery	16.36*	14.74–18.17
5 hrs after surgery	17.01*	15.45–18.73
7 hrs after surgery	16.77*	14.88–18.91
24 hrs after surgery	14.60	13.05–16.33
Postoperative administration group		
Before surgery	13.44	12.36–14.62
At the end of surgery	19.84*	19.11–20.59
1 hr after surgery	16.59*	14.90–18.46
3 hrs after surgery	19.82*	17.93–21.90
5 hrs after surgery	18.33*	16.10–20.87
7 hrs after surgery	18.13*	15.93–20.64
24 hrs after surgery	14.04	13.11–15.05
Nonadministration group		
Before surgery	13.52	12.45–14.69
At the end of surgery	19.43*	18.43–20.49
1 hr after surgery	17.15*	15.28–19.25
3 hrs after surgery	21.10*	19.14–23.27
5 hrs after surgery	20.46*	18.52–22.61
7 hrs after surgery	20.46*	18.07–23.17
24 hrs after surgery	16.16*	14.27–18.31

*Statistically significant difference from the preoperative intraocular pressure.

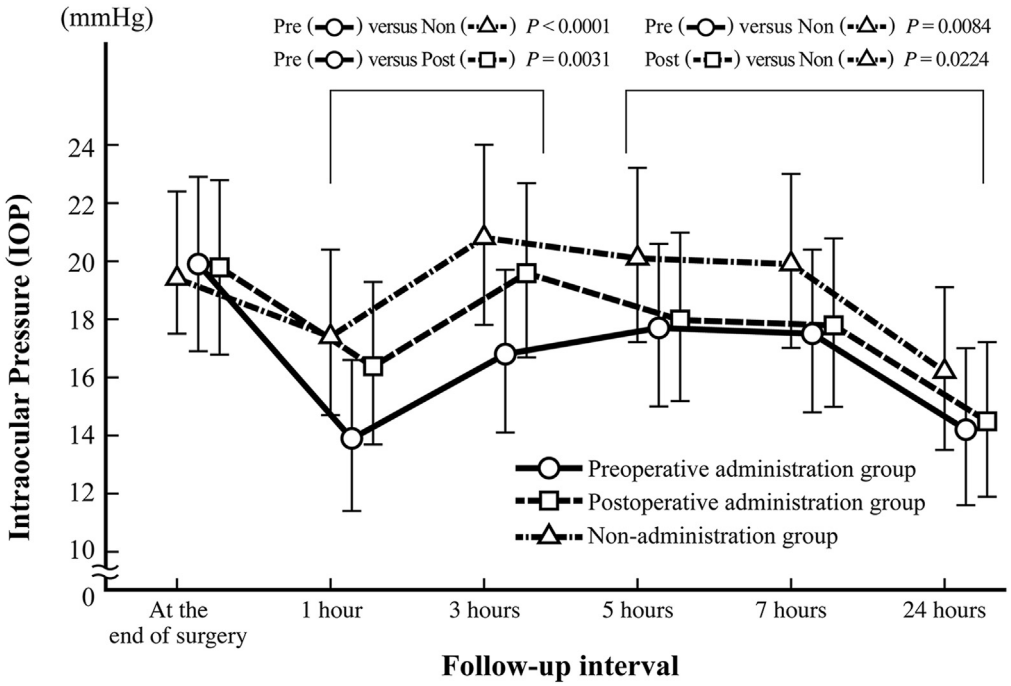

Figure 1. Graph comparing the exponential mean (±95% confidence interval) intraocular pressure (IOP) 1, 3, 5, 7, and 24 hours after surgery among eyes of patients taking oral acetazolamide 1 hour before surgery (preoperative administration group), eyes of patients taking oral acetazolamide 3 hours after surgery (postoperative administration group), and eyes of patients not administered oral acetazolamide (nonadministration group) using a linear mixed model. Mean IOP 1 and 3 hours after surgery was significantly lower in the preoperative administration group than in the postoperative administration and nonadministration groups, and the mean IOP 5, 7, and 24 hours after surgery was significantly lower in the preoperative administration group and postoperative administration group than in the nonadministration group.

A marked IOP elevation more than 100% more than the preoperative IOP occurred in 1 eye (3.3%) in the preoperative administration group, in 7 eyes (23.3%) in the postoperative administration group, and in 8 eyes (26.6%) in the nonadministration group; the incidence was significantly different among groups ($P = 0.0459$; Fig 2). The IOP elevation 26 mmHg or higher occurred in 5 eyes (16.7%) in the preoperative administration group, in 8 eyes (26.7%) in the postoperative administration group, and in 13 eyes (43.3%) in the nonadministration group; the incidence was significantly different among groups ($P = 0.0407$). With a criterion of an IOP elevation more than 100% more than the preoperative IOP, the incidence was significantly lower in the preoperative administration group than in the postoperative administration and nonadministration groups ($P = 0.0121$).

Mean flare intensity 5 hours after surgery was 39.23±21.03 mg/dl in the preoperative administration group, 29.19±21.11 mg/dl in the postoperative administration group, and 28.75±18.63 mg/dl in the nonadministration group; the means differed significantly among groups ($P = 0.0187$). Comparison of the flare intensity between each 2-group pair revealed that the flare intensity was significantly higher in the preoperative administration group than in the postoperative administration group ($P = 0.0135$) and nonadministration group ($P = 0.0163$), whereas there was no significant difference in the flare intensity between the postoperative administration and nonadministration groups.

The number of eyes with wound gaping at the epithelial side, wound gaping at the endothelial side, wound misalignment, or local detachment of Descemet's membrane was not significantly different among groups. Loss of coaptation along the stromal tunnel was not detected in any eye. The mean incision length did not differ significantly among groups ($P = 0.4567$). Seidel's test results were negative in all eyes. No complication resulting from the administration of oral acetazolamide occurred in this series.

Discussion

The findings of the present study demonstrated that a short-term IOP elevation in eyes with POAG occurred from 3 to 7 hours after cataract surgery when no antiglaucoma medication was administered. Mean IOP 1 and 3 hours after surgery was significantly lower in the eyes of the preoperative administration group than in eyes of the postoperative administration group and eyes of the nonadministration group. Furthermore, the IOP 5, 7, and 24 hours after surgery was significantly lower in eyes of the preoperative and postoperative administration groups than in the eyes of the nonadministration group. These findings indicate that the short-term IOP elevation was attenuated throughout the follow-up period (from 1 to 24 hours after surgery) by oral acetazolamide administered 1 hour before surgery, and the IOP elevation from 5 to 24 hours was attenuated by oral acetazolamide administered 3 hours after surgery.

The incidence of a marked IOP rise differed significantly among the 3 groups with both criteria. Specifically, it was significantly lower in the preoperative administration group than in the postoperative administration group and nonadministration group with the criterion of an IOP elevation more than 100% more than the preoperative IOP. Thus, the

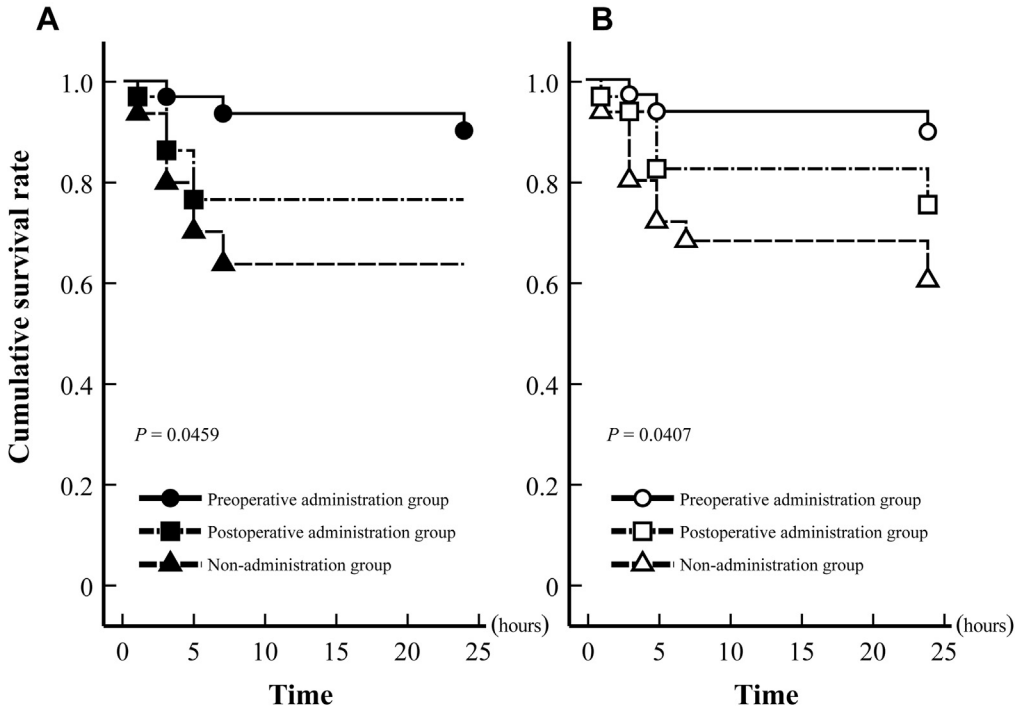

Figure 2. Graphs comparing the incidence of a marked intraocular pressure (IOP) increase among the eyes of patients taking oral acetazolamide 1 hour before surgery (preoperative administration group), eyes of patients taking oral acetazolamide 3 hours after surgery (postoperative administration group), and eyes of patients not administered oral acetazolamide (nonadministration group) based on Kaplan–Meyer survival analysis with 2 criteria: (**A**) IOP increase of more than 100% more than preoperative IOP, and (**B**) IOP increase 26 mmHg or higher. The incidence of a marked IOP increase differed significantly among the 3 groups with both criteria. When comparing between each pair of 2 groups, the incidence was significantly lower in the preoperative administration group than in the postoperative administration group and nonadministration group with the criterion of an IOP elevation more than 100% more than the preoperative IOP.

incidence of a marked IOP elevation in the immediate postoperative period could be reduced by the use of oral acetazolamide when administered 1 hour before surgery.

The flare intensity measured 5 hours after surgery was significantly higher in the preoperative administration group than in the postoperative administration group and non-administration group. Oshika and Araie[32] reported that oral acetazolamide significantly increases the aqueous protein concentration, which is determined as the flare intensity, for 2 to 10 hours after administration with a peak at 6 hours in healthy volunteers. The findings of the present study are consistent with those of their study. Thus, the drug effect of oral acetazolamide takes place rapidly, within several hours after administration, even in eyes with POAG.

The incidence of the 5 wound architectural features examined using AS OCT did not differ significantly among the 3 groups. Additionally, the wound length and width were similar among groups, and the Seidel test results were negative in all eyes. These findings indicate that wound status did not affect the differences in the IOP among groups.

The administration time of oral acetazolamide affected the difference in the IOP at various intervals. Administration of oral acetazolamide 1 hour before surgery led to a significant decrease in the IOP from 1 to 24 hours after phacoemulsification surgery in eyes with POAG, whereas administration 3 hours after surgery led to a significant decrease in the IOP from 5 to 24 hours after surgery. Oshika and Araie[32] reported that oral acetazolamide decreases IOP for 2 to 6 hours after administration with a peak at 4 hours in healthy subjects. Based on these findings, it is certain that oral acetazolamide decreases the IOP within several hours after administration. However, the reason for the long-lasting IOP-lowering effect 24 hours after surgery cannot be explained at this time. In any case, because the short-term IOP elevation occurred for 3 to 7 hours after surgery with a peak at 3 or 5 hours in eyes with POAG, oral acetazolamide is thought to be most effective for prophylaxis against the IOP elevation when administered 1 hour before surgery.

Intraocular pressure elevation occurs in the immediate or early periods after cataract surgery in eyes with glaucoma.[1–5] Previous studies examined the effectiveness of topical or systemic antiglaucoma medications as prophylaxis against short-term IOP elevation.[4,6,9–13] Although many topical medications, including prostaglandin $F_{2\alpha}$ analogs, topical carbonic anhydrase inhibitor, β-blockers, and topical α-adrenergic agonist, have been evaluated, the effect of the topical agents is still conflicting.[4,6,9–13] In contrast, studies revealed a substantial effect of systemic acetazolamide for prophylaxis against the short-term IOP spike.[14–18] Specifically, several studies demonstrated that the IOP-lowering effect of oral acetazolamide is more prominent than that of topical dorzolamide in eyes with or

without glaucoma.[16,17] In these studies, however, antiglaucoma medications were prescribed just before and after surgery. The present study demonstrates that oral acetazolamide is more effective for prophylaxis against short-term IOP elevation when administered 1 hour before surgery than when administered 3 hours after surgery.

This study has several limitations. First, we did not measure the IOP between 7 and 24 hours after surgery. It is possible that IOP continues to increase during this interval. Mean IOP, however, decreased between 7 and 24 hours in all 3 groups. Accordingly, it is unlikely that an IOP elevation sufficient to worsen glaucomatous optic neuropathy occurs again after 7 hours after surgery. Second, it is unclear whether prophylaxis against IOP elevation resulting from oral acetazolamide actually reduces optic nerve damage. However, we believe that it is safer to avoid the IOP spike, particularly in eyes with advanced-stage glaucoma.

In conclusion, short-term IOP elevation occurs in the immediate postsurgical period, with a peak 3 to 5 hours after phacoemulsification surgery in eyes with POAG. Administration of oral acetazolamide 1 hour before surgery decreased the degree of the short-term IOP elevation for 1 to 24 hours after surgery, whereas administration of oral acetazolamide 3 hours after surgery reduced the degree of the IOP elevation between 5 and 24 hours after surgery. Thus, administration of oral acetazolamide 1 hour before surgery is more effective than that at 3 hours after surgery for preventing the short-term IOP elevation in eyes with POAG. It remains unclear, however, whether this is true for eyes with pseudoexfoliation syndrome. Further studies are needed to examine the effect of antiglaucoma medication for prophylaxis against short-term IOP elevation in eyes with pseudoexfoliation.

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Abbreviations and Acronyms:
AS = anterior segment; **IOP** = intraocular pressure; **OCT** = optical coherence tomography; **POAG** = primary open-angle glaucoma.

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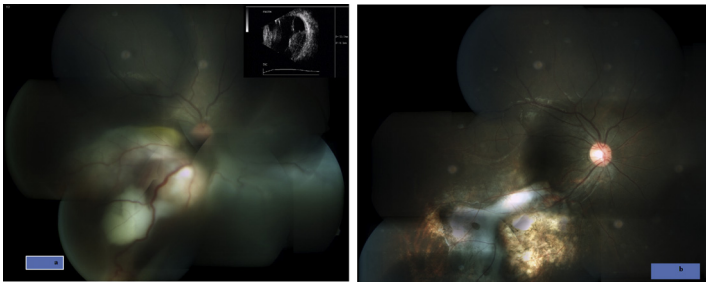
Pictures & Perspectives



Unusual Presentation of Choroidal Tuberculoma

A 19-year-old woman with decreased vision in the right eye for 2 months was referred for retinoblastoma. Best corrected visual acuity (BCVA) was 1.9 logMAR. A nodular subretinal lesion with exudative retinal detachment was noted (Fig 1**A**). Tuberculosis was suspected. Mantoux was 12×12 mm and Quantiferon was positive. Chest computed tomography showed hydro-pyo-pneumothorax with pleural thickening, a partially collapsed left lower lobe, and nodular consolidation with cavitation. Pleural fluid was positive for acid fast bacilli. Head magnetic resonance imaging showed left parietal tuberculoma. Inset: Ultrasonography showing mass lesion with high surface and low internal reflectivity, no calcification. Nine months after systemic therapy, the fundus showed healed tuberculoma with scarring (Fig 1**B**). BCVA was 0.5 LogMAR.

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