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Original

Pre- and Postoperative Ocular Events in Cataract Patients with Small Pupils who Underwent Cataract Surgery

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SUMMARY

Purpose：To analyze pre- and postoperative surgical events in cataract patients with small pupils who underwent cataract surgery.

Patients and methods：We reviewed the medical records of patients who underwent cataract surgery between January 2009 and May 2014 at Dokkyo Medical University Koshigaya Hospital. Surgery was performed by four experienced surgeons. We included 106 eyes from 83 patients with pupil sizes <5 mm in diameter who required iris retractors during the cataract surgery (small pupil group). The control group was comprised of 447 eyes from 319 patients with pupil sizes >5 mm in diameter who did not require a mechanical dilatation of the pupil during cataract surgery. Pre- and postoperative intra- or extraocular surgical events were analyzed.

Results：Preoperative intra- or extraocular surgical events were observed in 36 eyes (34.0%) in the small pupil group and 72 eyes (16.1%) in the control group, with a significant difference observed for those who underwent laser iridotomy ($P<0.001$) and trabeclectomy ($P<0.01$). Postoperative intra- or extraocular events were observed in 25 eyes (23.6%) in the small pupil group and 61 eyes (13.7%) in the control group, with significant differences observed for those who underwent the following procedures：trabeculectomy ($P<0.001$), sub-Tenon's injection of triamcinolone acetonide ($P<0.001$), and posterior capsulotomy ($P=0.012$).

Conclusion：Cataract patients with small pupils often have pre- and postoperative intra- or extraocular surgical events. It should be recognized that cataract surgery is only one step in the treatment of cataract patients with small pupils.

Keywords：cataract, lens, small pupil, visual acuity

INTRODUCTION

The advancement in cataract surgery has paved the way for improved surgical results. In addition, adaptation of surgery has increased, and several difficult cases have undergone cataract surgery；such cases include patients with small pupils. Phacoemulsification in patients with cataract with small pupils is often accompanied by risk factors, such as a small

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surgical field, dense cataracts with a thick lens[1], a shallow anterior chamber[1], and post-glaucoma surgery. Furthermore, these risk factors sometimes cause serious intraoperative complications such as ciliary zonule[2], posterior capsule rupture[2], corneal endothelial damage[1,2], and iris damage. These intraoperative complications may cause serious postoperative inflammation ; therefore, cataract surgery in patients with small pupils is a challenge to the surgeons.

There are various causes for small pupils, with the most common causes being pseudoexfoliation (PE) syndrome[2~6], eye trauma, previous eye surgery[2,6], uveitis[2,6], diabetes[2,5,6], and glaucoma medication (pilocarpine eye drops)[5]. Recently, the incidence of intraoperative floppy iris syndrome associated with tamsulosin (a systemic $\alpha 1$ adrenergic receptor antagonist) has increased because of small pupil cataract surgery[5,7,~9]. Furthermore, because of the increased use of tamsulosin in the elderly male population[5], more attention should be paid to the patients' medical history.

Although there are several reports regarding cataract surgery for small pupils[5,10~12], to the best of our knowledge, there are no reports regarding about associated pre-and postoperative surgical events. The frequency of cataract surgery for small pupils, defined as cases in which the mydriasis diameter is <5 mm, is approximately 1.4% of all cataract surgeries[12]. In the current report, we compared the pre- and postoperative intra- or extraocular surgical events between two groups of patients : those with pupil sizes of <5 mm in diameter who required iris retractors during cataract surgery (small pupil group) and those with pupil sizes of >5 mm in diameter who required no mechanical dilatation of the pupil during cataract surgery (control group).

MATERIAL AND METHODS

We reviewed the medical records of 83 patients (106 eyes) who underwent cataract surgery for small pupils between January 2009 and May 2014 (small pupil group). A small pupil was defined as a pupil with a completely dilated diameter <5.0 mm, and a disposable iris retractor (Alcon Grieshaber AG, Schasshausen, Switzerland), was used in all cases to maintain access to the surgical area. For the control group, we reviewed the records of 309 patients (447 eyes) with normal pupil sizes who underwent cataract surgery during the same time period. Normal pupil size was defined as a completely dilated pupil diameter $>$ 5.0 mm ; iris retractors were not used in any of these cases. All eyes received one of six types of foldable intraocular lenses (IOLs) : Acrysof SN 60WF or SN6CWS, Alcon Laboratories, Fort Worth, TX, USA ; Avansee PN6A, KOWA Pharmaceuticals, Montgomery, AL, USA ; AF-1 YA-65BB or Imics NY-60, HOYA Surgical Optics, Chino Hills, CA, USA ; Eternity Natural Uni W-60, Santen Pharmaceutical, Osaka, Japan). All subjects included in this study were followed up for a minimum of 6 months. This research adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of Dokkyo Medical University Koshigaya Hospital.

All cataract surgeries were performed by four experienced surgeons at Dokkyo Medical University Koshigaya Hospital. With the patient under local anesthesia, phacoemulsification was performed through a 2.2- to 2.4- mm superior or horizontal scleral incision, followed by insertion of one of the above-mentioned IOLs. The soft-shell technique was employed with the use of a dispersive [sodium hyaluronate 3.0% –chondroitin sulfate 4.0% (Viscoat)] and a cohesive [sodium hyaluronate 1.0% (PROVISC)] ophthalmic viscosurgical device (OVD). Through the side ports created with a 15° blade, approximately 0.1 mL of dispersive OVD was injected into the anterior chamber and 0.1 to 0.2 mL of cohesive OVD was injected below the dispersive OVD, so as to form a layer of the dispersive OVD beneath the corneal endothelium. In the small pupil group, four or five additional stab incisions were made with a 15° blade at the marked sites for the iris retractor. The iris retractor was inserted into the anterior chamber, and the needle holder was then turned so that the retractor could hook onto the edge of the iris and pull it toward the entry site. A continuous curvilinear capsulorhexis (CCC) measuring approximately 5.0 mm in diameter was created with a 25- or 27-gauge bent needle. In cases with poor visibility, as judged by the difficulty of CCC, the anterior capsule was stained with 0.1% trypan blue solution. After thorough hydrodissection and hydrodelineation, phacoemulsification of the nucleus and aspiration of the residual cortex were performed. The lens capsule was inflated with the cohesive OVD, and an IOL was placed in the capsular bag. After implantation of the IOL, all OVDs were thoroughly removed.

All eyes underwent preoperative examinations and were followed up for more than 6 months postoperatively. Corneal endothelial cell density (CECD) (cells/mm^2) was measured with a noncontact specular microscope (SP-9000 ; Konan Medical, Irvine, CA, USA). The video image in which the endothelial cell borders could be most clearly observed was transmitted to the image analysis computer, and the CECD was determined automatically. If the data were suspicious, then the CECD was determined by manual counting. The corrected distance visual acuity (CDVA) was preoperatively assessed on decimal charts and was defined as the best corrected visual acuity (VA) measurement at a minimum of 6 months postoperatively. The decimal VA data were converted into a logarithm of the minimum angle of resolution (logMAR). The ability of the patient to count fingers and distinguish hand motions and light and no light perceptions were converted into logMAR scores of 2.3, 2.6, 3.0, and 3.6, respectively[13]. The objective refractive status was measured with an autorefractometer (KR-7100 ; Topcon Corp., Tokyo, Japan). The manifest spherical equivalent (SE) value was determined as the spherical power plus half the cylindrical power.

The Emery–Little classification system was adopted to measure lens hardness[14]. During the cataract surgery, the surgical time (minutes), US time (seconds), and mean ultrasound power (percentage) were recorded. The cataract surgery machine used was Infinity™ (Alcon Laboratories).

STATISTICAL ANALYSIS

Differences between the small-pupil group and the control group in mean age, mean manifest SE value, preoperative and postoperative logMAR CDVA, preoperative and postoperative CECD, mean lens hardness, mean anterior chamber depth (ACD), mean surgical time, mean ultrasound time, mean ultrasound power, and time required for postoperative VA and CECD measurements were compared by unpaired t-tests. Discrete variables were compared between the two groups by the chi-square test or Fisher's exact probability test. These variables included sex ; the ratio of left eyes to right eyes ; combination of cataract with pseudoexfoliation (PE) syndrome, uveitis, or diabetes ; use of pilocarpine hydrochloride ; leg amputation for diabetes ; hemodialysis for diabetes ; use of trypan blue ; CCC ; rupture of the posterior capsule or zonule of Zinn ; and any previous or following intra- or extraocular surgeries. Pearson's coefficient of correlation was calculated to determine the factors associated with pupil diameter. Multiple linear regressions were used with stepwise selection of variables with significance in the linear regression analysis. P values <0.05 were considered to indicate statistical significance.

RESULTS

Table 1 shows the patients' preoperative factors, intraoperative factors, and postoperative factors in the small pupil and control groups. There were no statistically significance between-group differences in age ($P=0.81$), sex ratio ($P=0.43$), the ratio of left eyes to right eyes ($P=0.47$), manifest SE value ($P=0.57$), combination with diabetes ($P=0.73$), TB ($P=0.56$), CCC ($P=0.23$), rupture of the zonule of Zinn ($P=0.12$), ultrasound power ($P=0.08$) or the time required for postoperative VA and CECD measurements ($P=0.92$). The pre-logMAR CDVA was higher in the small pupil group than in the control group ($P<0.001$). The pre-CECD was lower in the small pupil group than in the control group ($P=0.012$), and the lens was harder in the small pupil group than in the control group ($P<0.001$). The ACD was shallower in the small pupil group than in the control group ($P<0.001$). Combination with PE syndrome ($P<0.001$) or uveitis ($P<0.001$), and the use of pilocarpine hydrochloride ($P<0.001$), leg amputation for diabetes ($P<0.001$), hemodialysis for diabetes ($P=0.011$), and rupture of the posterior capsule ($P<0.01$) were more common in the small pupil group than in the control group. The pupil diameter ($P<0.001$) was smaller in the small pupil group than in the control group. Surgery time ($P<0.001$) and ultrasound time ($P=0.015$) were greater in the small pupil group than in the control group. The post-logMAR CDVA ($P<0.01$), and CECD loss rate ($P<0.001$) were higher in the small

Table 1 Preoperative, intraoperative, and postoperative factors in the small pupil and control groups

Factor	Small pupil group	Control group	P value
Mean age (y)	72.6 ± 10.8	72.4 ± 9.7	0.81*
Male/female sex (n)	34/49	112/197	0.43 †
Left/right eye (n)	48/58	220/227	0.47 †
Mean SE (D)	−1.62 ± 3.73	−1.81 ± 4.26	0.57*
Pre-logMAR CDVA	0.82 ± 0.81	0.45 ± 0.55	<0.001*
Pre-CECD (cells/mm^2)	2567 ± 245	2642 ± 231	0.012*
Mean lens hardness	2.65 ± 0.83	2.28 ± 0.71	<0.001*
Mean ACD (mm)	2.77 ± 0.45	2.99 ± 0.43	<0.001*
# PE syndrome (Y/N)	26/80	2/445	<0.001 †
# Uveitis (Y/N)	23/83	8/439	<0.001 †
# Pilocarpine hydrochloride (U/NU)	9/97	0/447	<0.001 †
# Diabetes (Y/N)	26/80	117/330	0.73 †
Leg amputation for diabetes (Y/N)	4/102	0/447	<0.001 †
Hemodialysis for diabetes (Y/N)	4/102	3/444	0.011 †
Pupil diameter (mm)	4.00 ± 0.93	7.55 ± 0.73	<0.001*
TB (U/NU)	55/51	218/229	0.56 †
CCC (C/IC)	104/2	444/3	0.23 †
Mean surgery time (min)	35.6 ± 12.8	19.1 ± 5.6	<0.001*
Mean US time (s)	132.8 ± 144.8	90.0 ± 64.6	0.015*
Mean US power (%)	18.5 ± 5.9	19.2 ± 6.0	0.08*
PC rupture (Y/N)	4/102	2/445	<0.01 †
Zinn zonule rupture (Y/N)	2/104	2/445	0.12 †
Post-logMAR CDVA	0.41 ± 0.70	0.15 ± 0.41	<0.01*
Post-CECD (cells/mm^2)	2334 ± 486	2575 ± 276	<0.001*
CECD loss rate (%)	9.1 ± 17.0	2.6 ± 9.4	<0.001*
Measurement time (months)	13.5 ± 11.9	13.8 ± 12.0	0.92*

Plus-minus values are means ± SD. SE : manifest spherical equivalent value, logMAR : logarithm of the minimum angle of resolution, Pre : preoperative, CDVA : corrected distance visual acuity, CECD : corneal endothelial cell density, ACD : anterior chamber depth, PE : pseudoexfoliation, Y : yes, N : no, U : used, NU : not used, TB : trypan blue, CCC : continues circular capsulorhexis, C : complete, IC : incomplete, US : ultrasound, IOL : intraocular lens, I : implanted, NI : not implanted, PC : posterior capsule, Post : postoperative.
*Unpaired *t*-test, † chi-square test, ‡ overlaps included.

pupil group than in the control group. The post-CECD was lower in the small pupil group than in the control group ($P<0.001$).

Table 2 shows the previous intra- or extraocular events in the two groups. The total number of ocular events was higher in the small pupil group than in the control group ($P<0.001$). In particular, laser iridotomy ($P<0.001$) and trabeclectomy ($P<0.01$) were performed more often in the small pupil group than in the control group. There were no statistically significance between-group differences in retinal photocoagulation ($P=0.51$), vitrectomy ($P=0.86$), or the other variables ($P=0.13$).

Table 3 shows the postoperative intra- and extraocular events. The total number of ocular events was higher in the small pupil group than in the control group ($P=0.011$). In particular, trabeculectomy ($P<0.001$), sub-Tenon's injection ($P<0.001$) and, posterior capsulotomy ($P=0.012$) were performed more often in the small pupil group than in the control group. There were no statistically significance between-group differences in intravitreal injection of anti- vascular endothelial growth factor ($P=0.20$), vitrectomy ($P=0.52$) or the other variables ($P=0.44$).

Table 4 shows the results of multivariate analysis of

Table 2 Previous intraocular and extraocular events by group

Event	Small pupil group	Control group	*P* value
Total surgeries	36/70	72/375	<0.001
*LI (Y/N)	17/89	5/442	<0.001
*Retinal PC (Y/N)	8/98	43/404	0.51
*Trabeculectomy (Y/N)	6/100	5/442	<0.01
*Vitrectomy (Y/N)	5/101	23/424	0.86
*Others (Y/N)	2/104	24/423	0.13

Y : yes, N : no.
LI = laser iridotomy ; PC = photocoagulation
* Overlaps included

Table 3 Following intraocular and extraocular events by group

Event	Small pupil group	Control group	*P* value
Total surgeries	25/81	61/386	0.011
*Trabeculectomy (Y/N)	7/99	4/443	<0.001
*Intravitreal injection of anti-VEGF antibody (Y/N)	8/98	20/423	0.20
*Sub-Tenon's injection of TA (Y/N)	6/100	2/445	<0.001
*Posterior capsulotomy (Y/N)	5/101	5/442	0.012
*Vitrectomy (Y/N)	2/104	5/442	0.52
*Others (Y/N)	7/99	40/407	0.44

Y : yes, N : no, VEGF : vascular endothelial growth factor, TA : triamcinolone acetonide.
*Overlaps included.

pupil diameter. We found that pupil diameter was closely related to uveitis (R = −0.456), PE syndrome (R = −0.354), laser iridotomy (R = −0.213), and ACD (R = 0.203) in a descending order of relationship strength.

Table 4 Multivariate analysis of factors related to pupil diameter

Ranking	Factor	Pearson's correlation coefficient
1	Uveitis	−0.456
2	PE syndrome	−0.354
3	LI	−0.213
4	ACD	0.203

PE : pseudoexfoliation, LI : laser iridotomy, ACD : anterior chamber depth.

DISCUSSION

In this study, both pre-and postoperative ocular events were observed more often in the small pupil group than in the control group. Laser iridotomy was more often performed in the small pupil group, and the rate of performance of this surgery was correlated with shallow ACD. Oka et al. reported that the center of the ACD was 1.94 ± 0.25 mm in narrow angle eyes and 2.72 ± 0.33 mm in open angle eyes as measured by a noncontact anterior segment analysis device (Pentacam ; Oculus, Wetzlar, Germany)[15]. Lee et al. reported that the center of the ACD was 1.55 ± 0.25 mm in glaucomatous attack eyes and 1.90 ± 0.24 mm in the unaffected eyes as analyzed by anterior segment optical coherence tomography[16]. Although these results cannot be compared simply because measuring devices differ, ACD has a strong correlation with narrow angle[15,17]. It is not surprising that a past history of laser iridotomy was often observed in the small pupil group. Furtheremore, trabeculectomy was often performed in the small pupil group.

Trabeculectomy, sub-Tenon's injection of triamcinolone acetonide, and capusulotomy were often observed as postoperative events in the small pupil group. These events seem to have a correlation with glaucoma, diabetic maculopathy, and cystoid macular edemas with uveitis are often observed in patients with cataract and small pupils. Furthermore, glaucoma indicates that PE syndrome and the use of pilocarpine eye drops are common in patients with cataract and small pupils. Hayashi et al. reported that 13 out of 40 eyes with PE syndrome and a maximum pupil size > 4 mm developed glaucoma[4)]. Yamamoto et al. reported that 35.2% of patients with PE syndrome developed glaucoma[18)], and Pohjanpelto reported that 35% of patients with PE syndrome underwent surgery for glaucoma over approximately 10 years of follow-up[19)]. This rate is almost double in the patients who have ocular hypertension without PE syndrome[19)]. There was no significant difference in the rate of diabetes between the two groups. However, leg amputation and hemodialysis for diabetes were more often observed in the small-pupil group. Small pupils are correlated with the systemic condition of diabetes. Iwase and Shimizu reported that the development of diabetic macular edema was strongly associated with small pupils[20)]. We did not assess whether good mydriasis and small pupils were associated with diabetes, and evaluation of these associations in future studies could provide useful information. Chae et al. reported that intravitreal injection of ranibizumab during cataract surgery may inhibit postoperative cystoid macular edema in patients with non-proliferative diabetic retinopathy[21)]. Postoperative cystoid macular edema is an important issue in uveitic cataract surgery, with a rate of 21.3% reported by Ram et al.[22)] and rates of 12% and 8% at 1- and 3-month follow-up, respectively, reported by Belair et al.[23)] Rahimi et al. reported that intravitreal injections of bevacizumab and triamcinolone acetonide were effective for the treatment of cystoid macular edema in uveitis[24)]. These cystoid macular edemas are not associated with cataract surgery. There are some reports of sub-Tenon's injection of triamcinolone acetonide for uveitis itself[26)]. In the present study, it is not surprising that sub-Tenon's injection of triamcinolone acetonide was often observed in the small pupil group.

According to multivariate analysis of pupil diameter, it was closely related to uveitis, PE syndrome, laser iridotomy, and ACD, in a descending order of relationship strength. Although diabetes causes small pupils[2,5,6)], our results did not show any correlation between these two variables.

Preoperative VA in the small pupil group was poor compared with that in the control group. PE syndrome sometimes results in the development of glaucoma, and uveitis may cause poor VA. Furthermore, the preoperative corneal endothelial density in the small pupil group was lower than that in the control group, and low preoperative corneal endothelial density may be associated with laser iridotomy. Although the rate of bullous keratopathy was very low, it can be caused by laser iridotomy[27)]. Moreover, PE material is produced and accumulates in corneal endothelial cells, resulting in a progressive change in the endothelium as a consequence of the PE syndrome process[28)]. Several clinical studies have reported decreased CECD in patients with PE syndrome[4,29)]. Although the mean lens hardness in the small pupil group was higher than that in the control group, we could not clearly discern the mechanism for this. Surgical time and ultrasound time were significantly greater in the small pupil group than in the control group. The time required to insert the iris retractor and lens hardness may have been the reasons for the above-mentioned differences. The rate of posterior capsule rupture has previously been shown to be high during phacoemulsification in small pupils[2)], in agreement with our results.

The postoperative visual prognosis was lower in the small pupil group than in the control group. This difference may be due to preoperative complications such as glaucoma and uveitis which may have caused this phenomenon. Both preoperative and postoperative CECD were lower in the small pupil group than in the control group. Hayashi et al. reported that corneal endothelial loss after cataract surgery in eyes with PE syndrome was greater than that in eyes without PE syndrome[4)].

Our findings suggest that patients with cataract and small pupils often experience pre- and postoperative intra- or extraocular surgical events. It should be recognized that cataract surgery is only one step in the treatment of patients with cataract and small pupils, and complications of glaucoma and uveitis should be considered. Temporal corneal incisions may sometimes be required in cataract surgery on patients with small pupils, because trabeculectomy may be required after surgery. In case of small pupils, we have to select a less invasive surgical method because some cases need a second surgery. In addition, cataract surgery in patients with small pupils is closely associated with pre- and postoperative VA, pre- and postoperative CECD, lens hardness, ACD, surgical time, and ultrasound time. All of these features should be considered when performing surgery.

Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

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