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The Effect of a Blue Light Filtering Intraocular Lens on Macular Edema

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Abstract: This study sought to compare the effects of either a blue light-filtering intraocular lens (blue-filtering IOL) or an ultraviolet light-filtering intraocular lens (UV-filtering IOL) on the incidence of angiographic macular edema (ME) 3 and 12 months after implantation. A prospective randomized parallel clinical study was performed at Showa University Hospital. Forty-five cataract patients randomly received either a blue-filtering IOL (n = 21) or a UV-filtering IOL (n = 24), and macular leakage was evaluated by fluorescence angiography. At 3 months, ME was 24% in the blue- and 25% in the UV-filtering IOL group. At 12 months, ME was 5% in the blue- and 21% in the UV-filtering IOL group. The recovery rate in the blue-filtering IOL group was higher than in the UV-filtering IOL group at 12 months after surgery (P = 0.0457). These results suggested that an implanted blue-filtering IOL is more effective for recovery of ME than a UV-filtering IOL.

Key words: intraocular lens (IOL), cataract, blue light, ultraviolet, macular edema

Introduction

Cystoid macular edema (CME) was reported as Irvine-Gass syndrome in 1969[1)]. Implanting an ultraviolet (UV)-filtering intraocular lens (UV-filtering IOL) instead of the previously used UV-transmitting IOL reduced the incidence of CME after cataract surgery[2)]; however, this solution is not completely effective and the problem of CME remains[3-5)]. Even after small-incision cataract surgery, the incidence of angiographic macular edema (ME) with no visual impairment was recently reported at 10–30% of patients[6)].

In 1994, a blue light and ultraviolet cut-off filtering intraocular lens (blue-filtering IOL) was developed to prevent cyanopsia after cataract surgery[8)]. Basic studies of retinal pigment epithelial cells[9)] and animal experiments[10, 11)] demonstrated that such IOLs had a protective effect on the retina. A blue-filtering IOL might therefore also decrease the incidence of CME compared with the UV-filtering IOL, and this hypothesis was supported by a retrospective clinical study by Miyake *et al*[7)] showing prevention of CME using the

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blue-filtering IOL. Herein, we report a prospective clinical study comparing the effects of a blue-filtering IOL versus a UV-filtering IOL on ME incidence 3 and 12 months after implantation.

Patients and Methods

Patients were recruited at the Showa University Hospital (Tokyo, Japan) from February 2003 to March 2004. Fifty patients were enrolled in the study. The patients had age-related cataracts and were all eligible for IOL implantation. Informed consent was obtained from all patients and the study was approved by the Showa University Institutional Review board.

Enrolled patients ranged in age from 50 to 80 years and the range of axial length was 24 ± 2 mm. Patients were excluded if they had undergone an intraocular operation or had hypertensive retinopathy, diabetic retinopathy, age-related macular degeneration, or no observable fundus. Any patients receiving treatment for systemic disease with macular lesion were also excluded. Patients were randomly assigned to receive a blue-filtering IOL (ENV-13, Menicon Co. Ltd., Nagoya, Japan) or a UV-filtering IOL (ES-13, Menicon). Both lens types were assigned code numbers by a person who did not take part in this study.

The two different IOL are made of poly (methyl methacrylate), and both have a diameter of 5.5 mm, a sharp edge, and a loop angle of 10 degrees (wing type). The blue-filtering IOL contains UV absorber of the benzotriazol type and azo dyes, and the UV-filtering IOL contains UV absorber of the benzotriazol type. The transmittance of the blue-filtering IOL in water is 64% at 430 nm, 76% at 450 nm, 87% at 480 nm, and 93% at 520 nm, while the transmittance of the UV-filtering IOL is 94% at 430 nm and 99% at wavelengths longer than 450 nm.

The cataract surgeries were carried out by two surgeons. During the operation, the patient's eyes were protected from the surgical microscope illumination light by blue and UV filters. Two hours before surgery, the patients received 5% phenylephrine (Santen Pharmaceutical Co. Ltd., Osaka, Japan), 0.5% tropicamide (Santen Pharmaceutical), and 0.1% sodium diclofenac (Wakamoto Pharmaceutical Co. Ltd., Tokyo, Japan) by topical instillation every 30 minutes. Just prior to surgery, subtenon anesthesia was given using 1 ml of 2% lidocaine. The cataract was removed by phacoemulsification and aspiration, and then the blue-filtering and UV-filtering IOLs were fitted randomly. All patients received the following postoperative treatment: a subconjunctival injection of 0.8 mg betamethasone (Shionogi & Co. Ltd., Osaka, Japan) and antibiotics. Topical application of 0.1% betamethasone phosphate (Shionogi & Co.), 0.1% diclofenac sodium, and antibiotics were started on the first postoperative day and continued at four times a day for six weeks.

After cataract surgery, the patients were examined using a slit-lamp biomicroscope and funduscope. Measurements of intraocular pressure, Snellen visual acuity, and refraction were carried out at 1 week and 3, 6, and 12 months postoperatively. At 3 and 12 months after

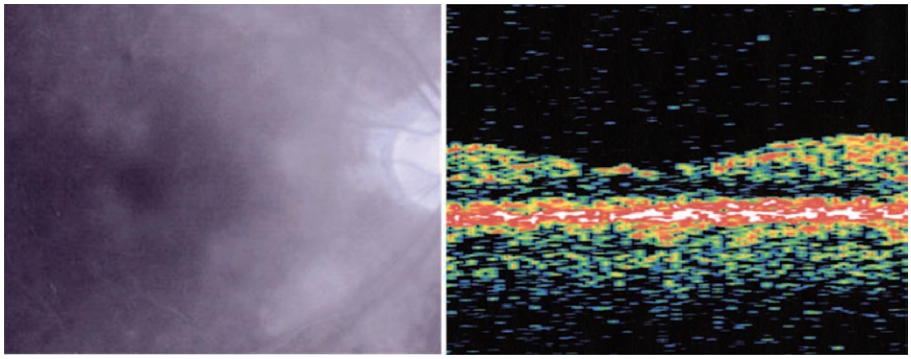

Fig. 1. Representative FA and OCT imaging of eyes with macular leakage. FA : fluorescence angiography fundus photograph showing macular leakage, OCT : optical coherence tomography showing macula thickness.

the surgery, macular leakage was determined by fluorescence angiography (FA). Following intravenous injection of 5 ml of fluorescein-mono-glucuronide (Alcon, Fort Worth, TX, USA), FA photographs were taken 10 and 20 minutes after the injection using a fundus camera (VX-10, Kowa Co., Tokyo, Japan) and digitally adjusted on a monitor using processing software. Macular edema (ME) was assessed based on the incidence of macular leakage by ophthalmologists blinded to the type of IOL (Fig. 1).

Macula thickness was determined by optical coherence tomography (OCT, OCT3000, Carl Zeiss Meditec, Jena, Germany) and the value was corrected based on axial length and refraction. Statistical analysis was performed using the Mann-Whitney U-test, and the Mantel-Haenszel chi square test was used to compare the recovery rates between the blue-filtering and UV-filtering IOL groups.

Results

A total of 50 patients were evaluated in this study. Twenty-four eyes received a blue-filtering IOL and 26 eyes received a UV-filtering IOL. Five subjects (3 in the blue- and 2 in the UV-filtering IOL group) withdrew from the study between 3 and 12 months after implantation for personal reasons. The number of eyes evaluated to completion of the study was 45. All patients were Japanese and the mean age was 71.4 years (range 56 to 80 years). There was no significant difference between the groups with regard to patient age : 71.4 ± 6.8 years old in the blue- and 71.5±6.7 years old in the UV-filtering IOL group ; gender (male/female) : 6/15 in the blue- and 5/19 in the UV-filtering IOL group ; axial length : 23.8 ± 0.7 mm in the blue- and 23.6±0.8 mm in the UV-filtering IOL group.

The cataract surgery was uneventful in all cases and the surgical time was less than 20 minutes : 16.5 ± 2.4 minutes in the blue- and 15.8±3.4 minutes in the UV-filtering IOL group (Table 1). In all cases, the posterior capsules were left without rupture. No intra-

Table 1. Baseline Data

	Blue-filtering IOL n = 21	UV-filtering IOL n = 24	P value
Age (years)	71.4 ± 6.8	71.5 ± 6.7	0.95
Gender (male/female)	6/15	5/19	0.56
Axial length (mm)	23.8 ± 0.7	23.6 ± 0.8	0.38
IOL power (D)	22.4 ± 2.2	22.3 ± 2.0	0.83
Surgical time (minutes)	16.5 ± 2.4	15.8 ± 3.4	0.41

Data represent mean ± SD. P values are Blue- vs UV-filtering IOL.

Table 2. Distribution of visual acuity at 3 and 12 months after IOL implantation

Post implantation	visual acuity	Blue-filtering IOL	UV-filtering IOL
3 months		n = 21	n = 24
	14/20	4	1
	16/20	5	3
	18/20	3	3
	20/20	3	8
	24/20	6	9
12 months		n = 21	n = 24
	16/20	3	2
	18/20	4	3
	20/20	7	6
	24/20	6	13
	30/20	1	0

operative complications occurred in the current series. The implanted IOL refractions were 22.4 ± 2.2 D in the blue-filtering IOL group and 22.3±2.0 D in the UV-filtering IOL group.

Postoperative inflammation in the anterior segment was observed in patients without intraoperative complications or signs of infections, but examination of the fundus using a slit lamp and a funduscope revealed no abnormal findings in any patients, including macular lesions. The inflammation was successfully treated within a week by topical administration of 0.1% betamethasone phosphate, 0.1% diclofenac sodium, and antibiotics. During the study period, no patients developed after-cataracts and therefore did not require follow-up Nd-YAG laser treatment. Visual acuity in all the patients was above 14/20 and no significant differences were observed at 3 and 12 months after IOL implantation between the groups (Table 2).

In the blue-filtering IOL group, FA results 3 months after IOL implantation were as follows: without ME in 16 eyes, with ME in 5 eyes. At 12 months after implantation, only

Table 3. Angiographic macular edema assessment at 3 and 12 months after blue- or UV-filtering IOL implantation

Post implantation	Distribution of Angiographic ME	Blue-filtering IOL	UV-filtering IOL
3 months		n = 21	n = 24
	without	16	18
	with	5	6
Incidence of macular leakage (%)		5/21 (24%)	6/24 (25%)
12 months		n = 21	n = 24
	without	20	19
	with	1	5
Incidence of macular leakage (%)		1/21 (5%)	5/24 (21%)

At 12 months, the recovery rate in the blue-filtering IOL group was significantly higher than that in the UV-filtering IOL group ($P = 0.046$).

Table 4. OCT at 3 and 12 months after IOL implantation

Post implantation	Blue-filtering IOL (μm) n = 21	UV-filtering IOL (μm) n = 24	P values
3 months	175 ± 40	174 ± 29	0.45
12 months	166 ± 38	172 ± 24	0.26

Data represent mean ± SD. P values are Blue- vs UV-filtering IOL.

one eye still showed ME, while all others had improved. In all cases, leakage was from perifoveal microvascular structures, and it was not caused by a window defect. No CME was observed in any of the patients who received a blue-filtering IOL. The incidence of macular leakage decreased from 24% (5/21) at 3 months to 5% (1/21) at 12 months in the blue-filtering IOL group. In the UV-filtering IOL group, FA results 3 months after IOL implantation showed 18 eyes without ME, and 6 eyes with ME. At 12 months, 19 eyes were without ME, while edema remained in 5 eyes. After UV-filtering IOL implantation, the incidence of macular leakage decreased only slightly from 25% (6/24) at 3 months to 21% (5/24) at 12 months. Thus, at 12 months after implantation, the recovery rate in the blue-filtering IOL group was significantly higher than that in the UV-filtering IOL group (Table 3, $P = 0.046$). OCT findings at 3 and 12 months after IOL implantation are listed in Table 4, and Fig.1 shows a representative OCT image showing macular leakage. The foveal thickness decreased from 175±40 μm (n = 21) at 3 months to 166±38 μm (n = 21) at 12 months after blue-filtering IOL implantation ($P = 0.43$).

Discussion

In this study, the incidence of ME was decreased by blue-filtering (visible light transmitting without blue light) IOL implantation, compared to UV-filtering (visible light transmit-

ting) IOL implantation 12 months after surgery, despite the same incidence of macular leakage at 3 months. We found that all patients who were free of ME at 3 months after surgery had not developed any leakage at 12 months. Thus, the recovery rate in the blue-filtering IOL group was higher than that in the UV-filtering IOL group.

It has been reported that the cause of CME is multifactorial including the release of bioactive substances such as prostaglandins, cytokines, and growth factors following cataract surgery[12-14]. We therefore proposed that the onset of CME after cataract surgery may relate to oxidative stress in the retina due to the following: 1) the retina absorbs short wavelength (UV and blue) light leading to a photochemical reaction that generates reactive oxygen species (ROS)[15], and resultant oxidative stress; 2) ROS activate transcription factors, such as nuclear factor kappa B[16] and mitogen-activated protein kinase (MAPK), and thereby increase cycloxygenase-2 activity; 3) these transcription factors then upregulate the cytokines, vascular endothelial growth factor (VEGF)[17] and interleukin-1 beta (IL-1 beta)[18], as well as prostaglandins in the retina; and then, 4) these biologically active compounds disrupt the tight junctions by inhibiting de novo synthesis of the required component proteins, leading to macular edema[19, 20] Gass *et al*[1] showed regression of edema in 50% of CME patients 6 months after cataract surgery and in 20% of patients between 1 and 3 years, with 30% of patients showing no improvement in 3 or more years. In the present study, the incidence of macular leakage was almost the same at 3 months in both groups, but the recovery rate in the UV-filtering IOL group was lower than that in the blue-filtering IOL at 12 months after implantation. The action spectrum of retinal phototoxicity increases logarithmically as the wavelength of irradiation decreases[21], thus exposure to short-wavelength (UV and blue) light induces severe oxidative stress in the retina. In the UV-filtering IOL group, the retina had therefore received blue light and oxidative stress, which could underlie the low recovery rate observed in the UV-filtering IOL group. Based on these results, a blue-filtering IOL may contribute to improving ME, but not to preventing onset. The energy of a surgical microscope and the duration of retinal illumination time could activate the ME onset, and future studies should investigate this effect.

This study evaluated the incidence of angiographic ME after cataract surgery as the endpoint of our comparison. In the retina, there are several chromophores[22, 23] that absorb blue light and generate ROS, which are immediately scavenged by antioxidants. However, the amount of antioxidants decreases with aging and inflammation[24], and thus ROS might easily attack the retinal cells during and following cataract surgery[25]. We recommend that a blue-filtering IOL implanted to prevent oxidative stress in the retina will be more effective in resolving ME after cataract surgery than a UV-filtering IOL.

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