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ORIGINAL ARTICLE

Changes in blood pressure and sleep duration in patients with blue light-blocking/yellow-tinted intraocular lens (CHUKYO study)

Kazuo Ichikawa on behalf of the CHUKYO study investigators

Blood pressure and sleep duration may be influenced by retinal light exposure. Cataracts may exert such an influence by decreasing the transparency of the crystalline lens. A large-scale clinical study was conducted to examine changes in blood pressure and sleep duration after intraocular lens (IOL) implantation during cataract surgery and to investigate how different types of IOL influence the degree of these effects. Using a questionnaire, we collected information, including blood pressure measurement and sleep duration, from 1367 patients (1367 eyes) before IOL implantation, 1 week after IOL implantation and 1 month after IOL implantation. Systolic and diastolic blood pressures were significantly decreased in the total patient group after implantation. The decrease in systolic blood pressure 1 month after implantation was significantly more in patients who received a yellow-tinted IOL than it was in those who received an ultraviolet (UV) light-filtering IOL. The post-implantation sleep duration, including naps, became shorter in patients who had slept too much and became longer in those who had slept too little before IOL implantation. Our observations suggest that a yellow-tinted IOL is better for patients with high blood pressure than a UV light-filtering IOL. Furthermore, the yellow-tinted IOL is as good as the UV light-filtering IOL for improving sleep duration. A pale yellow-tinted IOL is likely to be superior to a moderate yellow-tinted IOL in terms of allowing patients to discriminate different colors. Thus, the pale yellow-tinted IOL appears to be better for patients than the UV light-filtering IOL and the moderate yellow-tinted IOL.
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Keywords: blood pressure; blue light; cataract; intraocular lens; sleep

INTRODUCTION

In general, humans rely more heavily on vision than they do on their other senses. Thus, cataracts significantly impair quality of life. Cataracts not only make daily living activities difficult but can also exacerbate systemic conditions. These systemic conditions may simply be a result of deterioration due to aging because patients with cataracts are usually elderly and often have impaired activity levels and basal metabolisms; these metabolic disorders are associated with various comorbidities. However, a clinical study of 328 patients undergoing cataract surgery showed that their impaired sleep before surgery might have been improved postoperatively.[1,2] The disturbances in their systemic conditions might have been caused by an anxious state and physical inactivity derived from poor vision, possibly affecting the autonomic nervous system and basal metabolism. However, light exposure itself can affect circadian rhythm, metabolic regulation, sleep patterns and autonomic nervous system functions such as heart rate variability, blood pressure and body temperature regulation.[3–6] Sleep patterns are considered to be partially regulated by retinal photoreceptors, and cataracts can affect the systemic state through impaired light transmittance to the retina.[7–9] Signals from retinal photoreceptors travel via the suprachiasmatic nucleus, hypothalamus and pineal body.[10] The hypothalamus secretes several hormones that regulate the autonomic nervous system as well as endocrine and metabolic functions.[11] The pineal body secretes melatonin, which regulates circadian rhythm.[10] Production of melatonin is suppressed in bright environments and is increased in dim environments;[12,13] therefore, the melatonin level itself has a circadian rhythm, with diurnal decrease and nocturnal increase. Exposure to bright light during daytime enhances the nocturnal elevation of melatonin levels in healthy subjects, although the exact mechanism of this increase is not well understood.[14] Insomnia in the elderly was reported to possibly be improved by increasing melatonin levels.[15] Administration of melatonin before bedtime reduces blood pressure in patients with untreated hypertension.[16] Therefore, it is possible that improvement in the quality of light reaching the retina would improve melatonin secretion, circadian rhythm and systemic symptoms in patients with cataracts. Only a few small clinical studies have been carried out to test this hypothesis. Therefore, we conducted a large-scale clinical study to examine changes in sleep duration and blood pressure after cataract surgery.

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In cataract surgery, intraocular lens (IOL) implantation is usually performed after removal of the natural crystalline lens. The first-generation IOLs allowed transmittance of full spectral electromagnetic waves including ultraviolet (UV) light, which covers a wavelength of ~100–400 nm and is blocked by the natural lens.[17] UV light-filtering IOLs were developed after it became clear that the first IOLs were associated with an increased risk of postoperative cystoid macular edema.[18–20] However, visible light with short wavelengths of 450–495 nm, so-called blue light, can also be harmful, causing retinal damage or impairing the function of the retina.[21,22] Along with aging, the natural lens undergoes yellowing and its transmittance of blue light decreases.[23] Therefore, the next generation of IOLs was designed to be yellowish and to filter blue light similar to an aged, natural lens. However, such blue light-filtering IOLs also contained potentially harmful properties. Melatonin secretion, which is the key factor in circadian rhythm regulation, is suppressed most strongly in response to blue light.[8,13] Hence, the filtering of blue light could lead to unfavorable effects on sleep duration and the sleep cycle.[24] However, there is a conflicting report that showed blue light filtering to have no effect on sleep.[25] The effects of blue light filtering are even more controversial in terms of visual acuity, visual function and color vision in dim environments.[26–38] Therefore, the newest generation of IOLs is tinted a paler shade of yellow to moderately filter blue light.[39–41] Currently, a variety of IOLs is available with different spectral transmittance properties; these new lenses are categorized as UV light-filtering or blue light-filtering (yellow-tinted) IOLs (Figure 1).

These differences affect the spectral properties of light reaching the retina. Whether these differences affect systemic conditions, such as sleep duration and blood pressure after cataract surgery, has not been adequately studied. Thus, we also focused on these issues in the present investigation.

METHODS

This study was conducted in accordance with the ethical principles in the Declaration of Helsinki and the Ethical Guideline for Clinical Research established by the Ministry of Health, Labor and Welfare of Japan. This study was conducted in an exploratory manner as a consecutive case series, and data were collected in 13 medical facilities related to Social Insurance Chukyo Hospital, Aichi, Japan, between 19 January 2006 and 8 February 2009. Patient information was collected by questionnaire after obtaining informed consent from those who received IOL implantation to treat cataracts. Clinical data included age, gender, systemic complications, systemic medications, type of IOL implanted, Standard Pseudoisochromatic Plates (SPP3) color vision test results and blood pressure and sleep duration (in 0.5 h units) before IOL implantation and at 1 week and 1 month after IOL implantation. The IOLs studied were categorized as yellow-tinted or UV light-filtering types. Yellow-tinted IOLs were further categorized into pale yellow-tinted or moderate yellow-tinted types. The pale yellow-tinted IOLs were KS-AiN and KS-Ni (3-step and 2-step pre-set injection systems, respectively, with the same lens model AQ-Ni, STAAR Japan, Urayasu, Chiba, Japan) and Avansee (lens model AN6K, Kowa Company, Nagoya, Aichi, Japan). The moderate yellow-tinted IOLs were Hoya AF-1 series (lens model FY-60AD, Y-60H and YA-60BBR, HOYA Corporation, Shinjuku, Tokyo, Japan) and Alcon AcrySof series (lens model SN60AT and SN60WF, Alcon Japan, Minato, Tokyo, Japan). Other lenses that can filter UV light, regardless of the manufacturer, were considered to be UV light-filtering IOLs.

The primary end points of the study were changes in blood pressure and sleep duration. Statistical analyses were conducted using Prism (GraphPad Software, San Diego, CA, USA). Categorical data representing the baseline patient characteristics were expressed as the number and percentage of patients with each characteristic. Continuous variables were expressed as the means ± s.d. Differences in patient characteristics between groups were analyzed by applying analysis of variance or Pearson's χ^2 test. The differences in blood pressure and sleep duration at 1 week and 1 month after IOL implantation *vs.* baseline and the changes between 1 week and 1 month after IOL implantation were analyzed using analysis of variance followed by a one-sample *t*-test. For blood pressure, the changes were analyzed according to subgroups of patients with or without high blood pressure. High blood pressure was defined as systolic blood pressure (SBP) of 140 mm Hg or higher and/or diastolic blood pressure (DBP) of 90 mm Hg or higher before IOL implantation. Patients without high blood pressure were defined as those not meeting either criterion for high blood pressure. For sleep duration, changes were analyzed according to subgroups of patients with sleep durations of 6 h or less, between 6.5 and 8 h, or 8.5 h or more. These effects were compared among the three types of IOLs. If necessary, analysis of covariance was used to adjust for baseline value differences. The results of the SPP3 color vision test were analyzed as the rates of correct answers, compared among the three types of

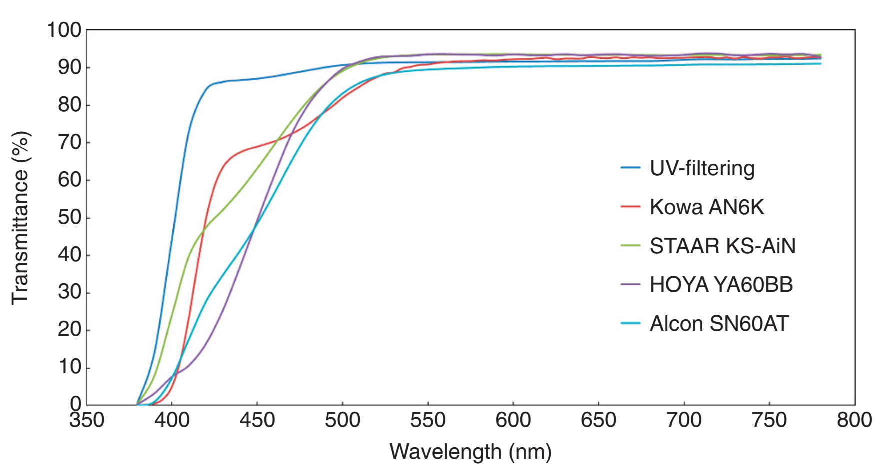


Figure 1 Spectral transmittance properties of several types of IOLs. The pale yellow-tinted IOLs (moderately filtering blue light) used in the patients in this study were KS-AiN and KS-Ni (STAAR Japan) and AN6K (Kowa Company). KS-AiN and KS-Ni are 3-step and 2-step pre-set injection systems, respectively, with the same lens model AQ-Ni. The moderate yellow-tinted IOLs (further filtering blue light) were FY-60AD, Y-60H and YA-60BBR (HOYA Corporation) and SN60AT and SN60WF (Alcon Japan). YA-60BB (not used in this study) and SN60AT are the examples of the moderate yellow-tinted IOLs by HOYA and Alcon, respectively. The others have slightly different but similar spectral transmittance properties in terms of those for wavelength of 400–450 nm. All of the other lenses filtering UV light (wavelength <400 nm) were considered to be UV light-filtering IOLs regardless of the manufacturer. The line of UV-filtering in Figure 1 is an example of those.

IOLs in 5-year age groups, from 20 to 95 years old, using analysis of variance and Student's *t*-test. All statistical tests were two-sided, and *P*-values <0.05 were interpreted as being statistically significant.

RESULTS

Patient characteristics are shown in Table 1. Patient information was collected for 1367 eyes in 1367 patients, of whom 40.0% were male and 54.4% had undergone IOL implantation in the right eye. The mean ± s.d. for age was 70.1 ± 8.4 years. Of the entire patient population, 65.3% were reported as those with hypertension. The SBP was 136.9 ± 21.1 mm Hg and the DBP was 78.0 ± 13.5 mm Hg; 23.9% were taking anti-hypertensive agents; and 47.5% had high blood pressure no matter whether they were taking anti-hypertensive agents or not—that is, SBP $\geqslant$140 mm Hg and/or DBP $\geqslant$90 mm Hg, before IOL implantation. Regarding other systemic complications, 15.6% of patients had diabetes mellitus, 13.8% had dyslipidemia and 11.6% had cardiovascular disease. Patient sleep duration was 7.1 ± 1.4 h. Patients received different types of IOL: 704 patients received pale yellow-tinted IOLs, 355 received moderate yellow-tinted IOLs and 308 received UV light-filtering IOLs. There were more males in the pale yellow-tinted IOL group ($P=0.0211$). The patients in the moderate yellow-tinted IOL group were older than those in the other groups ($P=0.0029$). The UV light-filtering IOL group included more diabetic patients ($P=0.0033$) and more patients with cardiovascular disease ($P=0.0337$).

Compared with the baseline values, the mean blood pressure of the entire patient population decreased significantly at 1 week and 1 month after IOL implantation (Figure 2). The decrease in the mean blood pressure was greater in patients with high blood pressure, whereas patients without high blood pressure before IOL implantation showed a slight increase (Figure 3). When the effects on blood pressure levels were compared by type of IOL, the mean changes in SBP at 1 month after IOL implantation were −3.0 ± 20.5 mm Hg in patients with UV light-filtering IOLs and −5.4 ± 19.8 mm Hg in those with yellow-tinted IOLs. The difference between these two groups was statistically significant (Figure 4). The decrease in SBP did not differ significantly between patients with pale yellow-tinted and moderate yellow-tinted IOLs (data not shown). The mean changes in DBP were −1.2 ± 12.7 mm Hg in patients with UV light-filtering IOLs and −1.9 ± 13.3 mm Hg in those with yellow-tinted IOLs, and these differences were not significant (data not shown).

The effect of IOL implantation on sleep duration, including naps, was also investigated. The mean sleep duration did not change in patients who slept between 6 and 8 h per day. However, the mean sleep duration after IOL implantation approached 6 h in patients whose preoperative durations had been 6 h or less (Figure 5), and the mean sleep duration approached 8 h in those whose preoperative durations had been 8.5 h or more (Figure 6). These effects did not differ according to the type of IOL.

Among the three types of IOLs, SPP3 color vision test results demonstrated that patients with pale yellow-tinted IOLs made the fewest errors (Figure 7). Patients with UV light-filtering IOLs made a modest number of errors, and those with moderate yellow-tinted IOLs made the most errors.

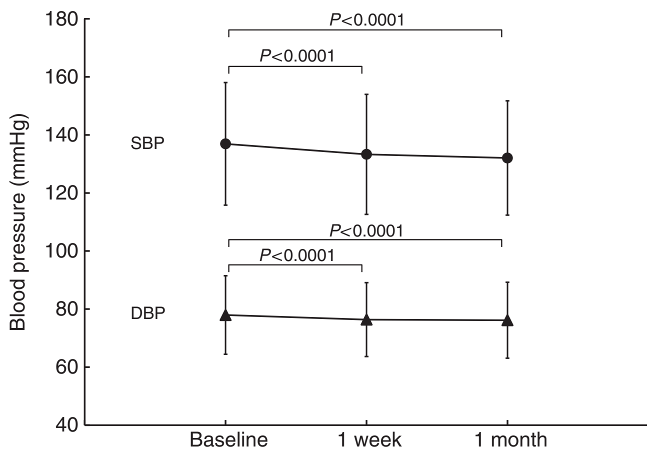


Figure 2 Changes in blood pressure from the baseline after IOL implantation in the entire patient population ($n=1367$). *P*-values shown are from *t*-tests for differences from baseline. *P*-values from analyses of variance for differences among baseline, 1 week and 1 month after cataract surgery are <0.0001 for SBP and 0.0005 for DBP.

Table 1 Patient background

	Total	*Pale yellow*	*Moderate yellow*	*UV*	P-*value*
Subjects[a]	1367 (100%)	704 (100%)	355 (100%)	308 (100%)	
Right eye	743 (54.4%)	395 (56.1%)	190 (53.5%)	158 (51.3%)	0.3446
Male	547 (40.0%)	304 (43.2%)	122 (34.4%)	121 (39.3%)	0.0210
Age, y	70.1 ± 8.4	69.6 ± 8.4	71.4 ± 7.7	69.8 ± 9.0	0.0029
Hypertension	893 (65.3%)	457 (64.9%)	234 (65.9%)	202 (65.6%)	0.9436
Diabetes mellitus	213 (15.6%)	89 (12.6%)	60 (16.9%)	64 (20.8%)	0.0033
Dyslipidemia	189 (13.8%)	97 (13.8%)	50 (14.1%)	42 (13.6%)	0.9848
Cardiovascular disease	159 (11.6%)	83 (11.8%)	30 (8.5%)	46 (14.9%)	0.0337
Anti-hypertensive	327 (23.9%)	168 (23.9%)	89 (25.1%)	70 (22.7%)	0.7787
SBP, mmHg	136.9 ± 21.1	137.1 ± 21.2	136.6 ± 22.2	137.1 ± 19.7	0.9544
DBP, mmHg	78.0 ± 13.5	78.1 ± 13.6	77.5 ± 14.0	78.1 ± 12.7	0.7757
SBP $\geqslant$140/DBP $\geqslant$90	650 (47.5%)	316 (44.9%)	176 (49.6%)	158 (51.3%)	0.1151
Sleep duration, h	7.1 ± 1.4	7.0 ± 1.4	7.1 ± 1.5	7.2 ± 1.4	0.1414

Abbreviations: ANOVA, analysis of variance; DBP, diastolic blood pressure; moderate yellow, moderate yellow-tinted intraocular lens; Pale yellow, pale yellow-tinted intraocular lens; SBP, systolic blood pressure; UV, ultraviolet light-filtering intraocular lens.
Age, SBP, DBP and sleep duration are indicated as mean ± s.d. and others as the number (%).
P-values shown are from ANOVA or Pearson's χ^2 test in comparison among three IOL groups.
[a]No subject was reported for both eyes implanted.

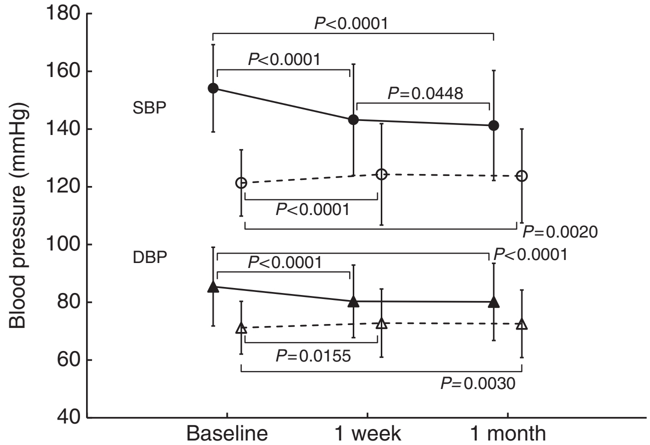


Figure 3 Changes in blood pressure from the baseline after IOL implantation in patients with and without high blood pressure ($n = 650$ and 717). Closed or open symbols indicate data of patients with or without high blood pressure, respectively. *P*-values shown are from *t*-tests for differences from baseline. *P*-values from analyses of variance for differences among baseline, 1 week and 1 month after cataract surgery are <0.0001 for SBP and DBP in patients with high blood pressure and 0.0005 for SBP and 0.0100 for DBP in those without high blood pressure.

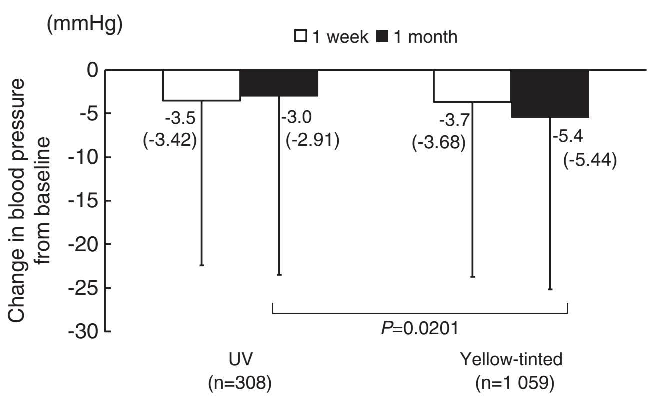


Figure 4 Changes in systolic blood pressure after cataract surgery in patients with UV light-filtering and yellow-tinted IOL. *P*-values shown are from analyses of covariance with the baseline as covariate. Least square means are expressed in parentheses.

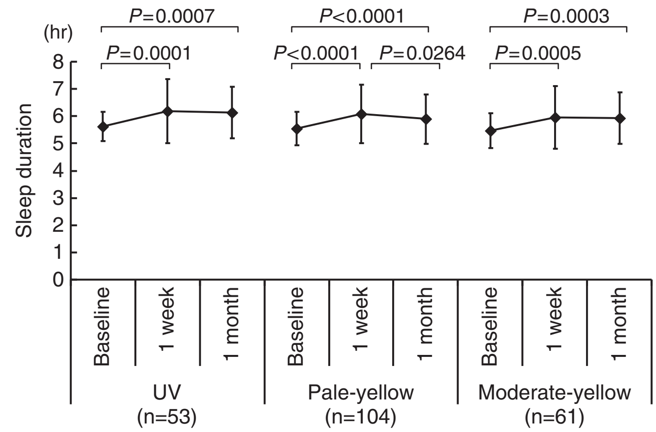


Figure 5 Changes in sleep duration after cataract surgery according to the types of IOLs in patients who slept 6 h or less including naps. *P*-values shown are from *t*-tests for differences from baseline. *P*-values from analyses of variance for the differences among baseline, 1 week and 1 month after cataract surgery are 0.0002 for UV light-filtering IOL, 0.0002 for moderate yellow-tinted IOL and <0.0001 for pale yellow-tinted IOL.

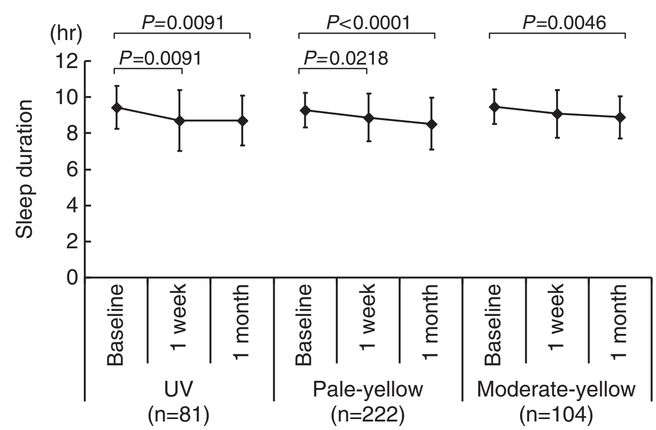


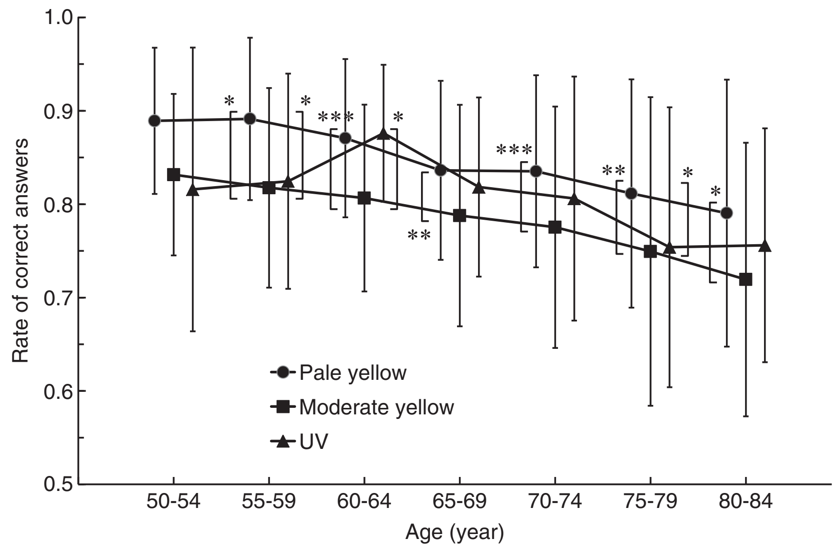
Figure 6 Changes in sleep duration after cataract surgery according to the types of IOLs in patients who slept 8.5 h or more including naps. *P*-values shown are from *t*-tests for differences from baseline. *P*-values from analyses of variance for differences among baseline, 1 week and 1 month after cataract surgery are 0.0109 for UV light-filtering IOL, 0.0152 for moderate yellow-tinted IOL and 0.0001 for pale yellow-tinted IOL.

DISCUSSION

Cataract patients may have systemic abnormalities involving control of body temperature and melatonin secretion as well as abnormal sleep duration and blood pressure due to dysfunctional light transmission to the retina through the crystalline lens.[1–16] This research confirmed that such systemic disturbances, which might be caused by cataracts, showed improvement after cataract surgery in a large number of patients. These improvements might be attributable to the acquisition of clear vision, amelioration of anxiousness or gains made in daily living activities, which may result in favorable autonomic nervous system and basal metabolism consequences. However, improvements in the quality of light might also be among the mechanisms that ameliorate the aforementioned conditions.[1–16] Although there were no significant differences in vision among the IOL groups after cataract surgery, there were differences in outcomes among the groups, implying that the difference in spectral transmittance properties might have resulted in different effects on the autonomic nervous system and melatonin secretion.

The decrease in SBP was greater in patients with yellow-tinted IOLs than in those with UV light-filtering IOLs. This may be because blood pressure is known to increase with blue light exposure in people with normal blood pressure.[42,43] Thus, blue light, which was not filtered by UV light-filtering IOLs, may counteract the blood pressure reduction after IOL implantation. It is possible that the changes in DBP did not differ between patients with UV light-filtering IOLs and those with blue light-filtering IOLs owing to the advanced ages of our subject population, as the mean was 70.1 years old. The elderly population has a lower DBP than the younger population because of their reduced arterial wall compliance, which should minimize the differences in DBP changes caused by different types of IOLs.

Sleep duration became shorter in patients who slept too much and became longer in those who slept too little, suggesting that sleep duration was improved by IOL implantation. There were no



Patient number							
Pale yellow	(19)	(46)	(107)	(116)	(191)	(137)	(57)
Moderate yellow	(5)	(15)	(37)	(62)	(104)	(84)	(30)
UV	(4)	(12)	(14)	(31)	(35)	(34)	(11)

Figure 7 Rates of correct answers in SPP3 test according to the types of IOLs. *P*-values show are from *t*-tests for differences between the types. $^{*}P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$.

differences in these effects among any of the types of IOLs used. Although the effects of UV light filtering and blue light filtering on sleep are controversial,[24,25,38] it is at least noteworthy that blue light-filtering IOLs were associated with an improvement in sleep duration similar to that achieved with UV light-filtering IOLs.

It has been reported that color vision in patients with blue light-filtering IOLs did not differ from patients with UV light-filtering IOLs.[30–35] However, the scores on the SPP3 test, which is a different method from the tests used in the aforementioned reports, differed according to the type of IOL. There might be differences in the perception of color vision among tested patients according to the type of IOL implanted. Such differences might have affected the mood status of our subjects, leading to variable degrees of blood pressure change. However, there was no consistent relationship between the changes in blood pressure and the SPP3 test results. Further studies are needed to elucidate whether changes in blood pressure and other systemic conditions after cataract surgery are attributable to changes in color vision or non-visual effects. As the natural crystalline lens becomes yellowish with aging,[23] patients with UV light-filtering IOLs, which are not tinted yellow, often report that their color vision changes after cataract surgery. However, patients with moderate yellow-tinted IOLs have color vision close to what they had before cataract development. As for improving color vision to the normal level, a pale yellow-tinted IOL, which shows the best results on the SPP3 test, is considered to be a good option.

Not only was improvement of sleep duration after IOL implantation observed, as has already been reported, but blood pressure reduction was also documented in this study. Yellow-tinted IOLs appeared to make a greater contribution to blood pressure reduction than UV light-filtering IOLs in patients with high blood pressure and to improve sleep duration to an extent similar to that of UV light-filtering IOLs. In addition, pale yellow-tinted IOLs appeared to be superior to moderate yellow-tinted IOLs in terms of distinguishing colors and are the best option among yellow-tinted IOLs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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