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Seasonal changes of 24-hour intraocular pressure rhythm in healthy Shanghai population

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Abstract

The aim of the present study was to investigate and compare the 24-hour intraocular pressure (IOP) rhythms in winter and summer in the healthy population of Shanghai, China.

This is a cross-sectional study in which 24-hour IOP measurements were taken for all eligible healthy volunteers in winter and summer, respectively, and the temperature, hours of sunlight (sunlight time), and circulatory parameters, including heart rate, systolic blood pressure, and diastolic blood pressure, were also recorded. The 24-hour IOP curves and IOP parameters (mean, peak, trough, and fluctuation of IOP together with the diurnal-to-nocturnal IOP change) in winter and summer were obtained and compared. The magnitude of IOP changes from summer to winter was also calculated.

A total of 29 participants (58 eyes), 14 (48.28%) male and 15 (51.72%) female, aged 43.66 ± 12.20 (19–61) years, were considered eligible for this study. Generally, IOP decreased progressively before noon, increased notably in the nocturnal period, and peaked at 12:00 AM in winter and at 2:00 AM in summer. The pattern of 24-hour IOP in winter and summer was significantly different ($P = 0.002$). The average IOPs from 4:00 PM to 8:00 AM, except for 6:00 AM, were significantly higher in winter ($P < 0.05$). However, no significant differences were shown after adjusting for temperature and/or sunlight time. From summer to winter, the extent of IOP increase was mostly around 0 to 3 mm Hg, and the IOPs increased more significantly in the nocturnal period than in the diurnal period ($P = 0.05$).

The 24-hour IOP rhythms were different in winter and summer, with higher IOP level in winter. Temperature and sunlight time, which are independent of heart rate and blood pressure, affected the 24-hour IOP rhythms in healthy people in Shanghai, China. Further investigations are expected for the rhythm of some endogenous substance secretion and the inner mechanism of regulation of IOP.

Abbreviations: AL = axial length, BCVA = best corrected visual acuity, CCT = central corneal thickness, DBP = diastolic blood pressure, GAT = Goldmann applanation tonometry, HR = heart rate , IOP = intraocular pressure, SBP = systolic blood pressure, SD = standard deviation.

Keywords: 24-hour intraocular pressure, healthy population, seasons

1. Introduction

Elevated intraocular pressure (IOP) is one of the most important risk factors for development and progression of glaucoma,[1–5] and reducing IOP is the only proven effective method for slowing the progression of the disease.[2,6,7] Thus, IOP is widely used for glaucoma diagnosis, setting treatment goals, and assessing the efficacy of treatments.[4]

It is believed that climate changes, mainly cold fronts, are one of the risk factors that are responsible for provoking the acute angle-closure glaucoma attack.[8] Previous studies have shown that IOP varies seasonally, generally being lower in summer and higher in winter, in healthy,[9–11] ocular hypertensive subjects[12] and glaucoma patients.[13] However, only a single IOP measurement was taken during the office hours in these studies,

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JC and MX contributed equally to this work.

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which could not show a complete picture of IOP patterns. IOP also varies throughout the day,[14] and 24-hour IOP measurement is more and more frequently used in glaucoma care, which could provide a more complete characterization of an individual's IOP.[15–20] The 24-hour IOP rhythm has been described,[17–23] and considering the variations in IOP throughout the year, the 24-hour IOP rhythm may also change, and this variability may hinder attempts to adjust management strategies timely.

Limited information is available about the seasonal changes in 24-hour IOP rhythm in healthy population of Shanghai, China. Therefore, the present study aimed to describe 24-hour IOP rhythms in winter and summer, identify differences between them, and determine possible factors that affect 24-hour IOP rhythm in this population.

2. Methods

2.1. Ethics statement

This study followed the tenets of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Eye and ENT Hospital of Fudan University in Shanghai, China. Written informed consent was obtained from all patients after explanation of the study.

2.2. Study subjects

Healthy and nonsmoking volunteers were recruited in February, 2015. Written informed consent was obtained. All subjects underwent a complete ophthalmic examination consisting of a medical history, best corrected visual acuity (BCVA) (E charts at a distance of 5 m), slit-lamp biomicroscopy (Type YZ5E, 66 Vision Tech. Co., China), Goldmann applanation tonometry (GAT; Haag Streit AG, Bern, Switzerland), funduscopy (CR-DGi nonmydriatic retinal camera, Canon, Japan), central corneal thickness (CCT; Tomey EM-3000), axial length (AL; IOL Master 500),and visual field testing (Humphrey automated perimetry 30–2, Carl Zeiss Meditech, Inc., Dublin, CA).

Inclusion criteria were: BCVA >0.8; diopter >−6D; IOP ≤21 mm Hg; AL ≤26 mm. Exclusion criteria were: having an irregular daily sleep schedule, the presence of ocular disease and systemic disease, the use of routine medication that could affect IOP, and visual field test results outside normal limitations.

2.3. 24-hour IOP measurement

Subjects were asked to maintain a daily 8-hour sleep period (10:00 PM to 6:00 AM) for 7 days before the measurement,[17] admitted to the hospital on February 7, 2015 and August 12, 2015, and underwent 24-hour IOP measurement with a noncontact tonometer (Full Auto Tonometer TX-F, Canon, Japan). All of the IOP measurements were taken by the same well-trained operator, and the indoor temperature was maintained around 23°C in winter and summer. The IOP of both eyes was measured every 2 hours from 8:00 AM to 6:00 AM the next day, specifically, at 8:00 AM, 10:00 AM, 12:00 PM, 2:00 PM, 4:00 PM, 6:00 PM, 8:00 PM, and 10:00 PM (diurnal period IOP), and at 12:00 AM, 2:00 AM, 4:00 AM, and 6:00 AM (nocturnal period IOP). Three measurements were taken for each eye at each time point, and the average value was used for analysis without correction for CCT. The subjects were instructed to continue normal indoor activities during the diurnal period and to go to bed after the measurement at 10:00 PM. From 12:00 AM to 6:00 AM, the subjects were awoken every 2 hours, and IOP was measured instantly in the sitting position. Circulatory parameters including heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured at the same time when the 8:00 AM IOP measurement was taken.

Using the average IOP values at each time point, 24-hour IOP curves were drawn. Mean IOP was calculated through 24-hour, and also separately for the diurnal period and the nocturnal period. Peak IOP and trough IOP were noted as the highest and lowest values among the 12 IOP values of the 24-hour IOP curve drawn. IOP fluctuation was calculated by subtracting the trough IOP from the peak IOP. The mean diurnal-to-nocturnal IOP change was determined by subtracting the mean diurnal IOP from the mean nocturnal IOP. The magnitude of IOP changes was calculated by subtracting the IOP values at each time point, mean IOP, peak IOP, and trough IOP in summer from the respective values in winter through 24 hours, and also separately for the diurnal period and the nocturnal period. The relative IOP change at each time point was calculated by the percentage of the IOP change normalized to the IOP value at each time point in summer.

2.4. Data and statistical analysis

The highest and lowest temperatures, and also sunrise and sunset times, were recorded according to the weather forecast. Sunlight time was defined as the duration from sunrise to sunset.

For all the eligible subjects, both eyes were included in the analysis. The 24-hour IOP curves were described and compared. Statistical analyses were performed using a commercially available statistical software package (SPSS for Mac, version 22.0). Categorical variables were described as frequency and constituent ratio, and analyzed by the chi-square test. Continuous variables were described as mean and standard deviation (SD), and statistical comparisons between 24-hour IOP pattern and parameters in winter and summer were made using a mix-model paired 2-tailed *t* test with Bonferroni adjustment.

3. Results

3.1. Demographics and ophthalmic characteristics of the subjects

A total of 29 volunteers (58 eyes), 14 (48.28%) males and 15 (51.72%) females, aged 43.66 ± 12.20 years (19–61), were

Table 1

Demographics and ophthalmic characteristics of the subjects.

Variables		Subjects
Number		29
Sex		
Male (n, %)		14 (48.28%)
Female (n, %)		15 (51.72%)
Age, y		43.66 ± 12.20 (19 to 61)
Diopter, DS	OD	−0.83 ± 2.13 (−7.25 to +2.00)
	OS	−0.85 ± 2.06 (−8.25 to +1.75)
CCT, μm	OD	541.55 ± 34.77 (475 to 617)
	OS	539.86 ± 34.07 (474 to 608)
Axial length, mm	OD	23.80 ± 1.62 (20.43 to 28.80)
	OS	23.75 ± 1.60 (20.45 to 28.99)

Categorical variables were described as frequency and constituent ratio. Continuous variables were described as mean ± SD.

CCT = central corneal thickness; DS = diopter of sphere, OD = oculus dexter; OS = oculus sinister.

Table 2

Circulatory parameters of the subjects in winter and summer.

Variables	Winter	Summer	*P*
Heart rate, bpm	76.34 ± 10.10	77.07 ± 9.75	0.0014
Systolic blood pressure, mm Hg	115.07 ± 15.05	111.52 ± 14.06	<0.001
Diastolic blood pressure, mm Hg	73.28 ± 12.33	71.66 ± 11.56	<0.001

Continuous variables were described as mean ± SD. Statistical comparisons between winter and summer were performed using a paired 2-tailed *t* test.

considered eligible for this study. The highest and lowest temperatures on the day when 24-hour IOPs were measured were 10°C and 3°C in winter, and 30°C and 25°C in summer. The sunrise times were 6:42 AM and 5:15 AM, and the sunset times were 5:34 PM and 6:44 PM, and the sunlight times were 671 and 798 minutes in winter and summer, respectively. Demographics, ophthalmic characteristics, and circulatory parameters of the subjects are shown in Table 1 and Table 2. Circulatory parameters (HR, SBP, and DBP) were significantly higher in winter than in summer.

3.2. Comparison of the 24-hour IOP curve between winter and summer

Figure 1 shows 24-hour IOP rhythms in winter and summer. Generally, IOP decreased progressively before noon, reached a small peak around 4:00 PM, increased notably at night beginning at 8:00 PM in winter and 10:00 PM in summer, and peaked at 12:00 AM in winter and at 2:00 AM in summer. IOPs at all time points were in accordance with normal distribution, with skewness ranging from −0.184 (2:00 PM) to 1.193 (8:00 PM), and kurtosis ranging from −0.984 (2:00 PM) to 4.344 (10:00 PM) (Fig. 2). In both seasons, peak IOP occurred in most of the cases at 2:00 AM (24.14%), secondly both at 12:00 AM (20.69% and together with 6:00 AM in summer), and thirdly both at 4:00 AM (13.8%).

The differences in 24-hour IOP patterns between winter and summer are significant ($P = 0.002$), and after adjusting for circulatory parameters, the differences still showed statistical significance ($P < 0.001$). However, after adjusting for temperature and/or sunlight time, no significant difference was shown between winter and summer ($P = 0.63$). After adjusting for circulatory parameters, IOPs at 8:00 AM ($t = -2.03$, $P = 0.04$), 4:00 PM ($t = -2.30$, $P = 0.02$), 6:00 PM ($t = -2.42$, $P = 0.02$), 8:00 PM ($t = -1.94$, $P = 0.05$), 10:00 PM ($t = -3.01$, $P = 0.003$), 12:00 AM ($t = -5.15$, $P < 0.001$), 2:00 AM ($t = -2.18$, $P = 0.03$), and 4:00 AM ($t = -3.02$, $P = 0.003$) were significantly higher in winter (Table 3). However, no significant differences were found between the IOP values at each time point in winter and summer after adjusting for temperature and/or sunlight time.

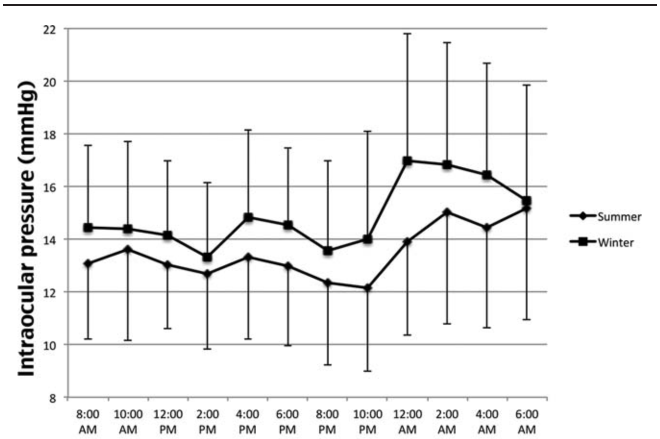

Figure 1. The 24-hour IOP curves in winter and summer. IOP curves were drawn with average IOP value of both eyes at each time points (n = 58). Error bars: SD. IOP = intraocular pressure.

3.3. Comparison of the IOP parameters between winter and summer

The IOP parameters, including 24-hour mean IOP, peak IOP, and IOP fluctuation in the diurnal period, were significantly higher in winter, before and after adjusting for circulatory parameters. However, no significant differences were found in other parameters or in IOP parameters after adjusting for temperature and/or sunlight time (Table 4).

3.4. Intraocular pressure changes from summer to winter

From summer to winter, the mean IOP increased more significantly in the nocturnal period than in the diurnal period ($P = 0.050$) (Table 5). However, when normalized to mean IOP in summer, no significant difference was found between the diurnal and nocturnal period.

The magnitude of this seasonal variation ranged from −8 to 16 mm Hg, but in most cases, the IOP increased by 1 to 2 mm Hg at 8:00 AM, 10:00 AM, 12:00 PM, 2:00 PM, 6:00 PM, 8:00 PM, 10:00 PM, 12:00 AM, and 4:00 AM; by 2 to 3 mm Hg at 4:00 PM and 2:00 AM; and by 0 to 1 mm Hg at 6:00 AM. The distributions of IOP changes from summer to winter were shown in Table 6 and Fig. 3. When normalized to mean IOP value in summer, IOP at each time point increased mostly by 10% to 20%, except at 12:00 PM, 2:00 PM, and 6:00 AM (0%–10%). Moreover, the relative IOP change at each time point in most cases increased by 10% to 20%, except at 12:00 PM, 2:00 PM, and 6:00 AM (0%–10%).

4. Discussion

The present study demonstrates that the 24-hour IOP curve was significantly higher, and peak IOP occurred earlier in winter than in summer; in most cases, IOP increased by 0 to 3 mm Hg from summer to winter, and IOPs increased more in the nocturnal period than in the diurnal period. These seasonal differences, independent of HR or blood pressure, might be related to temperature and sunlight time.

Intraocular pressure reached a peak value before dawn (around 2:00 AM), decreased progressively over the diurnal period, with a small peak in the afternoon (4:00 PM), and then increased again in the nocturnal period, which was consistent with previous studies by different IOP measure technologies.[17–23] However, the patterns of 24-hour IOP in winter and summer were significantly different, even after adjusting for circulatory parameters (HR, SBP, and DBP) ($P =$

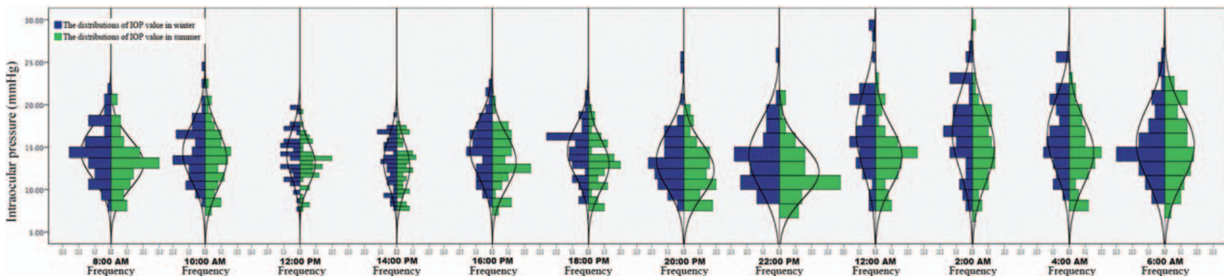

Figure 2. The distributions of IOP value at each time point, which is in accordance with normal distribution (n=58). Blue bar: the distributions of IOP value in winter, green bar: the distributions of IOP value in summer. IOP=intraocular pressure.

0.002 and $P<0.001$ before and after adjustment, respectively). According to the weather forecasts, sunrise time and sunset time in winter were nearly 90 and 70 minutes earlier, respectively, than in summer. Interestingly, both IOPs began to increase, and reached the peak about 2 hours earlier in winter than in summer, a difference that seems to be closely related to solar activities.

The average IOP values at almost all time points in winter were significantly higher than in summer, and the magnitude of this seasonal variation mostly ranged from 0 to 2 mm Hg, and by 10% to 20% normalized to IOP value in summer at each time point. In accordance with previous studies, seasonal effect on IOP was 1 to 3 mm Hg lower in summer than in winter,[8,9,11] and the IOP variations may differ due to differences in inherent constitution,[24] diet, and environmental conditions.[25]The 24-hour mean IOP and IOP fluctuation in the diurnal period were also significantly greater in winter. However, after adjusting for temperature and sunlight time, no significant differences were found. Furthermore, the magnitude of mean IOP change from summer to winter in the nocturnal period (1.79 ± 1.96) was higher than that in the diurnal period (1.25 ± 1.08) ($P=0.050$), although no significance was found when normalized to mean IOP in summer.

The present study suggests that, independent of HR or blood pressure, environmental conditions, including temperature and sunlight time, could affect the aqueous humor circulation and result in the IOP differences between winter and summer. Stoupel et al[25] suggested that environmental conditions, including daily geomagnetic and extreme yearly solar activity, could influence IOP significantly. Gerloff[26] reported that mean hours of daily sunlight exposure are slightly and inversely related with the mean IOP. They found that the IOPs of those who were exposed to sunlight less than 3 hours daily (15.3 ± 3.6 mm Hg) were higher than those who were exposed from 3 to 5 hours (14.8 ± 3.5 mm Hg) or for more than 5 hours (14.6 ± 4.2 mm Hg). Schmerl and Steinberg[27] found that IOP in rabbits decreased after injected with cerebrospinal fluid from humans who had been exposed to bright light. Qureshi et al[11] hypothesized that seasonal variations in IOP may be caused by changes in the amount of certain chemicals secreted by the pineal gland, which is affected by the amount of light entering the eyes daily. According to this hypothesis, prolonged sunlight affects certain secretions from the pineal gland, causing reduced IOP in summer, especially during the nocturnal sleeping periods.

Melatonin is secreted by the pineal gland, mainly during night-time darkness.[28,29] The characteristic diurnal cycle of pineal melatonin shows a sharp peak at night, and light could acutely suppress its production,[30,31] which is unique to melatonin. Considering the melatonin level also has a seasonal rhythm, being higher at night in winter than in summer,[32] we hypothesized that melatonin was involved in the regulation of 24-hour IOP and seasonal variation of IOP. It has been observed that melatonin

Table 3

Comparison of IOP at each time points in winter and summer.

Time points		Adjust HR, SBP, and DBP	Adjust temperature	Adjust sunlight time	Adjust temperature and sunlight time
	P	*P*	*P*	*P*	*P*
8:00 AM	0.05	0.04	0.37	0.75	0.32
10:00 AM	0.26	0.25	0.37	0.75	0.32
12:00 PM	0.12	0.10	0.37	0.75	0.32
2:00 PM	0.36	0.34	0.37	0.75	0.32
4:00 PM	0.03	0.02	0.37	0.76	0.32
6:00 PM	0.02	0.02	0.37	0.76	0.32
8:00 PM	0.06	0.05	0.37	0.75	0.32
10:00 PM	0.004	0.003	0.37	0.76	0.32
12:00 AM	<0.001	<0.001	0.37	0.77	0.32
2:00 AM	0.04	0.03	0.37	0.75	0.32
4:00 AM	0.004	0.003	0.38	0.76	0.32
6:00 AM	−0.40	0.69	0.37	0.74	0.32

Statistical comparisons between winter and summer were performed using a mixed-model paired 2-tailed *t* test, and Bonferroni adjustment was used.
DBP=diastolic blood pressure, HR=heart rate, IOP=intraocular pressure, SBP=systolic blood pressure.

Table 4

Comparison of IOP parameters in winter and summer.

Variables	Winter	Summer	*P*	Adjust HR, SBP, and DBP *P*	Adjust temperature *P*	Adjust sunlight time *P*	Adjust temperature and sunlight time *P*
Mean	14.91±2.96	13.48±2.77	0.05	0.05	0.45	0.88	0.85
Diurnal	14.15±2.60	12.90±2.63	0.07	0.06	0.73	0.81	0.84
Nocturnal	16.44±4.13	14.65±3.54	0.09	0.08	0.36	0.52	0.27
Change	2.29±2.50	1.75±2.22	0.43	0.44	0.54	0.30	0.32
Max	19.32±4.89	17.34±4.08	0.09	0.08	0.25	0.25	0.12
Diurnal	17.45±3.96	15.43±3.23	0.03	0.02	0.34	0.45	0.23
Nocturnal	18.69±5.13	16.91±4.37	0.15	0.14	0.38	0.37	0.23
Min	11.49±2.37	10.76±2.35	0.41	0.40	0.71	0.68	0.52
Diurnal	11.57±2.36	10.84±2.34	0.23	0.21	0.76	0.88	0.70
Nocturnal	14.37±3.59	12.63±2.97	0.08	0.08	0.14	0.78	0.14
Fluctuation	7.83±3.67	6.57±2.85	0.08	0.08	0.60	0.17	0.29
Diurnal	5.88±2.80	4.59±1.72	0.02	0.02	0.16	0.29	0.08
Nocturnal	4.32±2.49	4.28±2.37	0.68	0.68	0.46	0.42	0.72
Change	-1.56±2.85	-0.31±2.16	0.10	0.11	0.10	0.93	0.12

Continuous variables were described as mean±SD. Statistical comparisons between winter and summer were performed using a mixed-model paired 2-tailed *t* test, and Bonferroni adjustment was used.
DBP=diastolic blood pressure, HR=heart rate, IOP=intraocular pressure, SBP=systolic blood pressure.

Table 5

Change of IOP parameters in winter and summer at diurnal and nocturnal periods.

Variables	24-hour	Diurnal	Nocturnal	*P*
Mean (Δmm Hg)	1.43±1.05	1.25±1.08	1.79±1.96	0.050
Max (Δmm Hg)	5.88±2.73	4.89±2.53	4.77±2.91	0.746
Min (Δmm Hg)	−2.69±2.11	−2.02±1.90	−1.11±2.44	0.013
Relative mean	11.11%±8.61%	10.52%±9.56%	12.93%±13.63%	0.224

Continuous variables were described as mean±SD. Statistical comparisons between winter and summer were performed using a mixed-model paired 2-tailed *t* test. Intraocular pressure changes (Δmm Hg) were calculated as IOP value in winter minus that in summer.
IOP=intraocular pressure.

and some melatonin analogs are able to reduce IOP in several species.[33–40] Melatonin receptors have also been identified in the eye, which seems to be involved in the dynamics of aqueous humor.[41] In addition, topical application of melatonin can significantly reduce the IOP in normal albino rabbits and in glaucomatous monkeys.[42] Melatonin can also affect the anterior pituitary gland, resulting in an increase in the secretion of progesterone and estrogen, which could reduce IOP by increasing outflow.[43,44] Besides, there is evidence that levels of serotonin and melatonin may mediate events in the brain's sleep–wake cycle and the retina's cycle of disc shedding, and because the ciliary epithelium has an embryonic origin similar to those of the retina and the pineal gland, serotonin metabolism might also play an analogous role in the regulation of the diurnal cycle of aqueous secretion, which could affect the circadian rhythm of IOP.[45] Since the physiological mechanism of the substances mentioned above, responsible for the seasonal variations of IOP, still remains unclear, further studies are expected.

The present study also suggested that environmental temperature might play a role in seasonal variations of IOP. Shamshad et al[46] found that central retinal artery flow significantly increases upon warming and decreases upon cooling, but IOP showed insignificant alteration upon warming, and IOP returned to baseline after 10 minutes of cooling, even though IOP was significantly lower after cooling. Van de Veire et al[47] also showed that the temperature increase alone did not significantly

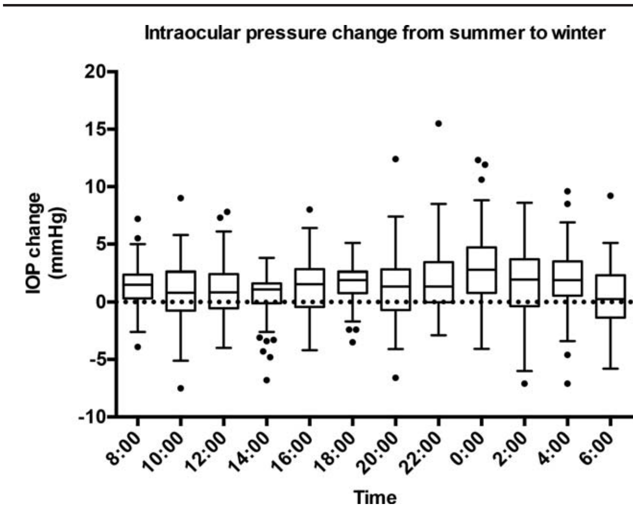

Figure 3. Box plots showed the distributions of IOP change at each time points (n=58). Intraocular pressure changes were calculated by IOP value in winter minus that in summer. The minimum, the 25th percentile, the median, the 75th percentile, the maximum and outliers (•) of IOP were presented. IOP=intraocular pressure.

Table 6

The distributions of IOP changes from winter to summer.

	8:00 AM	10:00 AM	12:00 PM	2:00 PM	4:00 PM	6:00 PM	8:00 PM	10:00 PM	12:00 AM	2:00 AM	4:00 AM	6:00 AM
Min (Δmm Hg)	−3.9	−7.5	−4.0	−6.8	−4.2	−3.5	−6.6	−2.9	−4.1	−7.1	−7.1	−5.8
25% (Δmm Hg)	0.33	−0.75	−0.55	−0.10	−0.43	0.78	−0.70	−0.03	0.78	−0.35	0.55	−1.35
Med (Δmm Hg)	1.50	0.80	0.85	1.10	1.55	1.90	1.35	1.35	2.75	1.95	1.90	0.25
75% (Δmm Hg)	2.38	2.63	2.43	1.63	2.83	2.63	2.80	3.43	4.70	3.68	3.50	2.33
Max (Δmm Hg)	7.20	9.00	7.80	3.80	8.00	5.10	12.40	15.50	12.30	8.60	9.60	9.20

The IOP changes (Δmm Hg) from winter to summer at each time points were calculated by subtracting the IOP values at each time point in summer from the respective values in winter. Number = 58.
25% = 25% percentile, 75% = 75% percentile, IOP = intraocular pressure, Max = maximum, Med = median, Min = minimum.

influence IOP. Findikoglu et al[48] analyzed physiological hemodynamic response to single head-out hot-water immersion and found a statistically significant decrease in IOP with an increase in HR, SBP, and DBP 5 minutes after immersion, but no statistically significant correlation between IOP and SBP or DBP. In these studies, IOP varies when temperature is changed, which was also independent of circulatory changes; however, these previous studies seemed to contradict to the notion that IOP is higher in winter when the temperature decreases. This may be because previous experiments gave the participants stimulations, which are not consistent with natural environmental conditions, and the temperature changes only took place for 5 to 10 minutes,[46,47] which is unlikely to lead to long-lasting physical reactions. Similarly in the present study, the indoor temperature was a transient condition; although it remained the same at 23°C in winter and summer, it could not cover the effects of outdoor environment temperature on seasonal IOP variations. This indicated once more that some inner mechanism related with environment temperature was involved in regulating IOP, and further studies are needed.

There were a few limitations of this study. First, although circulatory parameters (HR, SBP, and DBP) were measured in the present study, we failed to monitor dynamic circadian system changes, which may also have a seasonal and 24-hour rhythm affected by environmental conditions and other endogenous rhythms. Second, although we measured IOP immediately after awakening subjects at night to reduce the influence of posture as much as possible, the rhythm of some endogenous substance secretions like melatonin could have been disturbed. A continuous IOP tonometer, such as a contact lens-based sensor, is needed to exhibit biological conditions more accurately.[23] In addition, further studies are needed to measure substances that could be involved in IOP regulation. Apart from melatonin, serotonin, progesterone, and estrogen, many neuropeptides, such as vasoactive intestinal peptide, substance P, and the atrial natriuretic peptide, are also involved in the regulation of IOP. Indeed, a better understanding of the circadian regulation of IOP is needed for an appropriate treatment of ocular hypertension and glaucoma.[49] Finally, the study population consisted of healthy people in Shanghai, China, where the temperatures are moderate in winter and in summer, so the results of this study may only be representative of the 24-hour rhythms of populations in similar climates.

In conclusion, there are certain seasonal changes in 24-hour IOP rhythm, which are independent of changes in HR or blood pressure. Seasonal changes, including temperature and sunlight time, seem to be related to differences in 24-hour IOP rhythms. Further investigations are expected for the secretion rhythms of certain endogenous substances and the inner mechanism regulating IOP.

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