Twenty-Four-Hour Pattern of Intraocular Pressure in Young Adults with Moderate to Severe Myopia

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PURPOSE. To characterize the 24-hour change of intraocular pressure (IOP) in young adults with moderate to severe myopia.

METHODS. Nineteen young adults, ages 18 to 25 years, with moderate to severe myopia (myopia group) and 17 age-matched volunteers with emmetropia or mild myopia (control group) were housed for 1 day in a sleep laboratory. An 8-hour accustomed sleep period was assigned to each volunteer. Twelve measurements of IOP, axial length, blood pressure, and heart rate were taken at 2-hour intervals. In the wake period, blood pressure and heart rate were measured after a 5-minute bed rest. Axial length and IOP were measured in supine volunteers. Volunteers then sat for 5 minutes, after which IOP was measured. In the sleep period, measurements were taken in supine volunteers in bed.

RESULTS. In both the myopia and control groups, the average supine IOP in the sleep period was higher than the average sitting IOP in the wake period. However, the magnitude of this IOP elevation at night was significantly less in the myopia group. In the sleep period, IOP was less in the myopia group than in the control group. When only the 24-hour supine IOP data were considered, the trough occurred at 1:30 AM and the peak occurred around noon in the myopia group. In the control group, the trough was at 9:30 PM, and the peak at 5:30 AM. Least-square cosine fits showed 24-hour rhythms of supine IOP in both groups, but their phase timings were different. Axial length remained unchanged throughout the day and night in both groups. There was no difference in the 24-hour rhythms of mean blood pressure and heart rate between the two groups.

CONCLUSIONS. Considering habitual body positions, IOP increases at night in young adults with moderate to severe myopia, but the magnitude of the increase is significantly less than that in the age-matched control subjects. There is a 24-hour rhythm of supine IOP in the myopic group, but the phase timing is different from that in the control subjects. These variations of IOP in young adults with moderate to severe myopia are not related to changes in cardiovascular parameters. (Invest Ophthalmol Vis Sci. 2002;43:2351–2355)

Recent studies in experimental myopia with animals¹–⁴ raised an interesting question of whether the 24-hour variation of intraocular pressure (IOP) plays a role in the abnormal eye growth associated with myopia. In the literature, there has been very little information about the 24-hour pattern of IOP associated with human myopia. It is only known that when IOP of a nearsighted person is measured during a daytime office visit, the reading is likely to be higher than that of a person without myopia. This association of a high daytime IOP with myopia has been observed in children, young adults, and the aging population.⁵⁻⁻⁷ The likely IOP level at night in a nearsighted person is not known. However, it has been shown in the chick model of form-deprived myopia that the deviation of IOP in the myopic eye from the control eye is not consistent throughout the 24 hours.¹

We have studied the 24-hour pattern of IOP in healthy young adults.¹⁰⁻¹¹ In these studies, candidates with moderate to severe myopia (greater than −4 D) were excluded because of their potential for higher daytime IOP. Measurements of IOP were taken in the recruited volunteers in the sitting and supine positions in the laboratory. When data obtained in volunteers in habitual body positions (i.e., sitting during the day and supine at night) were considered, a significant elevation in IOP occurred during the sleep period. Considering only the supine IOP data throughout, a nocturnal IOP elevation still appeared. Physiological mechanisms causing this nonpostural elevation in IOP at night were unclear. As demonstrated by the longer axial length, the most characteristic feature of a myopic eye is its size.¹² Whether mechanisms responsible for the nocturnal IOP elevation in humans affect eyes of different sizes to the same degree is not known. This anatomic variable may influence the 24-hour IOP pattern in individuals with myopia.

In the present study, we collected 24-hour data of IOP, axial length, blood pressure, and heart rate from a group of young adults with moderate to severe myopia. Data were also collected from age-matched volunteers with emmetropia or with mild myopia as the control. Results should provide information on the 24-hour IOP pattern in moderate to severe myopes and possibly the physiological mechanisms in the regulation of IOP during the sleep period.

METHODS

The study adhered to the tenets of the Declaration of Helsinki and was approved by our institutional review board. Volunteers were recruited from university students and local residents. Informed consent was obtained after explanation of the nature and possible consequences of the study. Volunteers were selected for having a regular daily sleep cycle close to 11 PM to 7 AM. Candidates were healthy nonsmoking individuals, 18 to 25 years old, of both genders, and ethnically diverse. No candidate had had refractive surgery. Each candidate had a complete ophthalmic examination that demonstrated absence of any eye disease and a narrow iridocorneal angle. Refractive state was determined by the noncycloplegic method with subjective trial of lenses. Candidates with a refractive error between −2 and −4 D or with an interocular difference of more than 1 D were excluded. Successful recruits were divided into two groups. The myopia group had a
TABLE 1. Demographic Information for the Myopia Group and the Control Group

<table>
<thead>
<tr>
<th></th>
<th>Myopia Group</th>
<th>Control Group</th>
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</thead>
<tbody>
<tr>
<td>Gender</td>
<td>19 men, 9 women</td>
<td>17 men, 9 women</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>10 White, 7 Asian, 2 Hispanic</td>
<td>12 White, 4 Asian, 1 Hispanic</td>
</tr>
<tr>
<td>Age (y)</td>
<td>21.6 ± 2.1</td>
<td>21.8 ± 1.9</td>
</tr>
<tr>
<td>Height (in.)</td>
<td>67.7 ± 4.3</td>
<td>66.8 ± 3.5</td>
</tr>
<tr>
<td>Weight (lb.)</td>
<td>150 ± 37</td>
<td>157 ± 29</td>
</tr>
<tr>
<td>Refractive state (range) (D)</td>
<td>−6.8 ± 2.0 (−4 to −12)</td>
<td>−0.5 ± 0.6 (0 to −2)</td>
</tr>
<tr>
<td>IOP* (range) (mm Hg)</td>
<td>14.8 ± 1.8 (11–18)</td>
<td>15.1 ± 3.2 (9–20)</td>
</tr>
</tbody>
</table>

Calculated data are mean ± SD
* measured with the Goldmann tonometer during office hours.

refractive state greater than −4 D in each eye. The control group had a refractive state equal to or less than −2 D, which was used previously as the cutoff point for emmetropia in studies of the relationship between IOP and myopia.5,7 No latent hyperopia was found during the cycloplegic retinoscopy in the emmetropes in the control group. Demographic information in the myopia group and the control group is summarized in Table 1.

Experimental subjects were instructed to maintain a daily 8-hour sleep period for 7 days before the laboratory session. This assigned sleep period matched closely with the individual’s regular sleep cycle. Subjects wore a wrist monitor (Actiwatch; Mini Mitter, Sunriver, OR) for light exposure and physical activity and kept a wake-sleep log. Daily wake-sleep synchronization was enhanced by observation of regular patterns. Subjects were instructed to abstain from alcohol and caffeine for 3 days and not to use contact lenses for 24 hours (16 subjects in the myopia group and 3 subjects in the control group) before the laboratory session.

Subjects arrived at the laboratory at approximately 2 PM and stayed in individual studio apartments for the next 24 hours. Light intensity in the laboratory was held constant, unless indicated later, at 500 to 1000 lux at eye level when standing. The 8-hour period of darkness in the subject’s apartment was adjusted to correspond to each individual’s sleep period. Times for measurements were individualized to coordinate with this sleep period. Although the sleep periods and the measurement schedules were individualized, corresponding clock times were normalized for data presentation as if each subject had an assigned sleep period from 11 PM to 7 AM.

Measurements of IOP, axial length, blood pressure, and heart rate were taken every 2 hours. Intraocular pressure was measured with a pneumotonometer (model 30 Classic; Mentor O&O, Norwell, MA). It has been confirmed18 that different measuring angles with the pneumotonometer produced the same IOP (±0.5 mm Hg) against the manufacturer’s verifier. Axial length was measured using an A-scan biometer (model 5100; DGH, Exton, PA). One or two drops of 0.5% proparacaine were applied as local anesthetic before each measurement. Only the left eye was used for the measurement of IOP and the right eye for the measurement of axial length, to minimize potential complications (such as corneal abrasion) from repeated corneal contacts. Blood pressure and heart rate were measured with an automated wrist blood pressure monitor (model HEM-608; Omron, Vernon Hills, IL). Laboratory measurements were divided into three shifts and assigned to experienced researchers. Before the study, variations in the readings among the researchers were confirmed to be insignificant.

Before the assigned sleep period, measurements were taken at 3:30, 5:30, 7:30, and 9:30 PM. Subjects were instructed to lie in bed for 5 minutes before the measurement of blood pressure and heart rate. Measurements of axial length and IOP were taken afterward in supine subjects. Subjects then sat for 5 minutes before a sitting IOP was measured. We had found that subjects complied well with the supine-sitting measurements sequence, given the demands of numerous measurements and the requirement for 5 minutes of sitting before the sitting IOP measurement, and adopted this sequence as the protocol. Room lights were dimmed for this short period of data collection (approximately 10 to 15 minutes). Light intensity was less than 10 lux at eye level when subjects were lying in bed face-up, which helped the measurement of axial length by avoiding excess miosis. The reading of axial length was accepted when the standard deviation of 3 to 10 trials was less than 0.1 mm. For every measurement of IOP, a hard-copy record was visually inspected. The IOP was accepted if the tonograph pattern was normal and the standard deviation for 3-second recording was less than 1 mm Hg.15 In an unsatisfactory case, IOP measurement was taken again. Between the two trials, the IOP with the smaller standard deviation was selected. Subjects were encouraged to continue their normal indoor activities. Food and water were available, and meal times were not regulated.

Lights in individual sleep rooms were turned off at 11 PM. Measurements of blood pressure, heart rate, axial length, and IOP during the sleep period were taken in the supine position at 11:30 PM and 1:30, 3:30, and 5:30 AM. Before these scheduled measurements, room lights were turned on. The light intensity was at the same level (<10 lux) as during the daytime measurements. It has been shown that a short period of moderate light exposure (1000–1500 lux) at night does not affect IOP.13 Subjects were awakened, if necessary, and the measurements were taken immediately and completed within a few minutes. Lights were turned off after the measurements. Room activities were continuously videotaped using infrared cameras. When the assigned sleep period ended at 7 AM, room lights were turned back on to 500 to 1000 lux and subjects were awakened, if necessary. Measurements of blood pressure, heart rate, axial length, and IOP were taken at 7:30, 9:30, and 11:30 AM and 1:30 PM, as described earlier. Debriefing interviews were conducted to document how the subjects had slept.

Systolic and diastolic blood pressures were recorded. Mean blood pressure was calculated as the diastolic blood pressure plus one-third of the difference between the systolic and the diastolic blood pressures. Data analyses were similar to those of previous studies.10,15 Values are presented as mean ± SEM unless otherwise indicated. First, means of each parameter (IOP, axial length, mean blood pressure, and heart rate) from all the subjects in each group were calculated for each time point. The trough and the peak among these means were determined. Statistical comparisons of the means were made between the trough and the peak and between the wake and the sleep periods, using the paired t-test or the repeated measures ANOVA, when more than two means were compared. Student’s t-test was used for the comparisons between the myopia group and the control group. The criterion for statistical significance was P < 0.05.

Estimation of the 24-hour rhythm10,15 was performed for each parameter of IOP, axial length, mean blood pressure, and heart rate. Assuming the 24-hour rhythm resembled a cosine profile, the best-fitting cosine curve14 was determined from each individual’s data collected from the 12 time points. Each cosine curve had a fitted peak, the acrophase. The clock time of the acrophase estimated the phase timing of the rhythm.15 The null hypothesis of a random distribution of acrophases around the clock was evaluated statistically with the Rayleigh test.10 Lack of significance with this test indicated no consistent timing for 24-hour rhythms in experimental subjects, whereas the alternative conclusion showed that a 24-hour rhythm existed with synchronized timing in the group. The height of the fitted cosine curve (amplitude) estimated the magnitude of the 24-hour rhythm. Acrophases and amplitudes of the myopia group and the control group were compared using the Mann-Whitney rank sum test.

RESULTS

The 24-hour profiles of IOP in the myopia group and the control group are presented in Figure 1. Data were first ana-
The difference was not statistically signi-
fi-

cantly less than the difference of 0.4 mm Hg in the control group (P < 0.01). The acrophase in the myopia group was significantly less than the difference of 4.3 ± 0.3 mm Hg observed in the control group (P < 0.01). To exclude the postural influence on IOP, 24-hour IOP patterns in the two groups were analyzed, with only the supine IOP data used. The 24-hour supine IOP (data points shown as the triangles in Fig. 1) changed gradually in both groups, but timings for the trough and peak were different. The trough and peak IOP appeared at 1:30 AM and 1:30 PM in the myopia group and 9:30 PM and 5:30 AM in the control group. The trough-peak IOP differences were 2.6 ± 0.9 mm Hg in the myopia group and 3.0 ± 0.7 mm Hg in the control group (P > 0.05).

The supine IOPs in the wake period were compared (Table 2). The average supine IOPs for the myopia and the control groups were not different. For either group, the supine IOP in the sleep period was not significantly different from that in the wake period. However, the decrease of IOP from the wake period to the sleep period in the myopia group was different (P < 0.05) from the increase of IOP in the control group. Different phase timing for the supine IOP rhythm was evident from the cosine fits of the 24-hour supine IOP data (Fig. 3B). There were 24-hour rhythms in supine IOP in both subject groups (Rayleigh test; P < 0.05). The acrophase in the myopia group was at 11:39 AM ± 0.95 hour, whereas the acrophase in groups, but the deviation from the mean was greater in the myopia group than in the control group. The amplitude for the 24-hour rhythm was 1.9 ± 0.2 mm Hg in the myopia group, which was significantly less than the amplitude of 3.1 ± 0.4 mm Hg in the control group (P < 0.01).

TABLE 2. Difference in IOP between the Wake and Sleep Periods

<table>
<thead>
<tr>
<th></th>
<th>Wake (Sitting)</th>
<th>Wake (Supine)</th>
<th>Sleep (Supine)</th>
<th>Habitual Positions ΔIOP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H</td>
<td>17.3 ± 0.4</td>
<td>20.5 ± 0.4</td>
<td>19.6 ± 0.4</td>
</tr>
<tr>
<td>Myopia group</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H</td>
<td>16.2 ± 0.4</td>
<td>20.5 ± 0.3</td>
<td>21.3 ± 0.5</td>
</tr>
<tr>
<td>Control group</td>
<td>17</td>
<td></td>
<td></td>
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</tbody>
</table>

Data are mean (mm Hg) ± SEM.  
* P < 0.01, Repeated-measures ANOVA and post hoc Bonferroni t-test.
the control group was at 6:34 AM ± 1.12 hour (P < 0.01). The amplitudes were not statistically different in the two groups; 1.5 ± 0.2 mm Hg in the myopia group and 1.4 ± 0.2 mm Hg in the control group.

Axial length remained virtually unchanged throughout the 24 hours in both groups. The 24-hour average axial length was 25.82 ± 0.20 mm in the myopia group, which was longer than the average axial length of 23.50 ± 0.24 mm in the control group. After cosine-fits of axial length data, the Rayleigh test showed no 24-hour rhythm in either group. In both the myopia and the control groups, the peaks of mean blood pressure and heart rate occurred in the wake period, and the troughs occurred in the sleep period. Both 24-hour rhythms of mean blood pressure and heart rate were detected using the cosine fits and the Rayleigh test. However, no difference in the acrophases or the amplitudes appeared between the two groups (data not shown). It was noted that the IOP change was unrelated to, either in timing or in direction, the change in mean blood pressure and heart rate in both subject groups.

**DISCUSSION**

It is known that myopic young adults are likely to have higher daytime IOP than young adults without myopia. It might be supposed that IOP is also higher at night in a myopic eye than in an emmetropic eye. This hypothesis can be evaluated by comparing the nocturnal IOP levels of the two groups in the present study. Data showed that the nocturnal supine IOP of the myopia group was actually lower than that of the control group. In real life, IOP of a myopic eye at night in the recumbent position is most likely not higher than IOP of an emmetropic eye.

A positive correlation appeared between the refractive state and the habitual elevation of IOP in the sleep period (Fig. 2). A significant portion of this habitual IOP elevation is probably due to the postural change from sitting to supine. When we compared the daytime IOP difference between the sitting and supine positions, the myopia group had a lesser difference in IOP than the control group. It was also reported that high myopes had less daytime postural difference in IOP than low myopes. Postural change from sitting to supine causes redistribution of body fluid. The impact of redistributed body fluid in the eye, mainly the increase in choroidal vascular volume (uveal vascular engorgement), is likely to be modulated by the eye size. Observed under high-resolution magnetic resonance imaging, choroidal thinning is associated with moderate to severe myopia in humans. Therefore, the choroidal vascular volume does not increase proportionally as the increase of ocular volume in a myopic eye. Perhaps, the smaller habitual IOP variation in the myopia group is related to a weaker impact of uveal vascular engorgement. Postural change also causes an elevation of episcleral venous pressure and consequently affects IOP during the day and at night. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye.

Considering only the supine IOP data, the IOP trough and peak occurred differently in the two groups. In the control group, we observed an increase of IOP from the late wake period toward the end of the sleep period. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye. Considering only the supine IOP data, the IOP trough and peak occurred differently in the two groups. In the control group, we observed an increase of IOP from the late wake period toward the end of the sleep period. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye. Considering only the supine IOP data, the IOP trough and peak occurred differently in the two groups. In the control group, we observed an increase of IOP from the late wake period toward the end of the sleep period. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye. Considering only the supine IOP data, the IOP trough and peak occurred differently in the two groups. In the control group, we observed an increase of IOP from the late wake period toward the end of the sleep period. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye. Considering only the supine IOP data, the IOP trough and peak occurred differently in the two groups. In the control group, we observed an increase of IOP from the late wake period toward the end of the sleep period. Whether the episcleral venous pressure responds differently between the myopia group and the control group is unclear. The correlation between the habitual IOP change and the axial length could not be evaluated directly in the present study, because our data for IOP and axial length were not collected from the same eye.

It should be noted that there was a difference in the experimental conditions for the diurnal and nocturnal supine IOP measurements. Diurnal measurement was performed after a 5-minute bed rest. Nocturnal measurements, however, were taken after 0.5 to 6.5-hours’ continuous bed rest. If the nocturnal elevation of supine IOP in the control group is related to this long-term recumbent body position, this position probably has a different impact on an eye with moderate to severe myopia. The different phase timings in the supine IOP between the myopia and control groups may also reflect a difference in the endogenous hormonal rhythms. Plasma cortisol has been associated with the 24-hour rhythm of IOP. Although a cor-

**FIGURE 3.** Estimated 24-hour rhythm of intraocular pressure (IOP) in (A) habitual body positions and (B) the supine position, using the least-square cosine-fitting technique. The clock time of the acrophase (fitted peak) is shown with the amplitude (height of the fitted curve) in the radial scale (mm Hg). Nineteen control subjects. Sitting IOPs during the wake period (7 AM to 11 PM) and supine IOPs during the sleep period (11 PM to 7 AM) were used in (A).
relation of circulating cortisol and degenerative myopia in young adults was hypothesized, a link between the 24-hour rhythms of cortisol and IOP has not been investigated in myopic young adults.

We conclude that nocturnal IOP is not higher in young adults with moderate to severe myopia, compared with young adults with emmetropia or mild myopia. If a higher IOP is associated with myopia in young adults, the correlation is limited to the daytime IOP. The size of the globe is an important factor in determining the nocturnal IOP level, although it has received little attention. Our observations are based on data collected in young adults, and caution should be exercised in extending these conclusions to other age groups. Because our experimental subjects were not in the early stage of youth-onset myopia (as in some studies on the causal relationship between IOP and myopia), whether diurnal IOP or nocturnal IOP plays a role in youth-onset myopia cannot be judged by the present study. Similarly, these human observations may not inform us whether the 24-hour IOP pattern plays a role in the normal eye growth or the abnormal development of form-deprived myopic eye in chicks. Last, caution should be used in extending our conclusions to the aging population, in which an enlarging lens may modulate the effect of redistribution of body fluid at night in a myopic eye. A 24-hour monitoring of IOP in various body positions in children with developing myopia and in the aging population with moderate to severe myopia should provide needed information.

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References