Clinical Utility of Intraocular Pressure Monitoring Outside of Normal Office Hours in Patients With Glaucoma

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Objective: To determine whether intraocular pressure (IOP) monitoring outside of normal office hours adds clinically useful information.

Methods: We reviewed the records of all patients with glaucoma who were admitted for 24-hour IOP monitoring during 3 years. Applanation IOP was recorded in the sitting position from 7 AM until midnight and in the supine position at 6 AM.

Results: Thirty-two patients (22 women and 10 men) were enrolled (mean±SD age, 67.3±12.1 years). Mean±SD 24-hour IOP was 13.0±2.2 mm Hg. Mean±SD peak 24-hour IOP (16.8±3.2 mm Hg) was significantly higher than peak office IOP (14.7±3.2 mm Hg) (P<.001). Peak IOP was recorded outside of office hours in at least 1 eye in 22 patients (69%). Mean IOP fluctuation during 24-hour monitoring (6.9±2.9 mm Hg) was significantly greater than that during office hours (3.8±2.3 mm Hg) (P<.001). Peak 24-hour IOP was higher than the peak IOP noted during previous office visits in 40 eyes (62%). Results of 24-hour IOP monitoring led to immediate treatment change in 23 eyes (36%).

Conclusions: In glaucoma patients with advanced disease or progression that are disproportionate to known IOP measurements, 24-hour monitoring of IOP may reveal a greater role for pressure-related risk for glaucoma progression than previously suspected and may alter treatment strategies.

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ASSESSMENT OF INTRAOCULAR pressure (IOP) is a critical aspect of risk assessment and management for patients with or at risk for glaucoma. Lowering IOP remains the only proven method of preventing or slowing the rate of glaucoma injury. Studies1-4 suggest that the greater the lowering of IOP, the greater is the effect in preventing or slowing glaucomatous optic nerve damage.

Intraocular pressure varies throughout the diurnal and nocturnal periods.5-7 It is generally thought that peak IOP for most persons occurs in the morning.8,9 However, others10 have reported a steady daily increase in IOP in a group of patients being treated for glaucoma, and recent evidence11-17 suggests that nocturnal supine IOP may be higher for many individuals. It has also been suggested that fluctuation in IOP may be an independent risk factor for disease progression.18,19

In clinical practice, most ophthalmologists rely mainly on sporadic measurements of IOP obtained during daytime office visits. While some ophthalmologists schedule patient visits at different times of the day or obtain IOP measurements throughout the day, obtaining IOP measurements outside of normal office hours is uncommon.

Twenty-four–hour IOP behavior in glaucoma patients has implications for both disease pathogenesis and disease management. Despite the importance of this issue, there is a paucity of published data, especially on treated patients. In this study, we report on a consecutive series of patients admitted for 24-hour IOP monitoring. Specifically, we assessed whether IOP measurements outside of normal office hours revealed clinically important information.

METHODS

We reviewed the records of all glaucoma patients admitted for 24-hour IOP monitoring at The New York Eye and Ear Infirmary from September 1, 2001, to September 30, 2004. Patients were scheduled for 24-hour IOP monitoring for a variety of reasons but primarily when their previously recorded office IOPs did not seem to explain their present glaucomatous neuropathy or its progression. All patients were using their glaucoma medications when admitted.
Intraocular pressure was recorded in both eyes approximately every 2 hours in the sitting position from 7 AM until midnight with a Goldmann applanation tonometer and in the supine position at 6 AM with a Perkins handheld applanation tonometer, before the patient had gotten out of bed. During office hours (7 AM to 4:30 PM), IOP was measured by a clinical glaucoma fellow, an experienced technician, or an attending glaucoma specialist. During evening and nighttime hours, IOP was measured by either a fellow or a resident.

Peak and range (calculated by subtracting the minimum value from the maximum) IOP measurements recorded during office hours (office IOP) were compared with those recorded during the entire 24-hour period (24-hour IOP) using the paired, 2-tailed t test. In addition, IOPs recorded during up to 5 office visits before admission were recorded and analyzed. All data are given as mean±SD unless otherwise indicated.

RESULTS

Thirty-two patients were enrolled (22 women and 10 men; mean age, 67.3±12.1 years); all had open-angle glaucoma. The mean deviation on a 24-2 Humphrey visual field was available for 26 right eyes (–14.9±7.6 dB) and 27 left eyes (–13.1±7.8 dB); in the remaining eyes, advanced glaucomatous visual field loss was assessed only with the 10-2 threshold test owing to advanced disease. At the time of admission for 24-hour monitoring, glaucoma medications were being used in 24 right eyes (2.0±0.9 medications; 21 eyes treated with a prostaglandin analog, 9 with a β-blocker, 12 with an α1-agonist, and 7 with a topical carbonic anhydrase inhibitor). Medications were being used in 28 left eyes (2.2±1.0 medications; 23 eyes treated with a prostaglandin analog, 13 with a β-blocker, 12 with an α2-agonist, and 10 with a topical carbonic anhydrase inhibitor). Prior to admission, 12 eyes of 7 patients had undergone trabeculectomy, 1 eye had undergone laser trabeculoplasty, and 1 eye had received both laser trabeculoplasty and trabeculectomy. Of the 13 eyes with an earlier trabeculectomy, 9 were being treated with IOP-lowering medications.

The mean 24-hour IOP for all eyes was 13.0±2.2 mm Hg (range, 7.2-19.4 mm Hg). The mean 24-hour IOP for right eyes was 13.7±2.6 mm Hg; for left eyes, 13.3±1.8 mm Hg. The mean peak 24-hour IOP was higher than the peak office IOP (16.8±3.2 vs 14.7±3.2 mm Hg in all eyes [P=.001]; 16.4±3.5 vs 14.3±3.7 mm Hg in right eyes [P=.02], and 17.1±3.0 vs 15.1±2.4 mm Hg in left eyes [P=.005]). The difference between the 2 peaks was at least 2 mm Hg in 13 right eyes (41%) and 15 left eyes (47%) (Figure 1).

The peak IOP was recorded outside of office hours in at least 1 eye in 22 patients (69%). In 7 of these patients (11 eyes), the peak IOP was recorded only at the 6 AM supine measurement. In 7 of these eyes, that measurement revealed a higher IOP than during previous regular office visits. The difference between the 2 peaks was at least 2 mm Hg in 13 right eyes (41%) and 15 left eyes (47%). The difference between the 2 peaks was at least 4 mm Hg in 6 right and 6 left eyes (19% each) (Figure 1).

The peak IOP was recorded outside of office hours in at least 1 eye in 22 patients (69%). In 7 of these patients (11 eyes), the peak IOP was recorded only at the 6 AM supine measurement. In 7 of these eyes, that measurement revealed a higher IOP than during previous regular office visits.

The mean IOP fluctuation during 24-hour monitoring was significantly greater than that during office hours (6.9±2.9 vs 3.8±2.3 mm Hg in all eyes [P<.001], 6.7±3.0 vs 3.7±2.1 mm Hg in right eyes [P<.001], and 7.1±3.0 vs 3.9±2.5 mm Hg in left eyes [P<.001]) (Figure 2).

Intraocular pressure was recorded during a mean of 3.4 office visits before admission. Peak 24-hour IOP was

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**Figure 1.** Peak intraocular pressure (IOP) recorded during office hours and the entire 24-hour period in the right (A) and left (B) eyes of the study cohort.
higher than the maximum IOP noted during previous office visits in 40 eyes (62%), whereas peak office IOP was higher in 24 eyes (38%) (Figure 1). In 14 of these 24 eyes, continued monitoring after office hours revealed an even higher peak IOP. Thus, the highest measurement of IOP compared with previous office visits was obtained outside office hours in 30 eyes (47%). In 9 eyes (14%), peak IOP occurred only at the 6 AM supine measurement.

The mean difference between peak 24-hour and peak IOP recorded before admission was 2.1±3.6 mm Hg in right eyes (range, –5.0 to 10.0 mm Hg) and 2.8±4.0 mm Hg in left eyes (range, –4.0 to 10.0 mm Hg).

Results of 24-hour IOP monitoring led to an immediate treatment change in 23 eyes (36%) of 19 patients (59%). Trabeculectomy was undertaken in 7 eyes of 5 patients, laser trabeculoplasty was performed in 4 eyes of 3 patients, and medications were advanced in 12 eyes of 11 patients.

**COMMENT**

Most ophthalmologists manage their patients’ glaucoma on the basis of sporadic IOP measurements that are obtained during regular office hours. Measuring IOP throughout the daytime (often called the “office diurnal curve”) is relatively simple, but it is inconvenient to the patient and consequently used infrequently. Measurement of IOP during the evening and nighttime requires admission of the patient to the hospital and the presence of trained personnel to obtain the measurements. Even in the few places where this is available (eg, in hospitals affiliated with academic centers), frequent use is hindered by such obstacles as patient inconvenience, high cost, and the refusal of third-party payers to cover the associated expenses. We sought to evaluate the utility of 24-hour IOP monitoring and its impact on disease management for a selected group of individuals.

Glaucoma patients with advanced disease or progression that are disproportionate to known IOP measurements pose difficult diagnostic and therapeutic challenges. When confronted with such patients, the treating ophthalmologist may consider factors such as noncompliance, in which the patient uses medication properly only immediately prior to the office visit,20 and putative pathogenetic mechanisms unrelated to IOP.21,22 However, we show that in this group of patients, 24-hour IOP monitoring often reveals higher peaks and a wider fluctuation of IOP values than those found during typical office hours, either during the daily portion of the monitoring or during sporadic visits. These findings suggest a greater role for IOP-dependent mechanisms in the pathogenesis of glaucomatous progression than previously suspected. Moreover, identifying individual daily IOP patterns allows better tailoring of treatment, whether medical or surgical. For example, we have occasionally used a miotic agent before bedtime to blunt early-morning IOP peaks. Alternatively, in a patient with consistent, single-digit IOP during the day who is a candidate for IOP-lowering surgery, the identification of the evening or nighttime peak suggests that the target IOP may not need to be as low as previously assumed.

![Figure 2. Range of intraocular pressure (IOP) fluctuation recorded during office hours and the entire 24-hour period in the right (A) and left (B) eyes of the study cohort.](image-url)
In 11 eyes (7 patients), peak IOP was recorded during 24-hour monitoring only at the 6 AM supine measurement; in 7 of these eyes, that measurement revealed a higher IOP than during previous regular office visits. Intraocular pressure has been shown to rise when a patient is in the supine position by a similar degree of 3 to 4 mm Hg in both normal and untreated glaucomatous eyes during the day and night, superseding a rise in episcleral venous pressure. Recently, Mosaed et al suggested that peak nocturnal IOP can be predicted from the daytime supine measurement in untreated glaucoma patients. Regardless of the underlying cause, a significant rise in supine IOP in patients with progressive glaucoma should be diagnosed and treated. It remains to be elucidated whether supine IOP measured in the office after a short duration of lying down, or by some other means, can accurately predict nocturnal or early-morning supine IOP in treated, high-risk glaucoma patients. Zeimer et al studied 9 patients with treated primary open-angle glaucoma (POAG) who were previously identified by home self-tonometry as having early-morning peak IOP. These patients measured IOP upon waking and 30 minutes and 1 hour later on an average of 4.2 consecutive days. In 8 of the 9 patients, the authors observed high IOP peaks upon awakening that declined within 30 minutes. The results of this small study suggested that some glaucoma patients may have significant IOP peaks upon awakening, which inherently cannot be demonstrated in the ophthalmologist’s office.

There is much discussion in the literature—but few data—on the 24-hour behavior of IOP in patients with glaucoma, especially treated patients. Hughes et al showed that mean peak 24-hour IOP was on average 4.9 mm Hg higher than mean peak IOP recorded during previous office visits in 29 treated glaucoma patients. Methodological differences from our study included IOP measurement using a TonoPen (Medtronic, Inc, Jacksonville, Fla) and the omission of IOP measurements after midnight. The number of office visits included in their analysis was not mentioned.

David et al retrospectively analyzed 2272 daytime (7:45 AM to 7 PM) IOP diurnal curves that were obtained in a glaucoma clinic over a 10-year period. Included were outpatients with ocular hypertension and all types of glaucoma, some of them treated, and healthy subjects. Forty-one percent of the peak IOP values were found on the earliest measurement (7:45-9 AM) and 24%, on the second measurement (9:45-11:30 AM). The mean ± SD ranges of diurnal IOP values spanned 5.0 ± 2.7 mm Hg for healthy subjects, 5.8 ± 3.1 mm Hg for subjects with glaucoma, and 6.8 ± 3.2 mm Hg for subjects with ocular hypertension.

A different daily IOP pattern was reported by Rotta-Bartelink et al, who measured daytime (9 AM to 5 PM) IOP in 28 subjects with POAG who were treated with a topical nonselective beta-blocker. The authors observed a steady increase in mean IOP throughout the day, with the highest measurement at 5 PM. The mean daily IOP range spanned 5.7 mm Hg.

Other studies have investigated 24-hour IOP behavior in untreated glaucoma patients. Liu et al studied 24 patients with open-angle glaucoma in a sleep laboratory. Intraocular pressure was measured every 2 hours with a pneumotonometer and values from both eyes were averaged. The mean ± SD nocturnal (11 PM to 7 AM) supine IOP was 22.3 ± 0.7 mm Hg and was significantly higher than the sitting IOP (19.6 ± 0.7 mm Hg) measured during waking hours (7 AM to 11 PM) (P < 0.01).

Konstas et al compared 24-hour IOP measurements in 40 eyes with exfoliative glaucoma and 40 eyes with POAG. Patients were newly diagnosed and untreated. The mean 24-hour range of IOP values spanned 13.5 mm Hg in eyes with exfoliative glaucoma and 8.5 mm Hg in eyes with POAG. In 45% of patients with exfoliative glaucoma and 30% of patients with POAG, the peak IOP was measured outside of office hours (defined as 10 PM to 6 AM). Ido et al studied 82 patients with open-angle glaucoma, 73 of whom were diagnosed as having normal-tension glaucoma with IOP less than 21 mm Hg at all time points, and 9 of whom had POAG. The mean ± SD 24-hour range of IOP values spanned 5.5 ± 1.6 mm Hg in 146 eyes with normal-tension glaucoma and 6.0 ± 2.5 mm Hg in 18 eyes with POAG. The peak IOP was measured outside of office hours (6 AM to 6 PM) in roughly one third of the patients. De Vivero et al retrospectively analyzed IOP diurnal curves in 101 untreated subjects with low-tension glaucoma in whom measurements were obtained between 8 AM and 10 PM. They found a similar mean ± SD daily fluctuation of 5.2 ± 2.2 mm Hg. The highest mean IOP (17.4 ± 3.0 mm Hg) was measured at 10 AM and gradually decreased during the day to reach its lowest value (15.0 ± 2.7 mm Hg) at 10 PM.

There has been recent emphasis on using drops with a better 24-hour IOP-lowering profile in patients with glaucoma. It is notable that the magnitude of 24-hour IOP fluctuation we found was observed in a group of patients of whom most were being treated with currently available medications and, of these, most were receiving prostaglandin analogues.

In analyzing IOP during office visits before admission, we included consecutive visits regardless of whether the treatment was identical to that used during the 24-hour monitoring. This analysis provides a “real-life” account of IOP in glaucoma patients, and our results demonstrate the potential for significant additional information being obtained from 24-hour monitoring in clinical practice.

Finally, variations in central corneal thickness (CCT) have been considered a source of IOP variation. Shah et al measured CCT and IOP in 56 eyes of 28 patients with suspected glaucoma during a 12-hour period. They did not find a significant variation in CCT or a correlation between change in IOP and change in CCT. Wickham et al found fluctuation of CCT in 51 patients during a 6-month period: 9.6 ± 26.9 µm in right eyes and 19.0 ± 29.2 µm in left eyes.

In conclusion, our data suggest that in glaucoma patients with advanced disease or with progression that is disproportionate to known IOP measurements, 24-hour IOP monitoring can reveal higher peaks and wider fluctuation of IOP than those found during typical office hours, measured either in multiple office visits or repeatedly during a single day. In these patients, 24-hour IOP monitoring may suggest a greater role for IOP-related risk for glaucoma progression than previously suspected and thus may justify a more aggressive IOP-lowering treatment strategy. Until accurate self-tonometry devices become widely
available, or until a method is found to accurately predict the 24-hour peak and range of IOP in individual patients, we suggest that clinicians consider obtaining 24-hour IOP measurements for selected patients.

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