

## Evaluation of influence of non-office hours diurnal variation of intraocular pressure in management of glaucoma

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### Abstract

**Aim and Objectives:** This article attempts to elucidate the role of round the clock IOP control and its relevance to current glaucoma practice. **Materials and Methods:** A prospective observational study was carried out on 50 patients of POAG or CACG on medical management whose intraocular pressures were found to be controlled by daytime office hours IOP estimation. The diurnal IOP readings obtained with Clarkes Hand held Perkins applanation tonometer and Reicherts Tonopen at 7am, 10am, 1pm, 4pm, 7pm, 10pm, 1am and 4am. Comparison of office hours IOP, extended office hours DVT and 24 hours IOP was done.

**Results:** Fifty patients were enrolled (mean age:  $53.88 \pm 8.42$  years) in the study. The mean office hours IOP for both eyes was significantly less ( $16.31 \pm 2.46$ ) than extended office hours ( $17.18 \pm 2.50$ ) and 24 hours DVT ( $17.49 \pm 2.45$ ). There was significant difference in IOP fluctuation in office ( $3.72 \pm 2.14$ ) versus extended office hours ( $9.26 \pm 3.11$ ) and 24 hours DVT ( $10.28 \pm 2.76$ ). The mean office hours peak IOP was significantly lower than that of extended office hours and 24 hours DVT.

**Conclusion:** 24-hour IOP monitoring can reveal higher peaks and wider fluctuation of IOP than those found during typical office hours, it suggests a greater role for IOP-related risk for glaucoma progression. Thus may justify a more aggressive IOP-lowering treatment strategy.

**Keywords:** Chronic angle closure glaucoma (CACG), Clarkes hand held perkins applanation tonometer, Intraocular pressure (IOP), glaucoma, Primary open angle glaucoma (POAG), Reicherts tonopen.

### Introduction

Diurnal IOP behavior in glaucoma patients has implications for both disease pathogenesis and management. Peak IOP and IOP fluctuations are known to be independent risk factors for the progression of glaucoma.<sup>1,2</sup> Since the management of glaucoma subjects is commonly based on isolated IOP readings obtained during the office-hours visits, there is a chance that the peak IOP and IOP fluctuations may be missed. For these reasons, monitoring IOP during the daytime or over a 24 h period offers obvious theoretical benefits. 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 considering the cost and inconvenience caused to both patient and treating physician or optometrist.<sup>3</sup>

Measurement of IOP during non-office hours thus may be useful in determining why optic nerve damage occurs evident in the form of progressive disc and visual field changes despite apparently adequately controlled pressure in normal office timings.<sup>4</sup> It can result in early detection of unfavorable intraocular pressure patterns by identifying IOP fluctuations and spikes which can help in early identification of glaucoma onset and progression as or change of glaucoma management in the form of critical assessment of efficacy of anti-glaucoma medication he is currently on or the need of any surgical intervention. The ability to show uncontrolled intraocular pressure patterns to the patients and impact of anti-glaucoma treatment may be an effective intervention to improve adherence to treatment.<sup>5</sup> By monitoring IOP more closely and prescribing medication that best controls IOP with the least amount of fluctuation, ophthalmologists can

offer patients the best therapy for their glaucoma thus personalizing IOP control for optimal glaucoma management. Hence the present study was undertaken to evaluate the influence of non-office hours IOP monitoring in glaucoma management.

### Materials and Methods

This is a hospital based prospective observational study, carried out on 50 patients of primary open angle glaucoma or chronic angle closure glaucoma on medical management whose intraocular pressures are found to be controlled by daytime office hours IOP estimation. The study included patients having age above 20 years with or without history of previous glaucoma surgery or argon laser trabeculoplasty/Selective laser trabeculoplasty or medical treatment. Patients with clinically proven IOP control (IOP measured once or twice during office hours) found to be within target IOP range, patients were scheduled for 24 hours IOP monitoring mainly when their previously recorded office hour IOP s did not seem to explain their present glaucomatous neuropathy or its progression (either disc or field progression), the patients already on medical therapy were using their glaucoma medications when admitted, patients of POAG or chronic ACG with PI patent with peripheral iridotomy done at least 8 weeks prior to consideration under this study, patients having open angles on gonioscopy, the IOP measurements used for statistical analysis were already CCT corrected to avoid error due to falsely high or low IOP were included in the study. Patient having secondary glaucomas, congenital and developmental glaucoma, glaucoma with uncontrolled intraocular pressure, any other anterior segment or posterior segment pathology,

corneal disease interfering with applanation tonometry, unwillingness of patient to give informed consent were excluded from the study. All patients were undergoing full ocular examination, slit lamp examination and disc evaluation.

The patients satisfying inclusion criterion were admitted in the hospital and entire procedure was explained to them and written informed consent was obtained. The diurnal IOP measurements were recorded at 7am, 10am, 1pm, 4pm, 7pm, 10pm, 1am and 4am using Clarkes Hand held Perkins applanation tonometer and Reicherts Tonopen. During the daytime i.e 7am, 10am, 1pm, 4pm, 7pm IOP was recorded in sitting position and during night time i.e 10 pm, 1 am, 4 am in supine position before the patient had gotten out of bed to resemble the normal physiological posture during day and night by single observer. Both the instruments i.e. Perkins applanation tonometer and Tonopen were calibrated before start of measurements. At each time point, the eyes were anaesthetized with 0.5% proparacaine eye drops and the tear film stained with fluorescein strips and measurements were taken. A drop of antibiotic (Moxifloxacin 0.3%) was instilled at the end of measurement to prevent chances of infection in case of any epithelial defect.

The observed 24 hour IOP data was classified into three types- 1. Office hours IOP (readings included 10 am, 1 pm, 4 pm), 2. Extended office hours DVT (readings included 10 am, 1 pm, 4 pm, 7 pm, 10 pm, 7 am), 3. All 24 hour IOP readings (10 am, 1 pm, 4 pm, 7 pm, 10 pm, 1 am, 4 am, 7 am). For better analysis and comparison standard statistical tests were used to analyse the observations and draw inference.

**Data Analysis**

Statistical analysis was done using IBM SPSS 2.2 software. Comparison of office hours IOP, extended office hours DVT and 24 hours IOP was done with respect to Mean IOP, IOP Fluctuation, Target IOP Vs Mean IOP, Peak IOP using dependent T test. Comparison of Glaucoma severity with 24 hour IOP fluctuation was done by one way ANOVA.

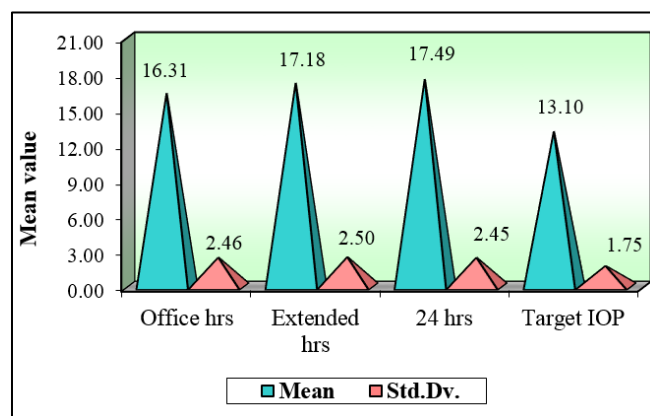
**Observations and Results**

The study included 87 eyes of 50 patients, of which 33 males (Mean age 54.85 ± 8.89) and 17 females (Mean age 52.00 ± 7.31). The mean age of total study population was 53.88 ± 8.42 years. During 24 hours IOP monitoring, 23 (46%) of patients had peak IOP at 4 AM, while 14 (28%) of patients had at 7 AM. 12 patients (24%) had maximum IOP at 7 PM, 1 (2%) had peak IOP at 10 AM. Thus majority of patients had their peak IOP outside normal office hours. Table 1 shows the details of the IOP measurements of the patients enrolled. The mean office hours IOP, office IOP fluctuations and office peak IOP for both eyes were statistically lower than observed in the extended office hours and 24 hours DVT. There was significant difference in mean IOP, IOP fluctuation and peak IOP in office versus extended office hours and 24 hours DVT.

**Table 1: Intraocular pressure (IOP) characteristics across the study population**

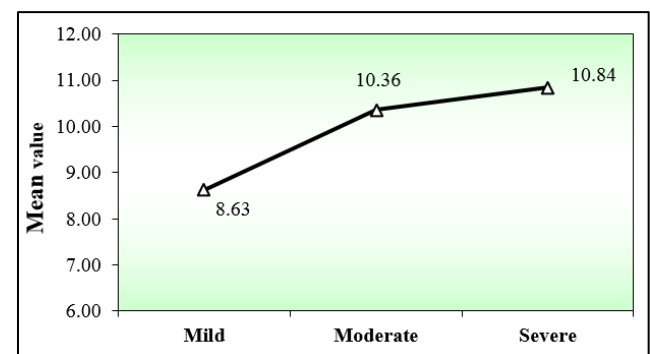
IOP (mmHg)	During office hours	During extended office hours	During 24 Hours DVT	P value
Mean IOP	16.31±2.46	17.18±2.50	17.49±2.45	0.0001
IOP Fluctuation	3.72±2.14	9.26±3.11	10.28±2.76	0.0001
Peak IOP	18.18±2.81	21.96±4.66	23.66±3.59	0.0001

We compared target IOP versus mean IOP at office hours, extended office hours and 24 hours. There was significant difference in right eye with respect to target IOP and office hours IOP. However, also found significant difference between target IOP and extended office hours and 24 hours DVT (Fig. 1).



**Fig. 1: Comparison of office hrs, extended hrs, 24 hrs with target IOP in both right and left eye with respect to mean score**

There was no significant difference between mild and moderate glaucoma (P =0.1028) as well as moderate and severe glaucoma (P = 0.7407) but significant difference observed between mild and severe glaucoma (P = 0.016) for mean 24 hour IOP fluctuation (Fig. 2).



**Fig. 2: Comparison of severity of glaucoma with IOP fluctuation**

The 24 hours IOP led to change of remedial measures either in the form of advancement of medical therapy or surgical treatment in 80 eyes. In right eyes, surgical treatment

was advised in 11 eyes (24.44%), augmentation of medical therapy in 29 eyes (64.44%), and no change of management in 5 eyes (11.11%). In left eyes, surgical treatment was advised in 12 eyes (28.57%), augmentation of medical therapy in 28 eyes (66.66%), and no change of management in 2 eyes (4.76%).

## Discussion

The current study included patients of POAG or CACG whose IOP was always normal in office hours but were still progressing in the form of disc or visual field progression. The office hours IOP data provide only a partial idea about the overall IOP, the main aim of the study was to find out how many patients reached higher IOPs or IOP fluctuation outside office hours and this was the novel point in our study.

The mean age of study population was 53.88 years, ranging from 40-70 years; the prevalence of primary open angle glaucoma was higher in men (66%) than in women (34%). This was comparable with different studies.<sup>3,6-8</sup> All our patients had visual acuity of 0.6 or more. Visual acuity testing is very important as it provides information to clinician regarding functional status of patient. In patients of glaucoma, visual acuity testing might not be completely reliable since patients have a good central vision (tunnel vision) in spite of advanced glaucomatous field damage. So, visual acuity testing should always be accompanied by testing of visual fields so as to assess patient's peripheral visual field. Central visual acuity may remain intact until the last stages of glaucoma. In cases of advanced glaucoma visual acuity plays an important role in selection of one treatment option over another.

The anterior segment examination becomes very important as it influences the outflow facility thus influencing intraocular pressure and its fluctuations. We had excluded all the secondary glaucomas. RAPD can give a status of optic nerve functioning of the patient. The pseudophakic patients have better outflow facility than patients with cataractous lens (lens being swollen). It also becomes important to assess the status of bleb in previously operated patients for trabeculectomy as well as the patency of peripheral iridectomy in patients of chronic ACG. So, it becomes important to evaluate all these factors as they affect IOP and in turn IOP fluctuation. We also assessed the number of POAG and chronic ACG patients. Our study showed a ratio of open-angle glaucoma to angle-closure glaucoma of 108/14 or 7.7:1. This ratio was similar to the ratio reported in some other Asian studies.<sup>2,7-13</sup> Optic disc examination is the most essential aspect of glaucoma evaluation and management. It helps in grading of the disease and plan treatment accordingly. IOP fluctuations affect disc damage. Based on Disc Damage Likelihood scale, 9 right eyes and 9 left eyes were having mild disc damage. The moderate disc damage was found in 12 right eyes and 14 left eyes. 24 right eyes and 19 left eyes were having severe disc damage amounting to total 43 (48.86%) eyes.

In current study, 6 right eyes and 2 left eyes were having IOP of 12 mmHg while IOP of 14 mmHg was found in 19 right eyes and 20 left eyes. However, 14 right eyes and 15 left

eyes were having IOP of 16 mmHg whereas IOP of 18 mmHg was found in 6 right eyes and 5 left eyes at first OPD visit during normal office hours. Assessment of visual fields is extremely mandatory because visual field progression in turn represents progressive constriction of fields which indicates glaucoma progression. We had calculated visual fields by Hodapp Parrish Anderson score. Total 22 eyes (11 rights and 11 left) were having advance damage on humphrey's visual field analysis. Early visual field damage was found in 18 eyes (9 right and 9 left eyes). 11 right eyes and 14 left eyes were having moderate damage on humphrey's visual field analysis. Severe visual field damage was found in 19 eyes (13 rights and 6 left). 3 eyes (1 right and 2 left) were showing normal disc on visual field analysis.

The status of current medication becomes important before undergoing 24 hour IOP measurement because it depicts how efficaciously the antiglaucoma drug is able to maintain uniform IOP throughout day and night. The way glaucoma medications affect IOP and its fluctuation becomes important in deciding glaucoma management. Out of 87 eyes, 42% eyes were on Bimatoprost, 23% were on Brimonidine, 16% were on Brinzolamide, 6% of eyes were on Dorzolamide, 24% were on Timolol Maleate, 9% were on Travoprost, 8% were not on any medication. Majority of the patients were on prostaglandin analogues. We calculated severity of glaucoma (AAO Classification) on the basis of disc and visual field damage. There was significant difference of mean 24 hour IOP fluctuation for mild and severe glaucoma ( $P = 0.016$ ). Severe glaucoma showed more IOP fluctuations. Total 16 eyes were having mild glaucoma; moderate glaucoma was present in total 28 eyes whereas 43 eyes were having severe glaucoma. Thus majority of our patients had severe glaucoma.

Peak IOP time can be picked up easily if attained at office hours, the normal office hours IOP may give false sense of security that intraocular pressures are under control, but when we did 24 hours IOP measurement, we found that in majority of patients, peak IOP was found early morning 4 am to 7 am. This clearly indicates that it is imperative to have 24 hours IOP monitoring at least in patients with disc and field progression and provide better alternative treatment strategies to have better round the clock IOP control. Many patients who are thought to be NTG after undergoing round the clock IOP monitoring can reveal peak outside office hours, thus the patients who are thought to be NTG turn out to be POAG. History also becomes important as in few patients who have shown peak IOP outside office hours gave an history of playing wind instruments or Valsalva maneuver (in the form of Yoga), thus lifestyle and even time of instillation of medication can influence Peak IOP.

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<sup>14</sup> and putative pathogenetic mechanisms unrelated to IOP<sup>15,16</sup> 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. IOP being a dynamic parameter is always subject to change, IOP fluctuation can be due to rise and dip in IOP, we found that in our study, IOP fluctuation was more due to rise in IOP thus explaining the need for more aggressive management strategies. Mean IOP is a strong predictor of glaucomatous damage. A desired therapeutic target is therefore uniform reduction of IOP throughout the 24 hours. The mean diurnal / 24 hr IOP in our study ( $17.49 \pm 2.45$  mmHg) was comparable to previous studies.<sup>3,8,17,18</sup>

Depending upon the disc findings and associated visual field changes, duration of disease, number of anti glaucoma medications and associated co- morbidities target IOP was set for each eye. It was found that target IOP was always lower than mean IOP at office hours, 24 hour IOP and extended DVT. Thus it indicates that 24 hour IOP measurement gives exact scenario of round the clock IOP of the patient. Since target IOP is always low than mean IOP more aggressive IOP controlling strategies either in the form of altering medical therapy or surgical management is needed. Our findings of 24 hour IOP monitoring suggested greater role for IOP-dependent mechanisms in the pathogenesis of glaucomatous progression. Moreover, identifying individual daily IOP patterns allows better decision about treatment, whether medical or surgical. 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 night time peak suggests that the target IOP may not need to be as low as previously assumed. In this study, 24 hour IOP monitoring lead to treatment change in 92% of patients, this was compare with study of Barkana et al<sup>8</sup> and Hughes et al.<sup>19</sup>

### Limitations of Study

A major flaw in the design of this study was that the glaucoma eyes were receiving treatment by one or a combination of different topical IOP lowering medications. The effects of each of these medications on the IOP profile are largely unknown. Drug compliance may have further influenced the results. The resulting IOP profiles were thus the combined effects of a mix of treatment, compliance, and disease issues.

### Conclusion

The present study suggests 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. In these patients, 24-hour IOP monitoring may suggest a greater role for IOP-related risk for glaucoma progression and thus may justify a more aggressive IOP-lowering treatment strategy. Extended DVT too revealed significant IOP peak and fluctuation. In view of patient inconvenience or requirement of admission, at least an extended DVT can be performed in such patients.

It is hoped that continuous 24-h IOP data may provide guidance to the identification of deleterious IOP patterns in

glaucomatous patients. Certain aspects of the 24-h IOP profile, such as the time and amplitude of peak IOP, frequency of spontaneous spikes, fluctuations, magnitude and duration of IOP rise and fall may be relevant as determinants of glaucoma development and progression.

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**Conflict of Interest:** None.

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