Commentary: Contact lens sensor-measured circadian intraocular pressure and glaucoma progression

Primary open angle glaucoma (POAG) is a multifactorial disease characterized by chronic optic neuropathy involving several risk factors. Intraocular pressure (IOP)[1] and alterations in ocular blood flow[2] contribute significantly to the onset and progression of glaucomatous optic nerve damage. Peak IOP and fluctuation[3] are also potential risk factors for glaucoma progression. Association between IOP peaks[4] and visual field deterioration in POAG has been documented in several studies, though role of IOP fluctuation continues to be debated. IOP measurements during routine office hours failed to detect peaks in a significant proportion of patients and detection of both IOP peak values as well as fluctuations was more accurate when 24 h IOP measurements[5] were made. More than 70% of IOP peaks are observed during the night and early morning hours. Repeated tonometry at regular time interval remains the clinically most practiced procedure to measure IOP fluctuation during day and night. However, such repeated IOP measurements to estimate 24 h diurnal variations is both impractical and an insufficient tool in clinical practice. Continued IOP monitoring, though critical in monitoring progression of disease, remains an unfulfilled need in glaucoma practices.

Several approaches are currently explored to study the circadian variation in IOP in normal and glaucomatous eyes. An interesting concept has been the use of a contact lens sensor (CLS) to measure corneal curvature variations linked to variations in IOP. An IOP variation of 1 mm Hg alters the radius of corneal curvature by 3 μm. Leonardi *et al*.[6] developed a soft contact lens embedded microstrain gauge that measures changes in corneal curvature and a good correlation between IOP variations and changes in corneal curvature was reported. Mansouri and Shaaraway[7] used these sensors to report 24 h variations in IOP and a nocturnal acrophase in two thirds of patients with POAG. Continuous 24-h IOP monitoring with the CLS revealed a nocturnal acrophase in healthy subjects and, more markedly, in glaucoma.[8] The diurnal IOP profile does not seem to predict the nocturnal rhythm, and hence the circadian IOP pattern should be evaluated in clinical practice and may be of significant import in management of glaucoma.

Rather than being a static variable, IOP fluctuates following a circadian rhythm. While healthy subjects reveal a 3–6 mm physiological increase in IOP at night, persons with glaucoma often have a more pronounced fluctuation exceeding 10 mmHg, which is considered an independent risk factor for disease progression. New devices to monitor IOP over 24 h, rather than snap-shot, single, day time office measurements in sitting posture are essential to assess and eliminate risk of progression. The SENSIMED triggerfish contact lens sensor (Sensimed AG, Lausanne, Switzerland) is a silicone contact lens with an embedded sensor that allows outpatient IOP monitoring as patients continue their routine activities. The CLS contains 2 titanium–platinum strain gauge or wire loops that detect fluctuations in the diameter of corneo scleral junction establishing a correlation between volumetric changes and IOP.[9] Measurements are taken for 30 s every 5 min for the entire 24 h period, generating a total of 288 responses. The lens transmits information through a battery powered antennae and data can be transferred through a bluetooth adapter for analysis. Measurements from CLS are in electrical units (milliVolts) and is represented graphically as IOP curves using an arbitrary unit of measure (millivolt equivalents, mV eq).

CLS-mediated diurnal IOP studies have made it possible to study the efficacy of treatments on the amplitude of IOP related fluctuation. Muniesa *et al*.,[10] for instance, observed that IOP fluctuation was greater in patients treated medically as compared to those who have had surgery, providing evidence to the effect that surgery could more efficaciously flatten the diurnal IOP curve as compared to medications. Not only did the patients in the medical arm have a more pronounced nocturnal acrophase compared to the surgical group, but a higher proportion of individuals on medical treatment had significantly elevated nocturnal IOP. Although medications effectively reduce mean IOP, they may not be as effective as surgical treatment in blunting IOP fluctuations. Surgeries probably preserve visual fields better by flattening the circadian rhythm of IOP. In a prospective, cross sectional study,[11] IOP related parameters obtained with 24 h recording with a CLS were correlated with the rate of visual field progression in treated glaucomatous eyes. Investigators of this study suggested CLS measured parameters may be useful in detecting eyes at higher risk of glaucoma progression while receiving treatment. IOP-related patterns throughout 24 h cycle

can be used to evaluate the effect of topical ocular hypotensive medications in blunting IOP fluctuations. Prostaglandin analogue,[12] but not other classes of medications, reduced the nocturnal IOP rise that accompanies the change in body position.

In the current issue, Dubey *et al*. have studied the relationship between nocturnal[13] intraocular pressure peak measured by CLS and glaucoma progression in treated eyes and have observed that thosewho progressed despite apparently normal day time IOP,were significantly more likely to experience nocturnal IOPspikes as compared to those who had not progressed onvisual field criteria. This study, however is limited by its small sample size and attempts to correlate a single parameter, the nocturnal peak IOP indicated by CLS as associated with visual field progression. De Moraes *et al*.,[14] in a similar, but a multi-centered study with a much larger sample size, have observed that 24 h CLS recordings may be associated with prior rates of visual field progression of glaucoma. Rather than merely nocturnal peak IOP, the investigators had observed several CLS variables that were associated with visual field progression that included mean peak ratio, night bursts ocular pulse frequency, and night bursts ocular pulse amplitudes. CLS variables had better association with glaucoma progression than Goldman applanation IOPs in a regression model.

The use of CLS to obtain patterns of electrical signals owing to volumetric changes in the eye, though does not measure the IOP, are correlated with fluctuations in IOP. In addition, the fact that CLS estimates how the ocular structures respond to pressure rather than IOP directly, provides far greater information than IOP alone in clinical management and understanding of structural alternations in glaucoma. From many of these studies of volumetric fluctuations of the eye obtained from CLS, it may be understood that in addition to the mechanical damage to retinal ganglion cell axons directly from elevated IOP, glaucomatous disc damage may also be a function of the response or resilience of ocular tissues to mechanical stress induced by IOP based on their biomechanical properties[14] as well. In summary, based on the current knowledge of CLS obtained parameters, it is possible to risk stratify treated patients with glaucoma, and be able to predict possible future visual field progression to make meaningful clinical decisions in glaucoma management. Future studies are essential to address practical barriers to routine use of contact lens sensor to identify individuals with diurnal peak pressures and appropriately treat them to achieve flattening of circadian fluctuations in IOP and prevent progressive visual loss from glaucoma.

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