Assessing the need and benefits of home tonometers in the management of patients with glaucoma

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Abstract: Intraocular pressure (IOP) measurement remains an integral part of managing patients with or at risk for glaucoma. The current gold standard, the Goldmann applanation tonometer, is influenced by ocular parameters, both extrinsic and intrinsic, that can lead to long- and short-term fluctuations and measurement errors. The biggest of all limitations of Goldmann-type tonometers is that the device provides a cross-sectional picture of IOP levels. To get an overall picture, including nocturnal IOP estimates, a home tonometry unit can provide valuable information. This article discusses the various sources that influence IOP measurement, home tonometers that are currently available, and the growing body of evidence that shows how home tonometry can be helpful in the care of individuals at risk for progression of glaucoma.

Keywords: home tonometry, intraocular pressure, sources of errors, telemetry

Introduction

Primary open-angle glaucoma is a slow, progressive, optic neuropathy with a characteristic optic disc excavation, progressive retinal nerve fiber layer loss, and acquired visual field loss. The exact pathophysiology of primary open-angle glaucoma is yet to be fully established, and a definite biological marker is not currently available. In the absence of this knowledge, various population-based studies¹–⁸ and clinical investigations have shed light on risk factors that predispose individuals to the disease. Intraocular pressure (IOP) is arguably the most important of the risk factors, as it remains the only modifiable risk factor that helps manage and control disease progression. With such importance placed on measured IOP, it becomes vital to measure this variable as accurately and frequently as possible. Thus, accurate measurements are required both in the office and at home. This article highlights the importance of IOP and physiological parameters, which can cause true and erroneous short- and long-term fluctuations in measured IOP values, thus making a case for the need of home tonometry. This article reviews various home tonometry devices and the evidence of its benefits in managing individuals at risk for glaucoma.

Importance of IOP in glaucoma management

Although IOP levels cannot fully explain glaucomatous pathology, its importance in managing patients with glaucoma should not be underestimated. Of the various risk factors known, such as age, race, family history, central corneal thickness, ocular perfusion, diabetes, and genetics, IOP is the only modifiable risk factor. Numerous population-based studies¹–⁸ have shown increased prevalence of primary open-angle glaucoma with an increase in IOP. In addition, numerous randomized controlled

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clinical trials have shown that reduction in IOP lessens the risk for visual field progression. These population-based studies and treatment trials cumulatively provide evidence that IOP plays an important role in pathogenesis of glaucoma. It must be remembered that having a cutoff level of IOP that is 21 mmHg or greater is an arbitrary cutoff and may yield low specificity as a diagnostic criterion. As low as 13%, or as high as 71%, of individuals having IOP values of 21 mmHg or greater, may signify glaucoma.

Factors influencing measurement of IOP

As clinicians, we look for data helpful in the management of disease, and we prefer data that are consistent, reproducible, accurate, and that do not greatly vary. IOP values, similar to many other physiological measurements, are in a state of flux and can vary both short- and long-term. Furthermore, to complicate the issue, there are numerous ocular biomechanical factors such as central corneal thickness, corneal curvature, corneal rigidity, and hydration that can lead to errors in clinical IOP measurement.17

There are numerous factors that lead to frank errors in IOP measurements, and there are other sources that lead to fluctuation in IOP levels.17 Since most current IOP measurement techniques only give an estimate at a given moment in time, short-term fluctuations can lead to a significant overestimation or underestimation of IOP from its true levels.

There are several factors that can lead to short- or long-term fluctuations of IOP. Overall IOP is thought to show polygenic inheritance, with a definite environmental contribution.18 The factors that can contribute to long-term fluctuations or variations in IOP are age, blood pressure, and seasonal variations.19-21 Although these factors tend to cause long-term fluctuations in IOP, its clinical importance is minimal. These factors are also very difficult to tease apart from those that induce short-term variations in IOP.

The factors that contribute to short-term variations in IOP values are diurnal variations, body posture, exercise, eye movements, activities causing Valsalva-like maneuver, and food and drug effects. These factors can pose a significant problem in clinical management, as IOP level is one of the integral measurements that helps decide the clinical efficacy of glaucoma medications and, to some extent, the management strategy in patients with or at risk for glaucoma. The diurnal variations in IOP levels are well known to occur in ocular-normal individuals. These IOP variations are to some extent exaggerated in patients with open-angle glaucoma.22-26 Although interindividual variations may be significant, on average IOP levels are highest before awakening and in the early morning hours, and are minimal late at night.27 This theory has been questioned recently, however: IOP may in fact increase at night,28-30 which may in part be responsible for progressive glaucomatous damage.30 Most of the variations in IOP that occur in the diurnal cycle are attributable to aqueous humor production, which varies as a function of levels of circulating cortisol and catecholeamines.31,32 Changes in aqueous humor inflow may not fully explain the diurnal fluctuations of IOP,30,31 and perhaps episcleral venous pressure variations contribute to the effect.30

The diurnal variation of IOP can be in the range of 3-9 mmHg, and obtaining this value may be fundamental to establishing a good estimate of target IOP range. In addition, diurnal variations become important in the long-term care of patients and in the follow-up of patients with glaucoma. Thus, the IOP measurement taken in the office becomes an important variable to be considered, particularly in follow-up visits related to IOP checks and when evaluating the efficacy of IOP-lowering medications in patients. Diurnal IOP measurement is very difficult to perform, particularly with clinical devices, and may require hospitalization. The availability of home tonometers will benefit in obtaining this difficult measurement.

Postural variations in IOP become significant because of measurement-related issues in clinics and because of lifestyle issues of the patients. Changes in body position from erect to supine or from erect to upside down can lead to changes in IOP on the magnitude of 16 mmHg and 30 mmHg, respectively.34 This short-term increase in IOP is a result of changes in the central venous pressure, which consequently produces changes in episcleral venous pressure.34 With the increase in popularity of yoga as a complementary and alternative medicinal technique,35,36 it is a fair question to ask whether these exercise postures, some of which require complete inversion, pose a risk to ocular health. In an observational prospective cohort, Baskaran et al36 show that assuming a complete inverted position leads to an immediate twofold increase in IOP from baseline that both persisted for the duration of the event and returned immediately to normal levels with assuming a seated position. This effect was seen in both Asian Indians and Caucasians.

Exercise has a variable effect on IOP: aerobic exercise causes lowering of IOP,37-40 whereas isometric exercises such as lifting weights may produce a small IOP increase during exertion.41 Such changes in IOP are not damaging in healthy adults42 but may play a role in open-angle glaucoma, particularly in progressive damage in patients with open-angle
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Both ocular healthy patients and patients with glaucoma, as postulated previously. Thus, caution is warranted among yoga-practicing patients with glaucoma. In addition, unilateral forced nostril breathing (UFNB), which occurs across a wide range of exertion from exercise, makes very specific changes to IOP because of its different effects on the autonomic nervous system. Right UFNB stimulates sympathetic activity by way of left-hemispheric stimulation, whereas left UFNB stimulates parasympathetic activity by way of right-hemispheric stimulation. As a result, IOP decreases with right nostril breathing and increases with left nostril breathing. Chen et al showed that right nostril breathing decreased IOP in right and left eyes significantly (9.6% and 6.7%, respectively), whereas left nostril breathing increased IOP an average of 5.7% and 2.5%, which was not statistically significant.

The increase in IOP during isometric exercise is a result of a Valsalva-like maneuver, which is an expiratory effort with the glottis closed. Proper breathing technique during exercises that involve lifting heavy weights is important to avoid elevation in IOP. Similarly, a lesser-known effect is a result of attempted inhalation against a closed glottis, called the Mueller maneuver, which causes a decrease in IOP. Both Valsalva and Mueller maneuvers have clinical significance, especially in nervous or anxious individuals who may hold their breath while IOP is being measured. The effect on IOP of holding one’s breath is further exaggerated by the strain produced while positioned in a slit lamp for measuring IOP, particularly in heavyset individuals.

Similarly, when positioned at the slit lamp, voluntary widening or attempted or involuntary narrowing of the palpebral fissure can produce a measurable transient spike in IOP. Prior work by Bain and Maurice in 1959 showed that if the venous flow is restricted by constriction around the neck, using a sphygmomanometer cuff to 40 mmHg leads to a doubling of IOP from baseline. It was postulated that restricting the venous circulation, particularly in the jugular vein, results in elevated episcleral venous pressure, which subsequently leads to elevated IOP. The same scenario is simulated to a lesser extent when wearing tight clothing, such as a tight necktie, which is shown to elevate IOP in both ocular healthy patients and patients with glaucoma. However, some other researchers have failed to confirm such an effect in ocular healthy individuals. The discordance in the outcome of these studies suggests that a more complex mechanism is involved in IOP changes resulting from tight clothing. Theelen et al found that the elevation in IOP resulting from tight clothing may be an artifact, and in reality, positioning of the patient in slit lamp is truly responsible for the elevation of IOP. In addition, it may be possible that the elevated venous pressure may have a difference in the amount of elevation in IOP in patients with glaucoma when compared with ocular healthy individuals.

Examining the normal physiological processes, we find that the measured IOP varies continuously with both cardiac and respiratory pulses and is seen in the pulsating mires when one performs Goldmann applanation tonometry. This is of limited importance in Goldmann applanation tonometry, as the mires are aligned midpoint of pulsations; furthermore, the time taken to perform tonometry is greater than the cyclic periodicity of the cardiac and respiratory pulse. However, this is of particular relevance to noncontact tonometry, as the measurements are obtained near-instantaneously. Thus, obtaining multiple measurements and averaging IOP is important when obtaining IOP using noncontact tonometers.

There are numerous instances when multiple measurements of IOP are needed. This may be in a nervous or uncooperative individual in whom the first measurement failed to yield reliable values, or it may be just to recheck measurements obtained. Repeated applanation using Goldmann-type tonometers is known to decrease IOP in the ipsilateral eye, as well as in the contralateral eye to a lesser extent. The decrease in IOP resulting from repeated applanation is a complex process, and neither tonographic effect nor changes in corneal biomechanics resulting from repeated applanation can fully explain the drop in IOP. The process of repeated applanation is not an issue when measurements are performed near instantaneously, as in noncontact tonometry, but it may be a problem if a time interval of a few minutes passes between repeated measurements using Goldmann-type tonometers and noncontact tonometry. It would be ideal to allow a 10-minute time interval if the measurements are to be repeated using Goldmann-type tonometers.

Other factors that lead to fluctuations in IOP measurement are related to the consumption of certain foods, beverages, and recreational drugs. Consumption of large quantities of water (500–1000 mL) has been shown to increase IOP in humans. Prior studies had proposed that a water-drinking test could be used as a predictive test to diagnose glaucoma. However, more recently, the water-drinking test has been used to identify peak increases of IOP. In healthy individuals, peak increases of an average of 2.24 mmHg occurred 10 minutes after water-loading. IOP increases on average of 5.00 mmHg were demonstrated in patients with glaucoma, with choroidal expansion also being associated with an increase in IOP, particularly in patients with angle-
closure glaucoma.\textsuperscript{72} Caffeine\textsuperscript{37,70} and excessive consumption of water can cause a transient increase in IOP\textsuperscript{37,71} whereas consumption of alcohol leads to a transient decrease in IOP.\textsuperscript{37,77} Smoking tobacco in the form of cigarettes can lead to a transient increase in IOP\textsuperscript{37,77} whereas smoking marijuana can lead to a decrease in IOP.\textsuperscript{75–78} Clinicians will have to pay particular attention to patients when IOP values do not match other clinical findings.

Ocular biometric factors such as myopia and accommodation can also cause fluctuations in IOP. A mean decrease of 1.8 mmHg was noted after an accommodation task in both young progressing myopes and emmetropes.\textsuperscript{79} These short-term variations in IOP make the case for having numerous IOP measurements and, possibly, measuring at different times of the day before initiating therapy or making changes to the management of patients. This may not be always possible in clinical setting or during office visits, and thus home tonometry becomes crucial in the management of glaucoma.

**Home tonometry**

Home tonometry as a concept has not picked up momentum because older attempts required topical anesthetics\textsuperscript{80,81} and involved expensive technology. In recent years, attempts have been made to make the device more affordable and not require anesthesia. Measuring IOP frequently and diurnally affords numerous advantages: home tonometry may give a truer picture of IOP values; measurements will not be influenced by errors induced in clinical settings, such as slit lamp position; and it may provide a decreased level of anxiety, particularly in nervous patients. On a more basic science level, measuring IOP around the clock provides better understanding of the aqueous humor dynamics, pathogenesis in glaucoma, and better understanding of the efficacy of IOP-lowering medications. Clinically, measuring the diurnal curve of IOP gives an idea of the fluctuations and range of IOP that can be used to better judge the risk level of patients and appropriately set up the target IOP range. Knowledge of diurnal IOP values may also be of great use in tailoring management in patients; that is, prescribing the appropriate medications when they are needed the most. It may help in the diagnosis and management of normal tension glaucoma and other patients with progressing glaucoma or suspect cases. In addition, high-risk cases such as pediatric glaucoma, where there is a need to closely monitor the efficacy of treatment, provide clinicians an insight that is not available by measurements obtained during an office visit.

**Proview home tonometer**

The Proview pressure phosphene tonometer developed by Fresco\textsuperscript{82} provided IOP measurements through the eyelids, did not require anesthesia, and was a fraction of the price of previous home tonometers. However, the measurements obtained by the Proview pressure phosphene tonometry were variable, and its agreement with the Goldmann applanation tonometer was moderate at best.\textsuperscript{82–88} Similar to other clinical tonometers, the Proview pressure phosphene tonometer only gives a snapshot of IOP in time.

**Icare rebound tonometer**

The Icare rebound tonometer (Icare; Helsinki, Finland) is a device that can measure IOP estimates without the use of topical anesthesia. It consists of an assembly of two coils coaxial to a probe shaft that bounce a magnetized probe off the cornea and detect the deceleration of the probe caused by the eye. A moving magnet within a coil induces changes in the voltage that are detected by the tonometer sensor. The voltage produced is proportional to the probe speed, and the deceleration speed seems to correlate best with IOP.\textsuperscript{89} The probe tip has a 1-mm-diameter plastic cover to minimize corneal damage. The probe tip is disposable between patients, so disinfection is not necessary.

When the device is activated for measurement, a spring drives the wire and probe forward rapidly. When the probe hits the cornea, it decelerates; the deceleration is more rapid if the IOP is high and slower if the IOP is low. The speed of deceleration is measured internally, and a chip calculates the IOP. As the contact with the cornea is momentary, no anesthetic is necessary.\textsuperscript{90}

This device is now modified for use as a home tonometer and is called Icare ONE. The ability of the Icare ONE to provide IOP estimates as a home tonometer has been evaluated in a few recent studies.\textsuperscript{91–93} Although it is known that rebound tonometry may be influenced by corneal parameter,\textsuperscript{94} its smaller design and the fact that it has no requirement for anesthetic before measurements makes it an ideal instrument for at-home and repeated use.

Studies have shown that the Icare ONE has a good agreement with the Goldmann applanation tonometer in about 70\% of cases.\textsuperscript{91,92} In addition, large fluctuations in IOP have been identified as an independent risk factor in glaucoma.\textsuperscript{95} Two recent studies have evaluated the use of Icare in pediatric population: Gandhi et al\textsuperscript{91} compared Icare ONE with the clinical gold standard in the pediatric population; good concordance in two-thirds of cases was found, and it was determined that the device was easy to understand and use.
by the caregiver. Flemmons et al.\textsuperscript{92} measured IOP diurnally, using Icare ONE, and concluded that about 30% of patients had a peak IOP measurement of 6 mmHg greater when measured diurnally versus at office measurement.\textsuperscript{92} Although a similar study with Icare ONE has not been performed in the adult population, one can hypothesize that such variations may exist in adults with primary open-angle glaucoma, and the measurements will be of great value in managing such patients.

Because the rebound tonometer has extremely short contact time with the eye, one may get a reading at any point in the IOP pulse cycle, and thus multiple readings need to be averaged to obtain a clinically useful value.

**Continuous monitoring of IOP**

All tonometers, both in the office and in the home, provide a snapshot of aqueous humor dynamics and IOP in time. The need for 24-hour continuous IOP measurement and types of devices are examined in detail in a separate review article.\textsuperscript{96} It would be ideal if IOP were measured automatically by a sensor inside or around the eye. This concept is not new: more than 40 years ago, Collins proposed that an encapsulated parallel capacitive circuit, when placed in the anterior chamber or in the posterior chamber, can measure IOP continuously and will not require an additional external power source.\textsuperscript{97} More recently, work from Walter and colleagues has led to the development of an intraocular lens that was capable of measuring IOP continuously.\textsuperscript{98,99} Chen et al.\textsuperscript{100} have successfully shown both in vitro and in vivo testing results of an implantable unpowered parylene-based micro-electro-mechanical-systems.\textsuperscript{100} The parylene-based sensor has been shown to be biocompatible, with minimally invasive implantation and no postoperative complications. This represents one of the most advanced techniques in wireless and continuous IOP monitoring devices. Fully implantable telemetry systems that allow continuous wireless monitoring of IOP were first tested in rabbits and rodents before their successful implantation in nonhuman primates.\textsuperscript{101} Although theoretically these permanent devices that are implanted inside the eye may give better IOP measurements that are less influenced by ocular biomechanical factors, the implantation of these permanent devices requires surgical procedures, and their long-term safety and biocompatibility are always a concern. A device that can be removed and that can be used on an ad hoc basis may be a safer alternative.

Prior attempts to create contact lens tonometers with built-in pressure sensors were limited because of the types of contact lens materials available. Rigid lenses were used, which were far from comfortable,\textsuperscript{102-104} and the data obtained were also not very reliable. In addition, the values obtained were influenced by ocular biomechanics, which caused variations in IOP measurement.\textsuperscript{103,104} These types of devices would have a vital role to play not only in 24-hour diurnal measurement of IOP but also in measuring ultra-short-term fluctuations in IOP that occur as a result of physiological changes such as saccadic eye movement.\textsuperscript{105}

More recently, Sensimed (Lausanne, Switzerland) has developed Triggerfish\textsuperscript{®}, a disposable silicone contact lens unit that is capable of measuring pressure variation in arbitrary units continuously. This was developed by Leonardi et al.\textsuperscript{107,108} and uses a soft contact lens with a strain gauge that allows the measurement of change in curvature of the cornea. A telemetry microprocessor and an antenna are also embedded into the contact lens for wireless power and data transfer. The principle of pressure measurement by Triggerfish\textsuperscript{®} is based on the fact that prior studies have shown that a change of 1 mmHg in IOP typically produces a change of 3 µm in corneal curvature in a cornea with a 7.8-mm radius of curvature.\textsuperscript{109,110} The pressure variation is measured every 5–10 minutes for a period of 30–60 seconds, giving a total of up to 144 measurements during a period of 24 hours. The Triggerfish\textsuperscript{®} is available in 3 base curves (9.0, 8.7, and 8.4 mm).\textsuperscript{111,112} The complete unit consists of a soft patch, worn around the eye, that allows an unobstructed view and that telemetrically receives data from contact lenses. A wire from the patch subsequently transmits data to a recorder attached to the patient’s clothes. The device is approved for use in Europe and costs about € 500 (approximately US$700), and is not available for sale in the United States. The published literature on clinical efficacy of Triggerfish\textsuperscript{®} is increasing. Freiberg et al.\textsuperscript{113} showed that there was a significant change in central corneal thickness (2.7%) after overnight wear of contact lens for IOP measurement. This change in corneal thickness was expected because of the hypoxic environment during eye closure. However, this change in corneal thickness was not significantly correlated to the IOP signal change obtained by the device.\textsuperscript{113}

The reproducibility of pressure patterns as measured by the contact lenses units was evaluated by Mansouri et al.\textsuperscript{112} in 37 patients who had a confirmed or suspected diagnosis of glaucoma.\textsuperscript{112} The researchers found that these units, which were worn for a 24-hour period twice (1 week apart), showed a fair-to-good reproducibility. That is, the correlation coefficient (Pearson correlation r) of the values generated by the device during the two sessions was 0.59 overall. The individuals not receiving glaucoma medications showed more variability...
(Pearson correlation r, 0.51) compared with individuals who were receiving glaucoma medications (Pearson correlation r, 0.63). The authors concluded that such a device may play a role in management of patients with glaucoma.

Mansouri and Shaarawy\textsuperscript{111} evaluated the contact lens pressure–measuring device in 15 patients with progressive damage resulting from open-angle glaucoma, despite controlled IOPs measured during office hours. They found that 69% of those patients had the highest IOP recorded during nocturnal periods, with prolonged peaks of pressure spikes greater than 1 hour seen in 80% of patients outside normal office hours. Obtaining the information of pressure fluctuations using the contact lens pressure measuring–device led to a change in management strategy in 73% of patients involved in the study.

The safety of this type of device was evaluated by two groups.\textsuperscript{112,113} As expected, the adverse effects for the overnight wear of these contact lens-based IOP measuring units were superficial punctuate keratitis and conjunctival hyperemia, which required no more than palliative treatment. Although blurred vision was reported by patients, the best corrected visual acuity remained unchanged before and after overnight wear of contact lenses.\textsuperscript{112}

Although excellent in its concept and for providing useful data, the measurements obtained using contact lens devices have significant room for improvement. There will be a transition phase before the arbitrary units that are generated by the devices are understood in terms of IOP that is measured and used in managing patients. The arbitrary units output by this device are affected by blinks and eye movement, both of which can be filtered mathematically, as these produce characteristic short spikes in measurement. The other factors that may affect measurement of these contact lens devices are change in stromal hydration throughout the day and night, corneal biomechanics, keratometry, corneal diameter, axial length, or scleral thickness and rigidity; these warrant further investigation.\textsuperscript{96}

Home tonometry is at an interesting point or phase of development, as prior units required anesthetic to measure IOP and were extremely expensive. The newer-generation devices do not require anesthetic, which is very welcome. With the advances in telemetric units, both implantable units and disposable noninvasive contact techniques, we are perhaps at the breaking point of obtaining information on aqueous humor dynamics that was not available previously. More research performed on the safety, validity, and clinical applicability of these devices will lead to establishing new clinical protocols on how to use them appropriately in clinical care.

**Disclosure**

The authors report no conflicts of interest in this work.

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