

Advances in 24-Hour IOP Monitoring

This technology will lead to more personalized care for patients.

BY ROBERT CHANG, MD

Is 24-hour IOP monitoring needed in glaucoma? This has been a difficult question to answer definitively. Until recently, there was no way to measure IOP continuously and, therefore, no answer on how additional data would change management. It has been well documented, however, that IOP fluctuates continuously over 24 hours, akin to a circadian rhythm but also with random variation. Making decisions on glaucoma based on only a few periodic IOP measurements during office hours is suboptimal. Furthermore, because IOP is the only major modifiable risk factor for the development and progression of glaucoma, the current, imperfect method of assessment using Goldmann applanation tonometry is ripe for improvement.

THERAPEUTIC EFFICACY

Demonstrating therapeutic efficacy requires accurately detecting changes in IOP, which can be difficult when the difference in millimeters of mercury can be as small as the standard deviation error of the measurement itself or artificially large due to an inaccurate baseline (regression to the mean). To better assess IOP fluctuation, some specialists have obtained repeated in-house diurnal IOP readings over a 24-hour period. This process is inconvenient, however, and does not provide a true reading during sleeping hours, because patients are awoken for the measurement.

Continuous ambulatory IOP monitoring would provide more information and might even identify novel patterns of IOP fluctuation. Arthur Sit, MD, made a strong case for 24-hour IOP monitoring in his review in the *Journal of Glaucoma*.¹

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IMPORTANT QUESTIONS

A long-debated matter is whether or not short-term fluctuation or long-term variability in IOP matters. Is the peak pressure more important? To define *abnormality*, one must first be able to define *normal fluctuation* for any given patient. Data from multiple clinical trials have provided mixed evidence on the importance of short-term and long-term fluctuations to the progression of glaucoma.

Again, however, the question is difficult to answer using today's imprecise methods of IOP measurement and current definitions of progression, which rely on subjective tests.² Studies have been confounded by IOP variation with sitting versus supine body positions as well as measurement errors owing to factors such as eye position, corneal biomechanical differences, Valsalva maneuver, and the fluorescence level of the tear film. The essentially constant variation due to external factors such as cardiac cycle, breathing pattern, eyelid and eye muscle movements, and physical activity have been presumed to have a minimal effect overall, but what about the nocturnal

period when the IOP tends to rise? Is preventing nocturnal IOP elevation more critical, particularly because some glaucoma medications have reduced IOP-lowering efficacy at night? The picture becomes even muddier when the ophthalmologist tries to take into account the ocular perfusion pressure and the translamellar gradient pressure.

PRESSURE SENSOR METHODS

Approaches

Advances in technology are reducing variability in IOP measurement and finally achieving 24-hour readings. The two main pressure sensor methods are temporary, noninvasive, external monitoring and permanent, invasive, internal monitoring. The permanent monitors have been implanted in rabbits and nonhuman primates, and several companies are studying implantable IOP transducers in humans.

Sensimed Triggerfish

The most well-known external IOP monitor is the Sensimed Triggerfish CLS (Sensimed), which provides an automated recording of continuous changes in ocular dimensions, a surrogate for IOP, over 24 hours. It is CE Mark approved but is currently pending FDA approval.

The Triggerfish is a soft contact lens. An embedded, miniaturized, telemetric, strain gauge sensor detects circumferential changes in the area of the corneo-scleral junction for 90 seconds about every 8.5 minutes. The information is sent wirelessly to a portable recorder via a flexible adhesive antenna worn around the eye for 24 hours. The technology is based on the assumption that a 1-mm Hg variation in IOP causes a 3- μ m change in the corneal radius of curvature.³ Interpretation of the results poses a challenge, however, because the output is an arbitrary unit proportional to the electric signal (in mV). The raw data represent a 24-hour pressure curve, which is useful for determining an individual's circadian rhythm. In a study by Mansouri et al of 40 glaucoma patients, 63% had a repeatable nocturnal elevation from baseline.⁴

It remains to be seen if treatment effects can be detected by the Triggerfish. A small study of nine patients published by Holló et al indicated that an average 5-mm Hg reduction from a prostaglandin analogue (as measured by Goldmann applanation tonometry) was not mirrored in the raw data using the Triggerfish.⁵ Eventually, longitudinal data will be needed to understand the effects of IOP variation as measured with the new pressure sensors.

Pro-IOP Implantable Microsensor

Implandata Ophthalmic Products, a medical device startup company from Hanover, Germany, has created the Pro-IOP implantable microsensor. Currently surgically implanted at the time of cataract surgery, the device can

telemetrically record the true manometric-equivalent IOP via a wireless handheld device that powers the sensor.

The sensor is under clinical investigation. The successful 1-year safety and functionality results of the ARGOS-01 pilot study involving six human patients were recently reported.⁶

The Pro-IOP sensor measures IOP in millimeters of mercury. Promising initial results suggest that the device can detect changes in glaucoma therapy. The company is also planning to develop an externally placed version of the sensor.

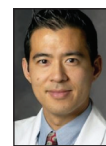
Other Devices

Two other companies are also racing to bring a permanent, implantable, wireless IOP sensor to market, including Solx and AcuMems. The latter is another startup that has implanted its microelectromechanical systems device in animals. Implantable IOP sensor technology has been continually refined for many years now to reach the point of a biocompatible, extremely small but accurate and safe low-powered device using radiofrequency identification.

CONCLUSION

It is an exciting time in the field of glaucoma. Continuous 24-hour IOP monitoring will almost certainly provide new information and lead to more personalized care for patients. For now, collecting many IOP readings throughout the day will truly qualify as "big data," so the next most important step is to determine the correlation of IOP fluctuation with existing structural and functional measures of glaucomatous progression. Maybe then, physicians will be able to determine what IOP pattern damages the optic nerve in a given patient. ■

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