24-hour intraocular pressure monitoring: past, present, and future

Monitoramento da pressão intraocular 24 horas: passado, presente e futuro

Sebastião Cronemberger[1]

[1] Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brasil.

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Corresponding author:
Sebastião Cronemberger
Faculdade de Medicina - Universidade Federal de Minas Gerais
Av. Prof. Alfredo Balena, 190, Sala 199,
Belo Horizonte, MG, 30130-100, Brasil
e-mail: secronem@gmail.com

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Primary open-angle glaucoma (POAG) is a complex neurodegenerative disease whose early diagnosis and treatment are crucial for preventing its progression. Millions of people worldwide still lose their sight due to POAG and the prediction is that, with longer life expectancy, more people would lose the vision.[1] Since the first research on glaucoma, the 24-hour intraocular pressure (IOP) monitoring, herein called diurnal curve of IOP (DCPo), is still a great challenge.

HISTORY

Richard Banister (1622) was the first to associate the loss of vision by glaucoma with high levels of IOP.[2] Adolph Weber (1855) was the first to establish the concept of glaucoma as an optic neuropathy.[2] In 1864, eserine and physostigmine (miotics) were introduced as the first drugs extracted from a plant used to treat the progression of glaucoma.[2] It is well known that elevated or uncontrolled IOP cause the excavation of the optic disc (glaucomatous excavation) and visual field (VF) loss. Since 1996, optic neuropathy and VF loss characterize the manifest glaucoma.[1,3] However, some patients may have an elevated IOP without VF defect or retinal nerve fiber layer (RNFL) loss.[3] Others may present pre-perimetric glaucoma characterized by RNFL loss detected by optical coherence tomography (OCT) in the absence of VF defect.[4] Until 1955, there were no standardized tonometer in Europe.[2] Since Leydhecker's investigations, it has been known that there is an interval of around 5 to 10 years between early detection of POAG and the first signs of optic neuropathy (pre-perimetric Glaucoma) or, even later, of functional changes.[5] This interval represents the resistance of the optic nerve to ocular hypertension (OH). In addition, the risk of conversion to glaucoma in patients with OH decreases approximately 14% for each mmHg of IOP reduction.[6]

GENERAL CONSIDERATIONS ON INTRAOCULAR PRESSURE

It is fundamental to know that an isolated IOP measurement does not reflect the patient's IOP. Much more information is necessary. However, the question that arises is why many patients still lose their vision despite all advances in diagnosis (OCT, OCT-A, Swept-OCT, VF (24-2, 10-2, 24-2c), brain research, etc.), in clinical (new drugs, fixed combinations, etc.) and surgical (trabecular surgery, etc.) treatment? We believe the answer is an inadequate and incomplete propaedeutic providing fault of early diagnosis and treatment.

ADEQUATE INTRAOCULAR PRESSURE CONTROL

Being a highly dynamic parameter with several influencing factors (ocular rigidity, central corneal thickness [CCT], corneal hysteresis, eyelid compression, psychic and

respiratory block, body position etc.) the 24-hour IOP monitoring is crucial, mainly for those patients with high suspicion of glaucoma and those whose glaucoma is progressing. Therefore, it is inconceivable to try to diagnose glaucoma or assess its progression with a single IOP measurement, especially in the afternoon. Visual field (subjective) and OCT (objective) are exams that present fewer variations than those found in the IOP assessment. With OCT, it is possible to characterize the rate of progression of RNFL loss as slow, moderate or rapid, but the glaucoma progression has an IOP peak as the cause that needs to be detected through a 24-hour IOP monitoring. Variations in IOP over 24 hours were first demonstrated by Sidler-Huguenin through bi-digital tonometry.[7] Using his tonometer, Maslenikow reported that in normal eyes the amplitude of the IOP oscillations did not exceed 2mmHg.[8] In 20 glaucomatous eyes, the IOP was highest in the morning. He found IOP fluctuations of up to 10mmHg and 23mmHg in one of the patients.[8] Thiel performed nocturnal tonometry and showed that IOP increases between 5:00 and 7:00 a.m., followed by a progressive decrease from morning to afternoon. He attributed this to cerebral and ocular venous stasis.[9] Sampaolesi et al. introduced a new method of evaluating DCPo performed with IOP measurements at 7:00 and 9:00 a.m., 12:00 a.m.; 3:00 p.m., 6:00 p.m., 9:00 p.m., and 12:00 p.m. by analyzing two parameters: mean IOP (IOPm) and variability (V).[10] Sampaolesi et al. introduced DCPo to evaluate the clinical and/or surgical treatment of glaucoma.[11] In Brazil, Fialho was the first to perform DCPo on 50 normal eyes using a Schiøtz tonometer. He reported that in the morning the IOP is higher than in the afternoon, and the oscillation of both eyes is parallel; 20% of the eyes showed an unchanged IOP at different times; the oscillation amplitude in most curves did not exceed 2mmHg and, exceptionally, oscillations of 4 to 5mmHg occurred. In 10% of the patients, he found reversed DCPo with lower morning values.[12] Sustaining constant IOP while reducing peaks may be as important as a low IOP in terms of disease progression, especially in patients who progress at low IOPms.[13] As a consequence, monitoring patients through DCPo provides the ophthalmologist with good advantages for the treatment sequence: precision, reliability, daily administration time of eye drops, combination of hypotensive medications and the choice of the best medication or medications for each patient. Calixto et al. studied DCPo in 86 normal eyes distributed in four age groups (15 to 25, 26 to 35, 36 to 45, and 46 to 58 years) and established the values of IOPm and V.[14] Subsequently, Calixto et al. carried out work with DCPo, including in the age group of 5 to 15 years and in congenital glaucoma. An important issue is that the normal values of IOP and DCPo were different abroad. In Brazil, Calixto et al. and Cronemberger et al. found 18mmHg as the normal superior limit of IOP and 13mmHg for the average in adults.[14,15] For children aged zero to 79 months, the normal IOP ranges from 7.1 to 11.8mmHg.[16] In DCPo of normal eyes of adults, the IOPm is equal to 17.3mmHg and V is equal to 2.2 as normal superior limits. In Argentina, Sampaolesi et al. found values similar to those in Brazil. The average IOP is equal to 15.5mmHg with the IOPm of 19.2mmHg and is V equal to 2.1 as normal superior limit.[10] For children, the IOP values were still more similar, average 8mmHg and 12mmHg as the normal superior limit for children zero to 60 months. However, in Europe the IOP values were higher than those found in Brazil and Argentina: average of 15.5mmHg with a normal superior limit equal to 20.5mmHg using the Goldmann applanation tonometer (GAT; 1957) or the Schiøtz tonometer.[5] In the United States, the normal superior limit of IOP is 21mmHg for adults and children. This value is higher than those found in Belo Horizonte and is elevated for children aged zero to 60 months. Analyzing IOP peaks during DCPo, Cronemberger et al. found the peak IOP (IOP at 6:00 am in bed and darkness) in 66.3% of 232 glaucoma suspects and 68.6% of 140 glaucoma patients whose IOP has appeared normal or apparently controlled in the office.[15] Rodrigues et al. compared DCPo at 6:00 a.m. in bed and darkness, mini-curve and isolated IOP measurement at 6:00 a.m. in terms of detecting IOP peak, and concluded that DCPo detected more IOP peaks than the mini-curve; the average IOP at 6:00 a.m. was higher with the patient lying down; the IOP at 6:00 a.m. with the patient lying down was higher than the average IOP of DCPo and the mini-curve.[17] In treated congenital glaucoma, the DCPo may be inverted with maximum IOP values occurring between 9:00 and 12:00 a.m. (74.7%), and the minimum values at 6:00 a.m. and 12:00 a.m.[18] This inverted DCPo can occur in patients who change their habits mainly when they work at night and sleep during the day. Therefore, 24-hour IOP monitoring is the best workup for detecting the IOP peak in glaucoma. The only disadvantage is that, in practice, it is not feasible, and it is time consuming for both patients and doctors, in addition to being expensive. Susanna et al. reported that the mean peak IOP and the percentage of change in IOP during the water drinking test (WDT) were significantly higher in patients with progression of VF loss compared to patients who did not progress.[19] In a comparative study between DCPo and the association of the ambulatory curve with WDT in POAG, NPG, and normal eyes, Meirelles et al. concluded that the association of the ambulatory curve with WDT was not effective in predicting DCPo peaks and fluctuations.[20] The ambulatory curve and the WDT must be analyzed separately. The authors reported that the most

effective procedure to predict the peak and fluctuation IOP was the ambulatory curve.[20] On the contrary, Vasconcelos-Moraes et al. compared WDT with a modified mini DCPo (IOP measurements taken during office-hours) and concluded that IOP peaks can be detected during WDT.[21] WDT can be used in clinical practice to estimate the peaks observed during daytime DCPo and to evaluate the state of exit of aqueous humor. However, they found limited agreement between IOP peaks of the methods.[21] Analyzing reproducibility, Medina et al. reported that 75% of the IOP peaks in DCPo performed on consecutive days showed a variation greater than 20%, similar to the findings for WDT.[22] They also reported that WDT shows low levels of agreement when performed at different times of the day, a limitation to its applicability for the diagnosis and follow-up of patients with glaucoma. However, due to the significant number of articles and editorials recently published in several international centers and with hundreds of patients studied, the potential of this stress test provides important additional information in the IOP peak assessment in glaucoma patients. One frequent issue in 24-hour IOP monitoring is what should we consider: IOP peak or IOP fluctuation? The answer is that as occurs with blood pressure, glycemia, leukocytes, etc., IOP presents a normal circadian fluctuation (1 to 6mmHg). The peak of IOP is nothing more than an abnormal IOP fluctuation, which means an IOP variation> 6mmHg. Cronemberger et al. evaluated the sensitivity and specificity, positive and negative predictive values and false positive and false negative probability of WDT, ibopamine test, FDT, blue-yellow perimetry and DCPo in glaucoma suspects.[23] DCPo showed greater sensitivity with greater positive predictive value. The FDT showed a very low probability of false negative. The ibopamine test, WDT and blue-yellow perimetry showed a very high probability of false positive.[23] In normal pressure glaucoma (NPG) that was suspected or diagnosed based on isolated IOP measurements, 24-hour IOP monitoring is indispensable to rule out diagnosis.[24] Many patients who have the diagnosis of NPG can present an IOP peak at 6:00 a.m. in bed and in darkness.[24] Cronemberger et al. reported that CCT does not present significant variation during the DCPo and, in consequence, does not have relationship with IOP variation.[25] Cronemberger et al. have studied the correlation between the thickness of the RNFL and the variation in IOP in suspected glaucoma and patients with POAG.[26] They concluded that IOP at 6:00 a.m. and ΔIOP had negative correlations with RNFL thickness quadrants in POAG. In suspected glaucoma, this negative correlation of RNFL thickness occurred between the IOP taken at 6:00 a.m. and the inferior quadrant. These findings may indicate potential risk factors for glaucoma progression.[26] The Contact Lens Sensor (CLS) Sensimed Triggerfish® approved by the Food and Drug Administration (FDA) in 2016 has been used to detect IOP-related changes in one eye over a 24-hour period.[27] However, it does not give real IOP values and presents controversial results in relation to other methods of measuring IOP.[27] Sharma et al. showed that 24-hour CLS IOP measurement is safe and well tolerated in glaucoma patients.[28] There were no short-term or permanent complications or side effects. However, there was a weak correlation between changes in Triggerfish® data and IOP measurements with the GAT. Contact Lens Sensor does not allow an estimation of the IOP in mmHg and cannot fully replace GAT. It could complement and add useful information on the innovative 24-hour continuous IOP profile and nocturnal measurements not covered by static clinical GAT.[28] Artificial intelligence (AI) has the potential to transform glaucoma treatment. Research will be crucial in the coming years to solve current problems and develop rigorous performance evaluation protocols. However, prospective studies on the impact of using AI algorithms are necessary to assess the real benefit in clinical practice.[28] A work carried out at São Geraldo Hospital evaluated the maximum IOP forecast at 6:00 a.m. in patients who performed 24-hour IOP monitoring.[29] The authors used machine learning to predict the IOP spikes at 6:00 a.m. in patients suspected and having POAG. They included 98 eyes of 98 patients who underwent 24-hour DCPo (including IOP measurements at 6:00 a.m. in bed and in darkness). The DCPo was defined as a series of three measurements at 8:00 a.m., 9:00 a.m. and 11:00 a.m. from the 24:00-hour DCPo. Two new variables were introduced: slope and concavity. The slope of the curve was calculated as the difference between the IOP measurements at 9:00 a.m. and 8:00 a.m. and reflected the change in IOP in the first hour. The concavity of the curve was calculated as the difference between the slopes at 9:00 a.m. and 8:00 a.m. and indicated whether the curve was higher or lower. The authors found three groups related to the forecast risk of the IOP peak at 6:00 a.m.: low risk for eyes with IOP <19mmHg at 8:00 a.m. and curve concavity < 2.3; intermediate risk for eyes with IOP <19mmHg at 8:00 a.m. and curve concavity ≥2.3 and the best predictors of IOP 6:00 a.m. >21mmHg were IOP 8:00 a.m. ≥19mmHg and DCPo concavity ≥2.3.[29] The proposed model achieved a sensitivity of 100% and a specificity of 86%, resulting in an accuracy of 93%. This new approach to the DCPo may become a widely used tool in daily practice and the indication of a 24-hour monitoring IOP could be rationalized according to risk stratification.[29]

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