Continuous Intraocular Pressure Fluctuation in Glaucoma and Glaucoma Suspect

Glokom ve Glokom Şüphesinde Sürekli Göz İçi Basınç Dalgalanması

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ABSTRACT

Purpose: The aim was to evaluate the circadian rhythm of intraocular pressure in glaucoma patients and patients with glaucoma suspect using the Sensimed Triggerfish® system.

Materials and Methods: The Sensimed Triggerfish® system was applied to nine patients. Before the application, a full ophthalmic examination was performed in all patients. Patient graphics were evaluated for diurnal variation and peak intraocular pressure.

Results: The patient diagnoses were pseudoexfoliation glaucoma (4 patients/44.4%), glaucoma suspect with pseudoexfoliation (3 patients/33.4%), primary open angle glaucoma (1 patient/11.1%), and pigmentary glaucoma (1 patient /11.1%). Two patients (22.2%) could not complete the 24-h measurement. After the application, the treatment modalities of four (44.4%) patients were changed. All had a diagnosis of pseudoexfoliation glaucoma. In addition, medical treatment was prescribed to two (22.2%) glaucoma suspect with pseudoexfoliation patients. All curves of patients with pseudoexfoliation showed an elevation during the nocturnal period and the peak intraocular pressure curves were observed between 01:00-09:00.

Conclusion: A 24-h intraocular pressure measurement is important for the diagnosis of glaucoma, the selection of treatment modality, and the evaluation of treatment efficacy.

Key Words: Diurnal variation, glaucoma, sensimed triggerfish system.

ÖZ

Amaç: Sensimed Triggerfish® sistemi ile glokom şüphesi olan hastalarda ve glokom hastalarında göz içi basıncının sirkadyen ritminin değerlendirmesi.

Gereç ve Yöntem: Sensimed Triggerfish® sistemi 9 hastaya uygulandı. İşlem öncesi hastaların hepsine detaylı oftalmolojik muayene yapıldı. Hastalara ait grafikler; diurnal değişiklikler ve maksimum göz içi basıncı değerleri açısından değerlendirildi.

Bulgular: Hastaların tanıları; psödoeksfoliatif glokom (4 hasta/%44.4), psödoeksfoliasyonun eşlik ettiği glokom şüphesi (3 hasta/%33.4), primer açık açılı glokom (1 hasta/%11.1) ve pigmenter glokomdu (1 hasta/%11.1). İki (%22.2) hasta 24 saatlik ölçümü tamamlayamadı. Uygulamanın sonuçlarına gore 4 (%44.4) hastanın tedavisi değiştirildi. Tedavisi değiştirilen hastaların hepsinin tanısı psödoeksfoliatif glokomdu. Ayrıca glokom şüphesi olan psödoeksfoliasyonlu 2 (%22.2) hastaya medikal tedavi başlandı. Psödoeksfoliasyonu olan hastaların hepsinin grafiklerinde gece peryodunda yükselme izlendi ve bu hastaların maksimum göz içi basınç değerleri 01:00-09:00 arasında ölçüldü.

Tartışma: Yirmi dört saatlik göz içi basınç ölçümü glokom tanısının konulması, tedavi modalitelerinin belirlenmesi ve tedavi etkinliğinin değerlendirilmesi açısından önem taşımaktadır.

Anahtar Kelimeler: Diurnal değişiklik, glokom, sensimed triggerfish sistemi.

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Geliş Tarihi - Received: 28.07.2015
Kabul Tarihi - Accepted: 27.11.2015
Glo-Kat 2016;11:172-176

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INTRODUCTION

Glaucoma is a chronic neurodegenerative disease that affects 70 million people worldwide[1] and it is one of the main causes of irreversible blindness. Elevated intraocular pressure (IOP) is one of the risk factors for the development and progression of glaucoma.[2-4]

Lowering IOP is the only evidence-based treatment for preventing the development and progression of glaucoma. Therefore, the main target of glaucoma treatment should be reducing IOP. IOP has a diurnal fluctuation and the values change between 3-6 mmHg in normal eyes, though it can be 10 mmHg and higher in glaucoma patients.[5-7] Most studies have shown IOP values are higher in the morning and decrease in the evening in patients with different glaucoma types.[8,9] As well, studies that evaluate 24-h IOP showed the highest IOP values are most frequently during the nocturnal period.[10,11] Therefore, a single measurement is not enough for the diagnosis of glaucoma, the selection of treatment modality, and the evaluation of treatment efficacy.

In this study, the aim was to evaluate the circadian rhythm of IOP in glaucoma patients and patients with glaucoma suspect using the Sensimed Triggerfish® system, which monitors continuous IOP for 24h.

MATERIAL AND METHODS

Nine patients who were followed with a diagnosis of glaucoma or glaucoma suspect at Ankara University School of Medicine, Department of Ophthalmology were included in this study. The Sensimed Triggerfish® system was applied to evaluate the 24-h IOP profiles. All patients had suspicion of inadequate treatment. Ethics committee approval was obtained [Health Ministry/Drug and Medical Device Foundation, acception date: 28.06.2013, acception number: 71146310 (2013-AC-CE-25)] and all patients obtained informed consent before the application. This study was supported by Ankara University Scientific Research Support Department (Project Number: 13H3330001).

All patients underwent a complete ophthalmic examination. The IOPs were measured with Goldmann applanation tonometry (GAT). Gonioscopy and a dilated fundus examination were performed. Central corneal thickness (CCT) was measured by ultrasonic pachymetry (Alcon, OcuScan RxP). The optic nerve was evaluated by spectral domain optical coherence tomography (Cirrus high-definition OCT; Carl Zeiss, Meditec, Dublin, CA, USA).

The visual field examination was performed with the Humphrey 750i Visual Field Analyzer (SITA-Standard, Carl Zeiss, Meditec, Dublin, CA, USA).

Pseudoexfoliation glaucoma was diagnosed by the presence of pseudoexfoliation in the anterior segment, elevated IOP (>21 mmHg), typical glaucomatous optic nerve changes (notching, thinner neuroretinal rim, and increased cup-to-disc (c/d) ratio), and glaucomatous visual field defects. Primary open angle glaucoma was diagnosed by elevated IOP (>21 mmHg), open angle at gonioscopy, typical glaucomatous optic nerve changes, and glaucomatous visual field defects. The diagnostic criteria of pigmentary glaucoma was trabecular meshwork pigmentation, the presence of a Krukenberg spindle and mid-peripheral iris transillumination, elevated IOP (>21 mmHg), open angle at gonioscopy, typical glaucomatous optic nerve changes, and glaucomatous visual field defects.

The Sensimed Triggerfish® system is the first commercially available continuous 24-h IOP monitoring system that contains a telemetric contact lens sensor, an antenna, and a portable recorder. The contact lens is made of a disposable, soft hydrophilic silicone material with two embedded platinum–titanium strain gauges. These gauges detect the circumferential changes in the area of the corneo-scleral junction. When the IOP increases, the circumference of the cornea increases and this change is detected by the strain gauges. Then, the signals acquired from the contact lens are perceived by a flexible adhesive antenna worn around the eye. The data is transmitted through a thin flexible cable from the antenna to the portable recorder device worn around the patient's waist, and then recorded profiles are visualized graphically on a computer interface.

Before the application of the Sensimed Triggerfish® system, IOP measurements with GAT were taken three times at 5-min intervals and then the contact lens system was fitted to the eye. Patients were informed about the recording of their daily activities during the application time. Then, 24 h later, the contact lens was removed and 5 min later, GAT IOP was measured three times at 5-min intervals again. Data from the portable recorder were transferred to a computer. The IOP profiles were evaluated along with the other findings, such as visual field and retinal nerve fiber layer changes. Treatment modalities were organized according to the ophthalmic examination findings, ancillary test results, and 24-h IOP profiles together.

RESULTS

The Sensimed Triggerfish® system was fitted to nine patients (4 female, 5 male). The mean age was 62.4 (52-71) years. The diagnoses of patients were pseudoexfoliation glaucoma (4 patients/44.4%), glaucoma suspect with pseudoexfoliation (3 patients/33.4%), primary open angle glaucoma (1 patient/11.1%), and pigmentary glaucoma (1 patient/11.1%). All patients except those with glaucoma suspect with pseudoexfoliation were under medical treatment.

None of the patients had dry eye before the contact lens system application and all of them tolerated the contact lens system easily with a minor complication of superficial punctate keratitis and conjunctival hyperemia. These findings resolved within 24 h.

Two patients (22.2%) could not complete the 24-h measurement due to battery insufficiency and technical device malfunction. The recording times for these patients were nine and 20 h. One was glaucoma suspect with pseudoexfoliation and the other was pseudoexfoliation glaucoma.

After the contact lens system application, treatment modalities of four (44.4%) patients were changed. All had a diagnosis of pseudoexfoliation glaucoma. Although one patient with pseudoexfoliation glaucoma could not complete the 24-h measurement, medical treatment was changed because of the elevation of the IOP curve in the recording period. In addition, medical treatment was prescribed to two (22.2%) glaucoma suspect with pseudoexfoliation patients. IOP curves of all pseudoexfoliation patients showed an elevation during the nocturnal period and the peak IOP curves were observed between 01:00–09:00.

We here reported clinical findings and the Sensimed Triggerfish® system results of three patients.

Case 1

A 64-year-old male patient had a medical history of travoprost and timolol maleate fixed combination once a day for the previous two years due to pseudoexfoliation glaucoma in the right eye. The maximum IOP value in the follow-up period was 22 mmHg and his central corneal thickness was 446 μm in the right eye. The c/d ratio was 0.3. The IOPs at the baseline and at the end of monitoring were 19 mmHg and 21 mmHg, respectively. The IOP curve increased continuously during the evening and nocturnal period (Figure 1). After the contact lens system application, a new anti-glaucomatous drug was added to the treatment.

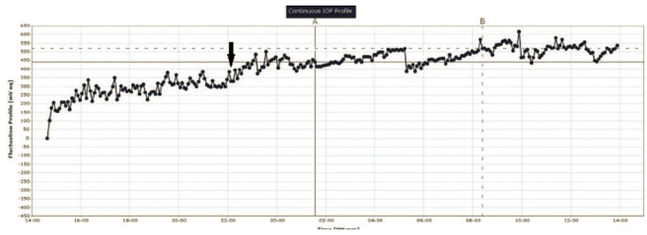

Figure 1: *The IOP curve showed elevation after 22:00 (arrow).*

Case 2

A 65-year-old woman with a diagnosis of pseudoexfoliation glaucoma in the left eye had a treatment of latanoprost ophthalmic solution once a day. During follow-up, the maximum IOP measurement was 28 mmHg, central corneal thickness was 580 µm, and the c/d ratio was 0.5. The IOP measurements before and after the application of the contact lens system were 24 and 27 mmHg, respectively. An elevation of the IOP curve was seen between 00:00–02:00 (Figure 2, arrows) and then the curve hit a plateau. Latanoprost medication was stopped and a fixed combination was prescribed.

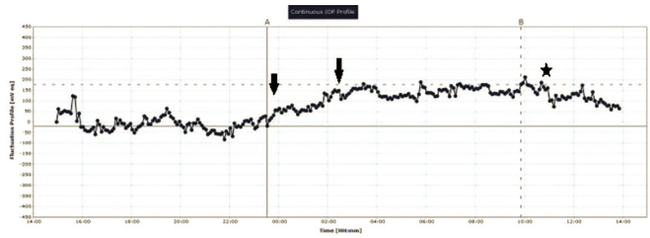

Figure 2: *The IOP curve showed elevation between 00:00-02:00 (arrows), had a plateau until 10:30 (star) and then started to decrease.*

Case 3

A 56-year-old female patient had glaucoma suspect in her right eye. On slit lamp exam, the pseudoexfoliative material was seen in the iris margins. The iridocorneal angle was grade 4 open. The maximum IOP measurement during the follow-up period was 22 mmHg. Central corneal thickness was 590 µm. There was a c/d asymmetry with the values of 0.5/0.3 in the right/left eye. In the right eye, borderline retinal nerve fiber layer thickness at one clock hour quadrant was detected by optic cube OCT. Because of these findings, a contact lens was fitted to the right eye. The IOPs at the baseline and at the end of monitoring were 22 mmHg and 24 mmHg, respectively. The IOP curve increased after 00:00 (Figure 4, arrow) and hit a plateau until 08:00 (Figure 3, star). Because of the elevation of the IOP curve in the nocturnal period, medical treatment was prescribed.

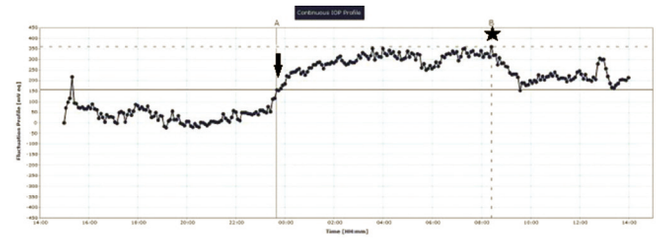

Figure 3: *The IOP curve showed elevation after 00:00 (arrow) and had peak curve during the nocturnal period (star).*

DISCUSSION

Intraocular pressure is a dynamic parameter with a circadian rhythm in healthy eyes. The elevation of IOP is more prominent in glaucoma patients. IOP measurements can increase up to 15 mmHg in patients with pseudoexfoliation glaucoma. These patients have a higher mean IOP range, as well as a higher maximum and minimum IOP than primary open-angle glaucoma.[12,13] Occasionally, the peak-level IOP of these patients could not be established during office hours and this could be the reason for the poor response to medical treatment. A 24-h IOP measurement is necessary, especially for pseudoexfoliation syndrome or glaucoma.

Hughes et al.,[14] showed that the treatment modality of most glaucoma patients changes due to the diurnal IOP variations. In addition, IOP fluctuation is a risk factor for glaucoma progression.[15] Therefore, diurnal IOP measurement should be a routine procedure in clinical practice.

Today, GAT is the gold standard procedure to evaluate IOP. However, the most important limitation of this method is not to evaluate IOP changes permanently. From 1957 until today, different recording methods were created for monitoring 24-h IOP.[16-21] However, none was able to bring a product to the market. Today, the most common method to evaluate the 24-h IOP is diurnal IOP measurements. In this method, multiple IOP measurements at different times are taken, but the patient should be hospitalized and for nocturnal measurements, the patient should be awake. One of the limitations of this method is to wake up the patient and change his or her body position.

To wake up the patient is a stress factor that can affect the measurement and cause artefacts.[22] In addition, IOP varies during the 24-h period in body positions. Malihi and Sit evaluated the effect of different head and body positions on IOP in non-glaucomatous individuals, and they showed the IOP is higher in recumbent (supine, right and left lateral decubitis) positions compared to sitting (with neck flexed, extended and neutral) positions.[23] In addition, in other studies, the average nocturnal IOP in supine position was found to be significantly higher than the average awake IOP in a sitting position in untreated glaucoma patients.[11,24] Another mechanism for the higher IOP measurements during the nocturnal period is thought to be increased episcleral venous pressure and redistribution of body fluid.[25]

In this study, diurnal IOP variations in patients were evaluated with the Sensimed Triggerfish® system, the first commercially available continuous 24-h IOP monitoring system. Treatment modalities of four (44.4%) patients were changed and antiglaucomatous treatment was prescribed to two (22.2%) patients after the application due to the diurnal variation, especially seen in the nocturnal period. All patients whose treatment modality changed had pseudoexfoliation glaucoma and two patients that began antiglaucomatous treatment had glaucoma suspect with pseudoexfoliation. It can be thought that 24-h IOP monitoring can be more important in patients with pseudoexfoliation. As well, Mansouri et al. performed this system on 15 eyes suffering from progressive open angle glaucoma with controlled IOPs during office hours and the treatment modality was changed in 73% of eyes.[26]

De Moraes et al.,[27] found that the peak IOP had a better predictor value of glaucomatous progression than the mean IOP or fluctuation. Therefore, 24-h monitoring of IOP should be an important parameter for disease management. Rao found that patients with pseudoexfoliation syndrome had higher IOP values during the latter part of the day, especially at 05:00.[28] However, in this study, IOP values were measured at certain times. Unlike this study, we evaluated 24-h IOP monitoring and we found the peak IOP curves of patients with pseudoexfoliation during the nocturnal period. The interval time of peak IOP curves was 01:00-09:00. This contact lens system can be a suitable method for IOP monitoring during this interval with the advantages of a stable body position and keeping the patient asleep.

Diurnal IOP variation is not only important for treatment decisions. It is also important for the selection of an antiglaucomatous drug. IOP-lowering medications have different efficacies during the nocturnal and waking periods. Although beta adrenergic blocking agents are effective during the diurnal period, they have no nocturnal efficacy.[29] Gulati et al. evaluated the diurnal and nocturnal efficacy of timolol maleate twice daily, dorzolamide hydrochloride twice daily, and latanoprost in the evening. It was shown that latanoprost lowered nocturnal IOP, while neither timolol nor dorzolamide affected the nocturnal IOP measurements.[30] Therefore, the time of the peak IOP value is important for the selection of adequate medication.

In our study, the 24-h IOP profile was not the only parameter for the decision of treatment modalities. Maximum GAT IOP values, central corneal thicknesses, glaucomatous visual field defects, and retinal nerve fiber layer changes were evaluated together.

The safety and tolerability of this system had been evaluated in different studies.[26,31-33] Lorenz et al.,[33] found similar safety and tolerability in healthy and glaucomatous eyes. Conjunctival erythema, conjunctival edema, epithelial microdefects, and lid edema were the main adverse effects. Results of the other studies were similar and these studies suggest this system demonstrates good safety and tolerability.[26,31,32] In our study, all patients tolerated this system and the only complication was superficial punctate keratitis and conjunctival hyperemia, which resolved within 24 h.

Although this system is important for monitoring a 24-h IOP profile, the main limitation is does not give a numerical value in mmHg. It only provides an indirect IOP measurement through changes in corneal curvature as mV (miliVolt). This system records IOP related conformal ocular dimensional changes at the corneoscleral junction. When IOP increases, this pressure disperse to the eye's external surface. A 1 mmHg change of IOP, causes a 3 μm change in the corneal radius of curvature. Therefore, direct comparisons to tonometry measurements cannot be obtained and only diurnal fluctuation can be evaluated. At the presence of a significant peak, the doctor cannot estimate the IOP value in mmHg. Also non IOP related corneoscleral junction changes (such as corneal shape and thickness changes) can cause artifacts. Another factor causing artifact is corneal biomechanical changes due to the barrier effect of contact lens.

The other limitation is the successful completion of this application. Patients must record their daily activity during the application period and carry this device on their body carefully. Hence, the patients for these applications should be chosen meticulously. Although, the selection of a favorable patient, battery insufficiency, and technical device malfunction may cause incomplete results, as we observed in two (22.2%) patients.

The Sensimed Triggerfish® system can provide significant information about 24-h IOP variations of glaucoma patients, especially with pseudoexfoliation, and these results can be helpful in the decision of treatment modalities. Further studies with large study groups are needed to use this system more commonly in clinical practice.

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