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ORIGINAL ARTICLE

Continuous IOP Fluctuation Recording in Normal Tension Glaucoma Patients

Bojan Pajic[1-3], Brigitte Pajic-Eggspuchler[1], and Ivan Haefliger[4]

[1]Swiss Eye Research Foundation, Eye Clinic ORASIS, Titlisstrasse, Reinach, Switzerland, [2]Division of Ophthalmology, Department of Clinical Neurosciences, University Hospitals of Geneva, Switzerland, [3]Eye Hospital VIDAR-ORASIS Swiss, University of Novi Sad, Faculty of Physics, Novi Sad, Serbia, and [4]School of Medicine, University of Basel, Basel, Switzerland

ABSTRACT

Background: Intraocular pressure (IOP) remains the only treatable risk factor of progressive glaucoma. Recently a device became available to continuously record IOP fluctuation in contrast to classical, discreet IOP measurements.

Objectives: To perform 24-h IOP fluctuation monitoring using a CE-marked silicone lens-embedded strain gauge sensor (SENSIMED Triggerfish) in five normal tension glaucoma patients in the presence and absence of anti-glaucomatous treatment and to show the clinical importance of this diagnostic tool.

Methods: 24-h continuous IOP fluctuation monitoring was performed on two occasions separated by at least 6 weeks in each patient. In the control session patients were untreated or previous IOP-lowering medication was washed-out for at least 6 weeks. In the treatment session patients received IOP-lowering medication for at least 6 weeks. The continuous recordings were analyzed for differences between daytime and nighttime data and for repeatability over time. Furthermore, profiles recorded in each patient in treated and non-treated conditions were compared.

Results: Highly individual and repeatable profiles were obtained. Data recorded during daytime portions of the recordings showed higher coefficients of variation than nighttime data. Positive and significant linear slopes for the transition period from wake time to sleep time were detected in all patients in the absence of anti-glaucomatous treatment, while in three patients of five no significant slopes were detected under treated conditions.

Conclusion: Our data suggest that the continuous IOP fluctuation monitoring device is sensitive to individual IOP rhythms and to differences in such rhythms due to anti-glaucomatous drug therapy.

Keywords: Glaucoma, IOP, fluctuation, monitoring, nocturnal, continuous

INTRODUCTION

Glaucoma is a progressive optic neuropathy leading to blindness if not adequately diagnosed and treated. In normal tension glaucoma (NTG), optic nerve damage occurs in the absence of elevated intraocular pressure (IOP). Despite normal IOP, NTG patients were shown to benefit from IOP-lowering through drug therapy or surgery.[1] The influence on NTG progression by other factors, typically the nocturnal interplay between IOP and arterial blood pressure, is being investigated.[2] In some patients the association of nocturnal blood pressure dips in association with increased IOP, despite IOP-lowering therapy,[3] may lead to insufficient perfusion of the optic nerve with subsequent to visual loss.

The dynamic behavior of IOP over the diurnal and nocturnal periods has been studied extensively. Wilensky investigated diurnal IOP patterns in both healthy subjects and glaucoma patients,[4] including NTG patients, using home tonometry and demonstrated the existence of a diurnal rhythm. When hospitalized in a sleep laboratory overnight, an increase in IOP during the nocturnal period was observed in both groups.[4] Recent work by Liu et al. has shown that a typical IOP pattern can be identified in glaucoma patients as well as in young and elderly healthy subjects.[5–7] Renard et al. collected 24-h IOP curves in the habitual body position (sitting during daytime and supine during nighttime) in normal tension glaucoma patients.[8] A nyctohemeral rhythm was found in 20 of 22 (91%) patients. Costagliola et al. also observed a 24-h IOP pattern in Caucasians with NTG.[9]

Zeimer et al. used the home tonometry approach to suggest a link between short-term IOP fluctuation

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Correspondence: Bojan Pajic, Swiss Eye Research Foundation, Eye Clinic Orasis, Titlisstrasse 44, 5734 Reinach, Switzerland.
E-mail: bpajic@datacomm.ch

and glaucoma progression.[10] They found that patients with progressive visual field loss exhibited more frequent IOP peaks as compared to patients with stable visual fields. Mansouri et al. have demonstrated that glaucoma patients assumed to be medically and surgically controlled show significant IOP fluctuations throughout the day and on provocative testing.[11] Recently, it was shown that 24-h IOP assessment resulted in a change of the clinical management in 23 of 29 (79.3%) reviewed glaucoma patients.[12] The clinical utility of extending IOP measurements to the 24-h period was further demonstrated by other authors, where peak IOP was observed outside regular office hours in 22 of 32 (69%) patients.[13] Based on evidence gained mainly in the last two decades, the clinical interest and relevance of studying the IOP behavior over the 24-h period has been established. Currently, the only approach to 24-h IOP monitoring is by using repeated tonometry. These measurements remain punctual and cannot be carried out in sleeping patients. Clinicians have expressed the need for a tool allowing continuous IOP monitoring.[14]

Recently, a novel device enabling continuous recording of IOP fluctuation has been described.,[15,16] The commercial product obtained the CE mark in 2009. Integrating the sensing elements in a soft contact lens enables monitoring during normal daily activities and during sleep. Mansouri et al. have previously reported the ability of the Sensimed Triggerfish device to record IOP changes over 24 h in a group of glaucoma patients.[17] Previously undetected IOP peaks and fluctuations were revealed by 24-h continuous monitoring in a majority of progressing glaucoma patients, despite office-hour IOPs considered to be within the target range. In this paper, we describe our experience with continuous recording of 24-h fluctuation profiles in NTG patients in two separate sessions with and without anti-glaucomatous drug treatment.

PATIENTS AND METHODS

Five patients diagnosed with NTG, defined as IOP without treatment less than 21 mmHg on diurnal testing, gonioscopic open anterior chamber angle, typical glaucomatous optic disc damage with glaucomatous cupping and loss of neuroretinal rim, visual field defect compatible with the glaucomatous cupping and progressive damage, underwent 24-h continuous IOP fluctuation monitoring on one eye on two occasions, at least 6 weeks apart. During the first session, IOP was monitored using SENSIMED Triggerfish (Sensimed AG, Lausanne, Switzerland) after a minimum 6 weeks washout of IOP-lowering medication (hereafter control session). Prior to the second session patients had received IOP-lowering medication for at least 6 weeks (hereafter treated session). Each subject served as his/her own control.

Patients were to undergo 24-h IOP monitoring. When offered the choice between monitoring under stationary conditions and ambulatory IOP fluctuation monitoring, all preferred the latter. Informed consent was obtained. No approval from the ethics committee was required since the device is approved for clinical use and CE-marked as class IIa device.

Visual field data, vertical cup-to-disc (C/D) ratio and average retinal nerve fiber layer (RNFL) thickness were obtained from patients' medical records. Data from the last follow-up visit were used. Visual fields were obtained using automated perimetry (Octopus101, program G2, Haag-Streit, Koeniz, Switzerland), RNFL assessment was carried out using confocal scanning laser tomography (HRT II, Heidelberg Engineering, Nurensdorf, Switzerland) and corneal topography and pachymetry were investigated with Scheimpflug camera (Pentacam, OCULUS, Wetzlar, Germany).

Following a complete ophthalmological examination including Goldmann applanation tonometry (GAT), the device was fitted and IOP fluctuation recording initiated. Sensors with a base curve radius of 8.7 mm were used. Recording proceeded for 24 h, including the nocturnal period with undisturbed sleep. Patients were instructed to instill IOP-lowering medication in the monitored eye during the IOP fluctuation monitoring according to their usual treatment schedule. Two patients were treated with latanoprost (Pfizer SA, Zürich, Switzerland) once daily, two patients were taking travoprost (Alcon Switzerland SA, Hünenberg, Switzerland) once daily and one patient was treated with travoprost once daily and dorzolamide (Merck Sharp & Dohme-Chibret AG, Opfikon-Glattbrugg, Switzerland) twice daily during the treated session. No control of the medication absorption during IOP fluctuation monitoring was done. Both IOP fluctuation monitoring sessions were performed under ambulatory conditions. With the exception of driving, showering and extreme exercise, no restriction of patient activity was required during the sessions. All patients completed an activity logbook during each session with particular attention to wake-sleep periods.

The SENSIMED Triggerfish enables continuous IOP fluctuation monitoring through a circular strain gauge and additional telemetry technology embedded in a disposable silicone contact lens (Sensor).[16,17] The strain gauge detects circumferential fluctuations at the limbus. The wireless Sensor is powered from a battery-containing portable recorder where monitoring data is stored for the duration of the monitoring session, lasting up to 24 h. After IOP fluctuation monitoring, the monitoring data is downloaded onto the ophthalmologist's computer using custom-made software. A qualitative fluctuation profile is produced, based on the median of the approximate 600 Sensor output values recorded over 60 s once every 10 min during the monitoring.

The corneal topography and pachymetry were measured just before fitting and after removing the SENSIMED

Triggerfish by the Scheimpflug camera. The contralateral eye was used as a control group measurement.

Statistical analysis

GAT IOP and pachymetry measurements taken before and after IOP fluctuation monitoring with SENSIMED Triggerfish were compared using a paired *t*-test for both sessions. The median Sensor output was calculated for each 60-s period of value recording. Missing data were not imputed and output values indicated as invalid by the device were excluded from the analysis. To assess the degree to which individual patient patterns were similar over the two sessions, Pearson correlation was computed between Sensor outputs in treated and control sessions for each patient separately. Between-patient similarity was assessed by: (a) computing pairwise correlations (e.g. the control session of a patient and that of each of the other patients) of Sensor outputs across sessions between each patient and all others, and (b) for each patient, averaging the pairwise correlations obtained with all other patients. The average of these pairwise correlations for each subject was used as his/her "inter-individual" correlation. The device records continuously for 60 s during every 10-min interval. For each continuous recording period the median was computed, producing six medians (data points) per hour and 48 points over the nighttime periods (9 PM to 5 AM). Correlations were obtained by pairing intervals across sessions (e.g. 5:00 PM to 5:10 PM in treatment to 5:00 PM to 5:10 PM in control) and computing the Pearson correlation.

Sensor output values recorded between 9 PM to 5 AM were used for evaluation of the nighttime period. Sensor sensitivity to treatment relative to control was assessed using two methods evaluating variation of Sensor output during the night: (1) computing coefficient of variation (CV) for treated and control nighttime sessions separately, with comparison via Levene's Test for Homogeneity of Variance, and (2) computing standardized Sensor Range=$((\text{Sensor}_{max}-\text{Sensor}_{min})/\text{Sensor}_{min})$. To eliminate the possible effects of outliers on this range statistic, computations were repeated with maximum and minimum outputs defined by 95th and 5th percentiles, and by 90th and 10th percentiles. Standardized ranges were compared between control and treated sessions over all subjects using a general linear model (GLM) with repeated measures. Analyses were done separately for each of the three standardized ranges (max–min, 95th–5th percentiles, and 90th–10th percentiles). The nighttime period, as defined here, was not the same as sleep period, which was deduced from the patient's activity logbook.

To assess the degree of change in Sensor output over time, a regression was fit to each patient's 9 PM to 5 AM data within sessions. The regression allowed for both linear and quadratic trends to be modeled. The linear slopes were tested for significance using a paired *t*-test.

For statistical testing $p<0.05$ was considered significant. All analyses were performed using SAS Version 9.2 or higher.

RESULTS

Five patients (3 male and 2 female), diagnosed with NTG, were admitted for 24-h continuous IOP fluctuation monitoring using the wireless contact lens sensor on two occasions separated by an average of 52 days (39–62). For one patient the sessions were separated by 39 days. Two right and three left eyes were monitored. Monitoring was initiated in the late morning in two patients and in the late afternoon in three patients. Mean age of the patients was 62 ± 5.9 (SD) years, ranging from 58 to 72. Last recorded visual field mean defect was 3.6 dB ± 2.48 (0.9–7.6) with a mean loss variance (LV) of 24.06 ± 27.46 dB (2.9–67.4), vertical cup-to-disc ratio 0.6 ± 0.15 (0.5–0.8) and average RNFL thickness 0.154 ± 0.06 mm (0.087–0.242) as measured by laser scanning tomography. In the control session patients were untreated or previous IOP-lowering medication had been washed-out for at least 6 weeks. All patients were under once-daily prostaglandin analogue monotherapy at bedtime and one (patient 1) had concomitant twice-daily carbonic anhydrase inhibitor (CAI) treatment (at 6 PM and at waking), all since at least 6 weeks at the time of the treated monitoring session.

GAT IOP taken both before and after 24-h continuous IOP fluctuation monitoring was lower in the treated session than in the control session. Mean IOP (range) in the control session was 17.8 ± 1.6 mmHg (16–20) before IOP fluctuation monitoring and 16.6 ± 2.2 mmHg (14–20) after, compared to 11.4 ± 1.1 mmHg (10–13) before and 11.8 ± 0.8 mmHg (11–13) after the treated session. Pre- and post-monitoring IOP were statistically lower in the treated session ($p=0.001$ for pre and $p=0.006$ for post). There was no statistically significant difference in IOP before and after IOP fluctuation monitoring in the control ($p=0.284$) or treated ($p=0.374$) session.

Figure 1A to 1E show the two 24-h monitoring profiles obtained for each patient. Eye blinks were observed as characteristic signals during daytime on all profiles, as was ocular pulsation during nighttime (Figure 2A and B). The correlation of IOP fluctuation profiles between the treated and control session was positive and significant in all patients (Table 1). All patients maintained normal indoor and outdoor activities throughout both monitoring sessions. These included both indoor and outdoor activities, including office and household work, social activities, and sport. According to patients' logbooks, bed time occurred around 10–11 PM and lasted until 5–8 AM the morning after. The only exception was patient 2, who arouse and was upright from 1.30 AM to 3 AM on both occasions. The nocturnal sleep period

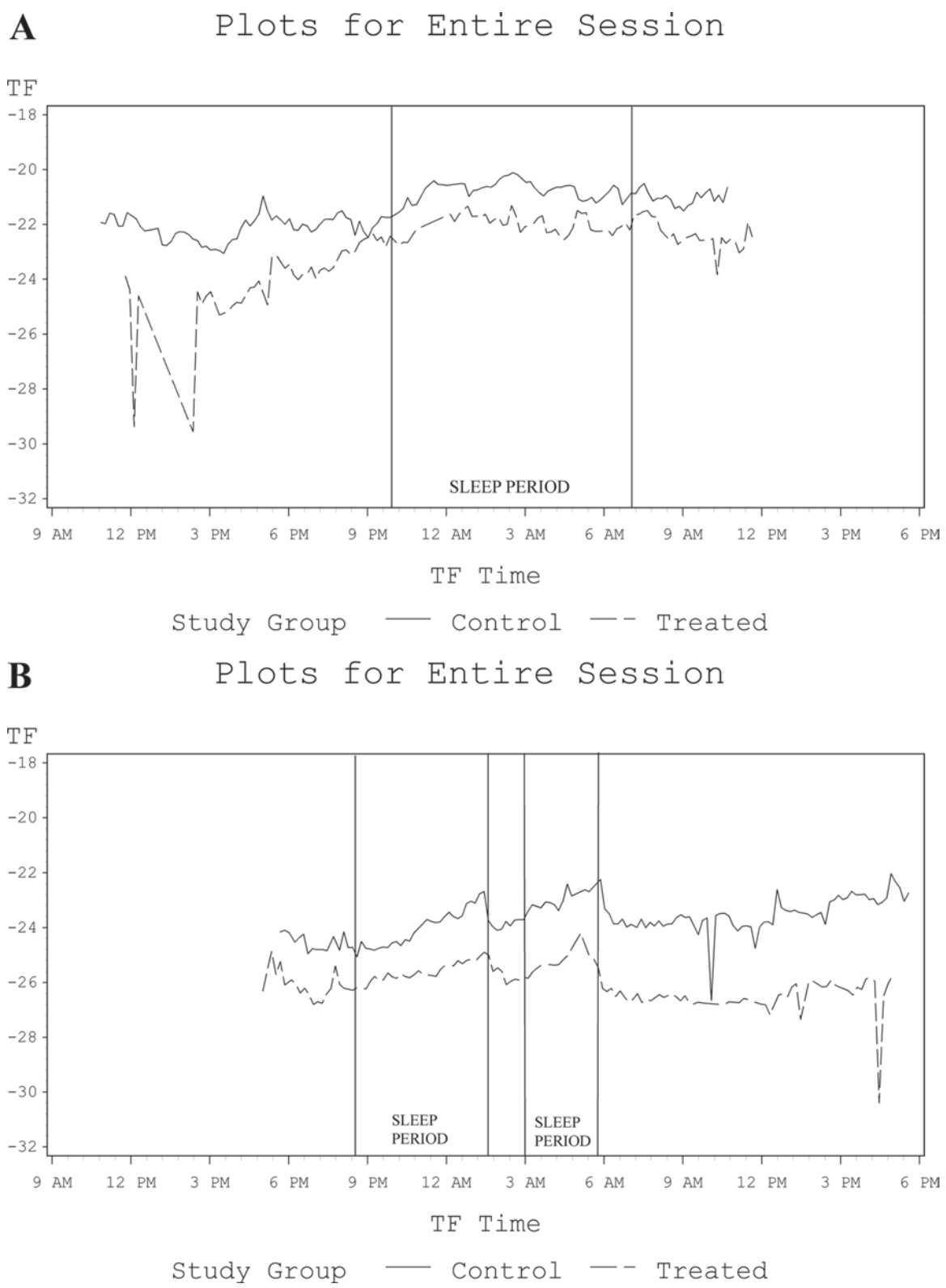

FIGURE 1 24-h IOP profiles recorded in absence (continuous lines) and presence (dashed lines) of IOP-lowering treatment in the five subjects on two occasions separated by an average of 7 weeks. (A) Patient 1; (B) patient 2; (C) patient 3; (D) patient 4; (E) patient 5. Sleep period are indicated by the vertical lines and are representative of both sessions. Patients 1, 3, 4 and 5 had one continuous sleep period in both sessions while patient 2 was awake and upright between 1.30 and 3 AM on both occasions. All patients took once-daily prostaglandin analog treatment at bedtime. In addition, patient 1 took CAI at 6 PM and at waking.

is indicated for each patient by the vertical lines in Figure 1. All patients slept in the habitual body position during nighttime. In addition to nocturnal sleep, all patients reported a resting period in the recumbent position during the day, with or without sleep, on both monitoring occasions. For patients 1, 2 and 4 the

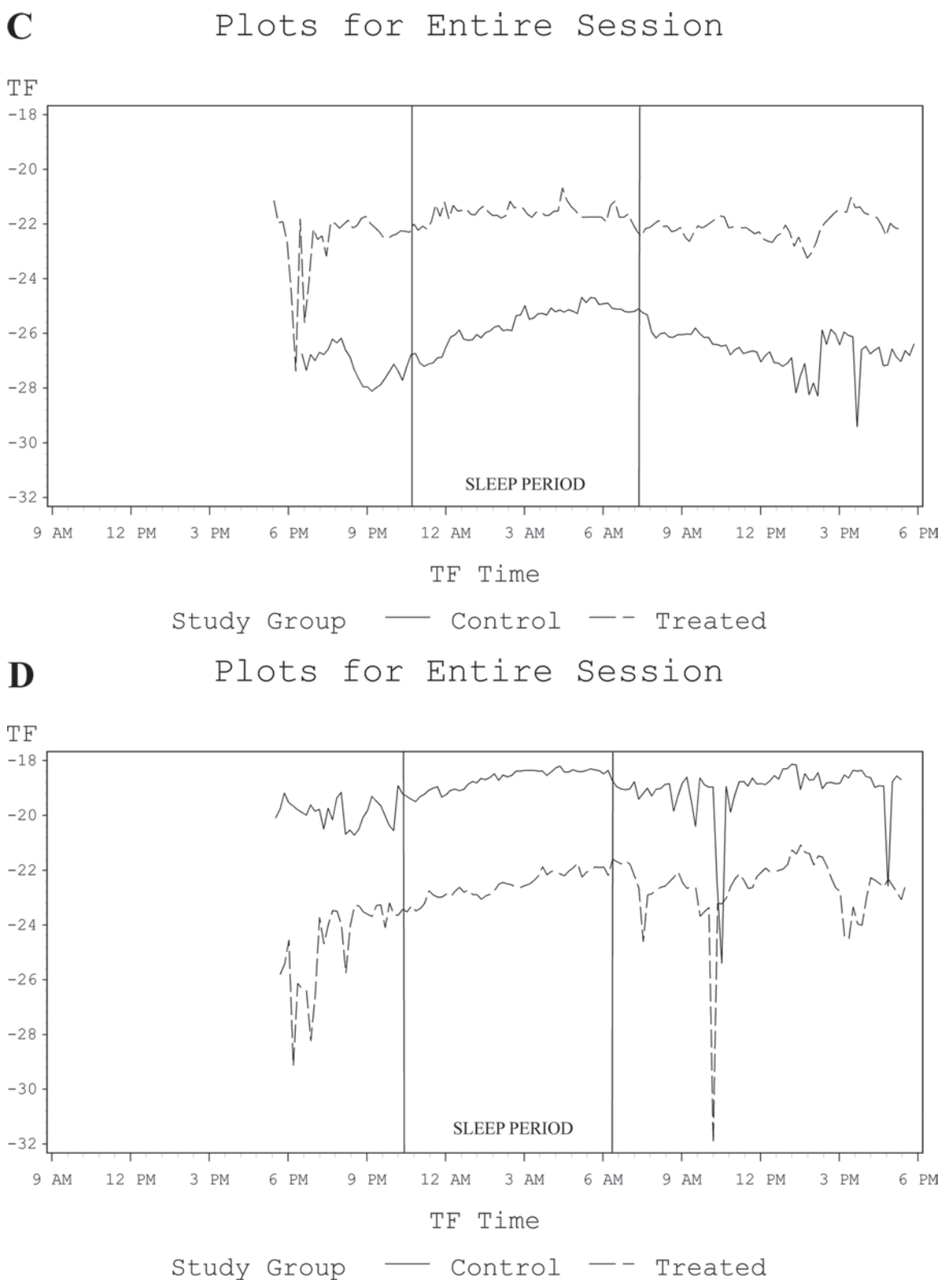

FIGURE 1 (Continued)

absolute device output values were generally higher with IOP-lowering treatment than without, while for patients 3 and 5 (Figure 1C and E) device output was lower in the control session than in the treated session. There was no relationship between the reference GAT IOP values before and after device recording and the respective initial and final device output (no statistical testing done).

When comparing nighttime (9 PM to 5 AM) data to that collected during the entire 24-h period in the

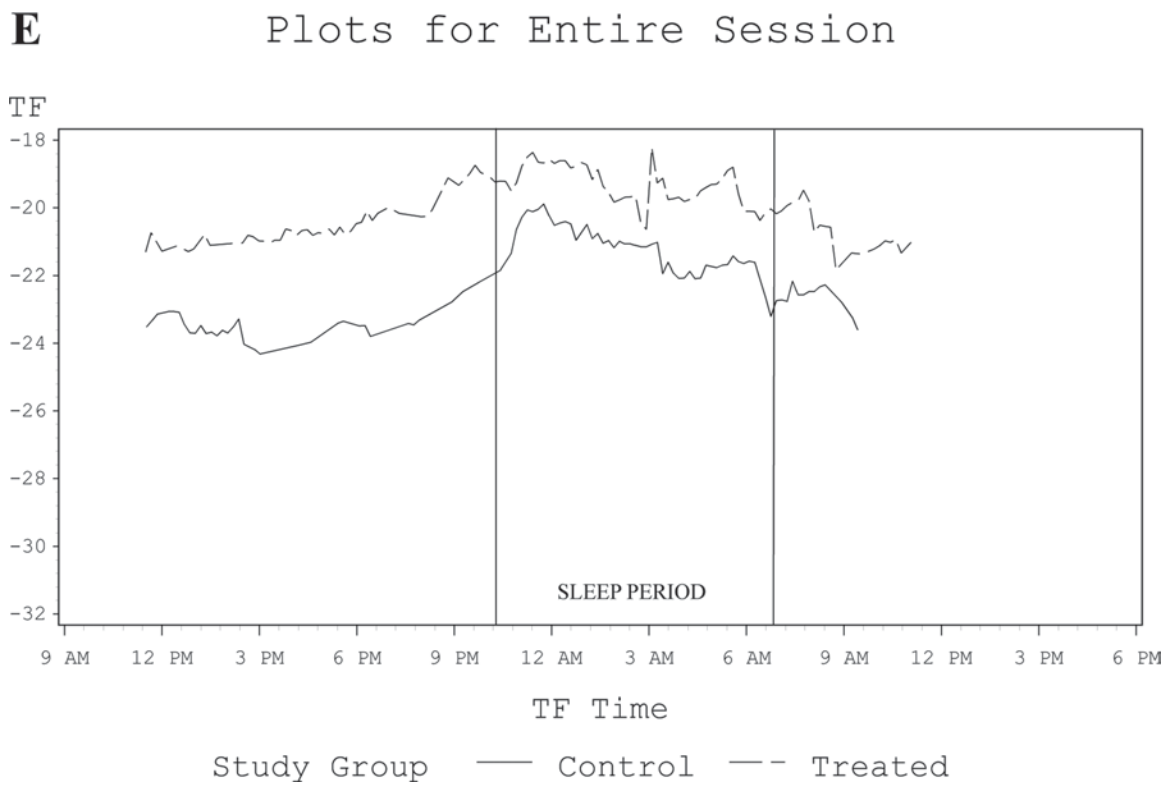

FIGURE 1 (Continued)

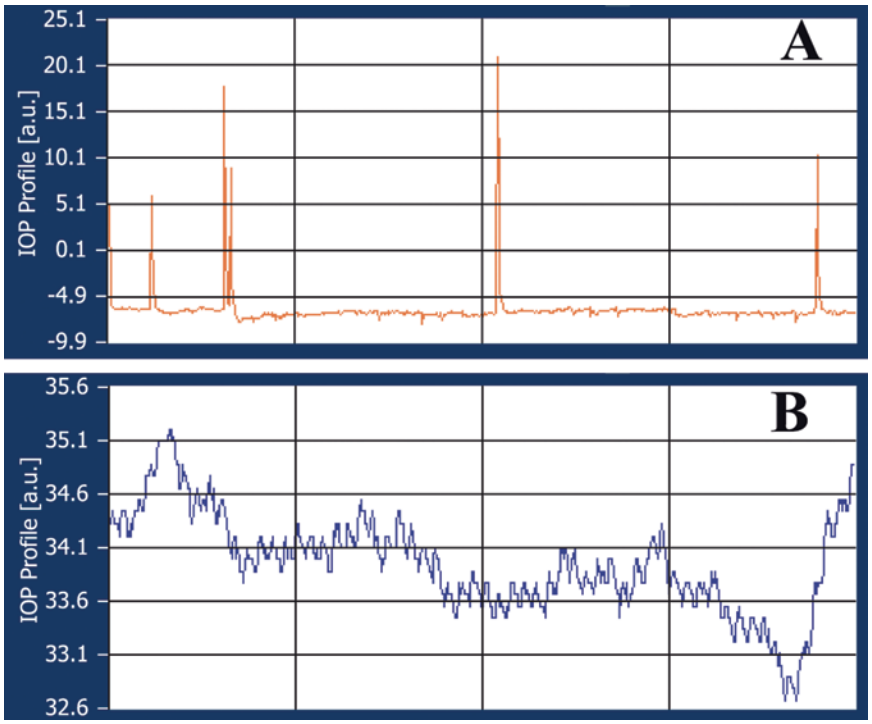

FIGURE 2 Detailed 60 s extracts of recordings. (A) Eye blinks were observed as characteristically recorded spikes. (B) Ocular pulsation during nighttime with closed eyes.

treated session, it can be observed that CV for nighttime data is much lower than CV for 24-h data (Table 2) and, naturally, even lower when compared to daytime hours only (not shown). In the control session, CV for nighttime data is smaller than for 24-h data except for patient 3. Also, CV from 9 PM to 5 AM is smaller in the treated session than CV for nighttime data in the control session for all patients (Table 2). This difference between treated and control session is statistically significant ($p < 0.0001$). This is further demonstrated

TABLE 1 Correlation between IOP fluctuation profiles recorded within and in-between patients. Pairs of Sensor output values at matching time points in either session were compared.

	Intra-individual		Inter-individual	
Patient #	*r*	*p*	*r*	*p*
1	0.68	<0.001	0.47	0.005
2	0.15	0.018	0.32	0.009
3	0.44	<0.001	0.23	0.204
4	0.39	<0.001	0.37	0.014
5	0.83	<0.001	0.21	0.236

TABLE 2 Coefficient of variation (CV) for nighttime and 24-h device recordings.

	Treated session		Control session	
Patient #	24-h period	9 PM to 5 AM	24-h period	9 PM to 5 AM
1	–5.78	–1.85	–3.46	–2.66
2	–2.64	–1.32	–2.98	–2.68
3	–3.46	–1.87	–3.36	–3.53
4	–6.36	–2.33	–4.74	–2.83
5	–4.36	–2.78	–5.41	–3.32

FIGURE 3 Example of standardized display of recorded profiles in absence (continued line) and presence (dashed line) of IOP-lowering treatment for patient 3.

by the statistically significant difference in the range of Sensor output values recorded in the treated versus the control session for the patients (max–min; $p = 0.03$). The comparison was also statistically significant for the 95th–5th percentile ($p = 0.02$) and borderline significant for the 90th–10th percentile ($p = 0.05$).

When regressions were fitted to the 9 PM–5 AM data for each session, a statistically significant linear slope was obtained for the control session in all patients. This correlation was greater than that obtained for the same patient during the treated session. For 3 patients of 5, the slope obtained for the treated session was close to zero and not statistically significant.

Mean (range) central corneal thickness (CCT) in the SENSIMED Triggerfish fitted eye without IOP-lowering treatment was pre-application 549.6 ± 34.0 µm (492–593) and after removal 547.4 ± 33.0 µm (495–597), a difference that was not statistically significant ($p = 0.51$). Mean CCT in the control eyes without IOP-lowering treatment was at baseline 553.8 ± 29.5 µm (508–594) and after the recording 552.6 ± 28.79 µm (505–592), hence showing no statistically significant difference ($p = 0.64$). Mean CCT in the SENSIMED Triggerfish fitted eye with IOP-lowering treatment was pre-application 549.4 ± 36.0 µm (486–592) and after removal 549.6 ± 34.0 µm (492–598), without statistically significant difference ($p = 0.94$). Mean CCT in the control group eyes without IOP-lowering treatment was at baseline 552.0 ± 36.8 µm (493–602) and after the recording 553.6 ± 28.79 µm (505–602), not statistically different ($p = 0.61$). No statistically significant difference in pachymetry was observed between the monitoring sessions at any time (control session pre-application

of SENSIMED Triggerfish $p=0.86$, control session after removal of the device $p=0.82$, treated session pre-application of the device $p=0.92$, treated session after removal of SENSIMED Triggerfish $p=0.87$, Wilcoxon test).

DISCUSSION

Continuous 24-h IOP fluctuation monitoring was carried out in five NTG patients. Each patient was monitored on two occasions separated by at least 4 weeks. Patients remained ambulatory during both monitoring sessions. All subjects showed a similar IOP pattern of the two monitoring sessions with the 24-h profiles being individual and recognizable. Intra-individual correlation between the control and treated 24-h profiles was moderate to strong in all patients. The profiles recorded were highly reproducible despite an average of 52 days (approximately 7 weeks) separating the two IOP fluctuation monitoring sessions. Moreover, IOP did not differ significantly, as measured by GAT, before and after each 24-h monitoring session, i.e. 1 day apart at the same time of day. The observation of a preserved IOP fluctuation pattern over time has been reported elsewhere, for the diurnal period,[18] including in 64% of open-angle glaucoma patients, and for the 24-h period.[5] Nocturnal and early morning supine IOP values measured with a pneumatonometer were higher than diurnal, sitting measurements in patients with early glaucomatous changes, this pattern being found in the profiles recorded in our series of glaucoma patients as well. Renard et al. found a nyctohemeral rhythm of IOP in 20 of 22 (91%) normal tension glaucoma patients subsequent to 24-h phasing.[8] Our data is in contrast to recent work by Realini et al., who reported poor repeatability of IOP patterns over time in treated glaucoma patients and in healthy volunteers.,[19,20] However, their work was based on seven tonometer readings throughout the day, and due to the limitations of static tonometry, may have captured insufficient IOP data to establish the true IOP pattern.

In three out of five patients, the values recorded by the device were generally higher in the treated session than in the control session, while IOP levels were lower in all patients in the treated session. Absolute values recorded with the device are not directly proportional to IOP, only changes in device output are related to fluctuations in IOP. Further, the device Sensor being disposable, IOP fluctuation profiles in treated and untreated conditions were recorded with two different Sensors in each patient. Variation in the absolute Sensor output value at a given IOP arises as there is some inter-Sensor variability in the electric output of the device strain gauge at equal stretch. It should hence be pointed out that the device is intended for the observation of relative changes only. Any one absolute device output value should not be considered alone, but device profiles should be analyzed in conjunction with reference tonometer values taken before and after device application. For the purpose of this report, we have chosen to maintain the originally recorded device output, thus presenting as raw data as possible. Given the device intended use, however, it would be more convenient, maybe even more appropriate, to display profiles on a standardized scale, enabling direct evaluation of differences in (selected parts of) the profile pattern. An example of standardized display for patient 3, with the initial value being set to the same for both profiles, is shown in Figure 3.

The nocturnal portions of the profiles recorded were in most cases associated with smaller CVs than those for the full 24-h profiles, which for their part had lower CVs than the diurnal portions of the profiles. Presumably, this is in part due to varied subject activity during waking hours. Furthermore, the additional pressure on the eye exerted by the eye lid during eye blinks generates a characteristic and important spike on the recorded profiles (Figure 2A). During the nocturnal period when patients were asleep, the amount of eye blinking is significantly reduced if not altogether eliminated. The rhythmic fluctuation observed on the profile extract (Figure 2B) is due to ocular pulsation, its frequency in the range of cardiac activity. It is plausible that eye blinks account for at least part of the higher CV for the diurnal period.

Reference IOP readings by Goldmann applanation tonometry were $32 \pm 6.95\%$ (21–40%) lower in the treated session. These treatment effects are in line with literature reports on the IOP-lowering effect of prostaglandin analog monotherapy,[21,22] with a presumed additional IOP-lowering effect of concomitant use of dorzolamide in one patient.[23] When comparing profiles recorded in the presence and absence of anti-glaucomatous drug treatment, CVs were significantly lower in the treated session than in the control session and the range (difference between maximal and minimal value recorded) of output lower in the treated session. This correlates with previous reports in which the IOP fluctuation over 24 h was reduced by the introduction of prostaglandin analog.[19,24] Addition of the carbonic anhydrase inhibitor dorzolamide to prostaglandin analog therapy reduced IOP fluctuation.[25] In contrast, Liu et al. observed a similar IOP range (IOP_{max}–IOP_{min}) when adding a carbonic anhydrase inhibitor to prostaglandin analog therapy, despite lower mean IOP.[26]

One patient (patient 1) received dorzolamide twice daily concomitantly to prostaglandin analog therapy, for its presumed positive effect on optic nerve perfusion, as published previously.[27] There was no obvious difference in the pattern recorded in presence of treatment for this patient as compared to recordings for the other four patients. The contribution of each of the two administered drugs on the recorded pattern is not known at this point, nor has a fluctuation profile been recorded in presence of prostaglandin analog therapy alone for

this patient. It should be noted that generally lower IOP in presence of dorzolamide throughout the 24-h period would have no influence on the profile recorded with the device since only relative variations are to be considered. Less fluctuation, expressed as a lower CV, was recorded with the device in presence of treatment in this patient and is in line with the above cited reports. The association between the recorded pattern and the individual drugs is not clear at this point, however, prostaglandin analogs have been shown to be the most potent IOP-lowering compounds currently available.[28] With the assumption that the addition of dorzolamide to prostaglandin analog therapy generates only little additional effect on IOP, the prostaglandin analog will predominantly influence the IOP fluctuation profile.

A statistically significant and positive linear trend was observed for the 9 PM to 5 AM portion of the profiles recorded in all patients in the control session. This is in line with the generally accepted concept that IOP increases from daytime, sitting position, to nighttime, supine position. In the treated session, however, no significant linear trend was obtained for three of the five patients (60%). In fact, no significant nocturnal rise could be detected for these patients in presence of drug therapy. This result is further underlined by the smaller range of device output values recorded in the treated session as compared to the control session in all patients. A flattening of the recorded 24-h profiles is observed after drug treatment introduction. Modulation of IOP or remodeling of the individual, 24-h IOP profile with maximal IOP reduction in association with a flattening of the nyctohemeral profile, are therapeutic approaches suggested by other authors.,[29,30]

There are several weaknesses to our study. The small number of subjects makes generalization of results difficult. Further, the relationship between the device output and IOP as measured with a tonometer is unknown. Simultaneous IOP readings in the monitored eye are not feasible since the device includes a soft silicone contact lens that covers the cornea throughout the monitoring. It cannot be excluded that artifacts such as corneal swelling, a commonly observed phenomenon with contact lenses and inversely proportional the oxygen transmissibility of the lens material,[31] are present and biasing the recorded profiles. Hypoxia with resulting metabolic shift and corneal swelling does predominantly occur during extended contact lens wear in the nocturnal period, when eye lids are closed, creating an additional barrier independent of the lens to oxygen uptake. However, the device used in this study is integrated into a silicone lens, with oxygen transmissibility in the extremely high range (125×10^{-9} D_k/t units) despite being several times thicker at its center than classic vision correction contact lenses made of silicone hydrogel or silicone elastomer, although the latter is rather uncommon. Sweeney et al. showed that less corneal edema was observed after 8 h of sleep in eyes wearing silicone contact lenses (2.0% ± 2.0) as compared to eyes not wearing any contact lens (3.6% ± 2.1).[32] The silicone material may act as an oxygen reservoir between the closed eyelid and the cornea during the sleep period. We could show that with the IOP fluctuation monitoring device, no statistically significant changes in CCT was detected after a 24-h wearing period in glaucoma patients.

CONCLUSION

Our data suggest that the continuous IOP fluctuation monitoring device is sensitive to individual IOP rhythms and to differences in such rhythms due to anti-glaucomatous drug therapy. Further research on the relationship between the device output and IOP as measured by tonometry is recommended.

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REFERENCES

[1] Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol*. 1998;126:487–497.

[2] Oh WH, Park KH, Kim JM, Kim DM. Circadian blood pressure and intraocular pressure patterns in normal tension glaucoma patients with undisturbed sleep. *Korean J Ophthalmol*. 2010;24:23–28.

[3] Kiuchi T, Motoyama Y, Oshika T. Influence of ocular hypotensive eyedrops on intraocular pressure fluctuation with postural change in eyes with normal-tension glaucoma. *Am J Ophthalmol* 2007;143:693–695.

[4] Wilensky JT. Diurnal variations in intraocular pressure. *Trans Am Ophthalmol Soc* 1991;89:757–790.

[5] Liu JH, Zhang X, Kripke DF, Weinreb RN. Twenty-four-hour intraocular pressure pattern associated with early glaucomatous changes. *Invest Ophthalmol Vis Sci* 2003;44:1586–1590.

[6] Liu JH, Kripke DF, Hoffman RE et al. Nocturnal elevation of intraocular pressure in young adults. *Invest Ophthalmol Vis Sci* 1998;39:2707–2712.

[7] Liu JH, Kripke DF, Twa MD et al. Twenty-four-hour pattern of intraocular pressure in the aging population. *Invest Ophthalmol Vis Sci* 1999;40:2912–2917.

[8] Renard E, Palombi K, Gronfier C et al. Twenty-four hour (Nyctohemeral) rhythm of intraocular pressure and

ocular perfusion pressure in normal-tension glaucoma. *Invest Ophthalmol Vis Sci* 2010;51:882–889.
[9] Costagliola C, Parmeggiani F, Virgili G et al. Circadian changes of intraocular pressure and ocular perfusion pressure after timolol or latanoprost in Caucasians with normal-tension glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2008;246:389–396.
[10] Zeimer RC, Wilensky JT, Gieser DK, Viana MA. Association between intraocular pressure peaks and progression of visual field loss. *Ophthalmology* 1991;98:64–69.
[11] Mansouri K, Orguel S, Mermoud A et al. Quality of diurnal intraocular pressure control in primary open-angle patients treated with latanoprost compared with surgically treated glaucoma patients: a prospective trial. *Br J Ophthalmol* 2008;92:332–336.
[12] Hughes E, Spry P, Diamond J. 24-hour monitoring of intraocular pressure in glaucoma management: a retrospective review. *J Glaucoma* 2003;12:232–236.
[13] Barkana Y, Gerber Y, Mora R, Liebmann JM, Ritch R. Effect of eye testing order on automated perimetry results using the Swedish Interactive Threshold Algorithm standard 24-2. *Arch Ophthalmol* 2006;124:781–784.
[14] Sit AJ. Continuous monitoring of intraocular pressure: rationale and progress toward a clinical device. *J Glaucoma* 2009;18:272–279.
[15] Leonardi M, Leuenberger P, Bertrand D, Bertsch A, Renaud P. First steps toward noninvasive intraocular pressure monitoring with a sensing contact lens. *Invest Ophthalmol Vis Sci* 2004;45:3113–3117.
[16] Leonardi M, Pitchon EM, Bertsch A, Renaud P, Mermoud A. Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes. *Acta Ophthalmol* 2009;87:433–437.
[17] Mansouri K and Shaarawy T. Continuous Intraocular Pressure Monitoring With a Wireless Ocular Telemetry Sensor: Initial Clinical Experience in Patients With Open Angle Glaucoma. *Br J Ophthalmol* 2011 Jan 7.
[18] Wilensky JT, Gieser DK, Dietsche ML, Mori MT, Zeimer R. Individual variability in the diurnal intraocular pressure curve. *Ophthalmology* 1993;100:940–944.
[19] Realini T, Weinreb N, Wisniewski S. Short-Term Repeatability of Diurnal Intraocular Pressure Patterns in Glaucomatous Individuals. *Ophthalmology* 2010 Aug 13.
[20] Realini T, Weinreb RN, Wisniewski SR. Diurnal intraocular pressure patterns are not repeatable in the short term in healthy individuals. *Ophthalmology* 2010;117:1700–1704.
[21] Ang A, Reddy MA, Shepstone L, Broadway DC. Long term effect of latanoprost on intraocular pressure in normal tension glaucoma. *Br J Ophthalmol* 2004;88:630–634.
[22] Ang GS, Kersey JP, Shepstone L, Broadway DC. The effect of travoprost on daytime intraocular pressure in normal tension glaucoma: a randomised controlled trial. *Br J Ophthalmol* 2008;92:1129–1133.
[23] Cheng JW, Cai JP, Wei RL. Meta-analysis of medical intervention for normal tension glaucoma. *Ophthalmology* 2009;116:1243–1249.
[24] Ishibashi S, Hirose N, Tawara A, Kubota T. Effect of latanoprost on the diurnal variations in the intraocular and ocular perfusion pressure in normal tension glaucoma. *J Glaucoma* 2006;15:354–357.
[25] Stankiewicz A, Wierzbowska J, Siemiatkowska A et al. The additive effect of dorzolamide hydrochloride (Trusopt) and a morning dose of bimatoprost (Lumigan) on intraocular pressure and retrobulbar blood flow in patients with primary open-angle glaucoma. *Br J Ophthalmol* 2010;94:1307–1311.
[26] Liu JH, Medeiros FA, Slight JR, Weinreb RN. Comparing diurnal and nocturnal effects of brinzolamide and timolol on intraocular pressure in patients receiving latanoprost monotherapy. *Ophthalmology* 2009;116:449–454.
[27] Pajic B, Pajic-Eggspuehler B, Häfliger IO. Comparison of the effects of dorzolamide/timolol and latanoprost/timolol fixed combinations upon intraocular pressure and progression of visual field damage in primary open-angle glaucoma. *Curr Med Res Opin* 2010;26:2213–2219.
[28] Stewart WC, Konstas AG, Nelson LA, Kruft B. Meta-analysis of 24-hour intraocular pressure studies evaluating the efficacy of glaucoma medicines. *Ophthalmology* 2008;115:1117–1122.e1.
[29] Caprioli J, Coleman AL. Intraocular pressure fluctuation a risk factor for visual field progression at low intraocular pressures in the advanced glaucoma intervention study. *Ophthalmology* 2008;115:1123–1129.e3.
[30] Blaise P, Guillaume S. [Circadian variations in intraocular pressure and their clinical implications]. *J Fr Ophtalmol* 2005;28:317–325.
[31] Fonn D, Sweeney D, Holden BA, Cavanagh D. Corneal oxygen deficiency. *Eye Contact Lens* 2005;31:23–27.
[32] Sweeney DF, Holden BA. Silicone elastomer lens wear induces less overnight corneal edema than sleep without lens wear. *Curr Eye Res* 1987;6:1391–1394.