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Research Article

Blood Flow in the Optic Nerve Head Changes after Disc Hemorrhage in Primary Open Angle Glaucoma

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Abstract

Purpose: To evaluate hemodynamic changes in the optic nerve head (ONH) after disc hemorrhage (DH) in patients with primary open angle glaucoma (POAG), we applied laser speckle flowgraphy and optical coherence tomography angiography.

Subjects and Methods: We evaluated 28 eyes from 14 patients with POAG who had been using a topical prostaglandin analogue for more than 6 months. Intraocular pressure (IOP), mean deviation (MD) on Humphrey visual field test, ONH blood flow, and ONH vessel density indices were measured when DH was detected, and at 6 and 12 months after the first measurement.

Results: The blood flow in the ONH tissue significantly decreased 12 months after detection of the DH only in DH eyes, whereas non-DH eyes showed no changes. However, no significant changes were found in the ONH vessel density indices in both eyes. In addition, no significant changes in IOP and MD were found for both eyes.

Conclusions: We observed a decrease in the blood flow in the ONH tissue and no significant change in the ONH vessel density 12 months after DH occurred in patients with POAG.

Keywords: *Disc Hemorrhage; Optic Nerve Head; Blood Flow; Laser Speckle Flowgraphy; Optical Coherence Tomography Angiography*

Abbreviations

DH: Disc Hemorrhage; ONH: Optic Nerve Head; POAG: Primary Open Angle Glaucoma; LSFG: Laser Speckle Flowgraphy; OCTA: Optical Coherence Tomography Angiography; IOP: Intraocular Pressure

Introduction

Glaucoma is a multifactorial degenerative optic neuropathy and is the second leading cause of blindness worldwide [1]. There have been many reports suggesting that disc hemorrhage (DH) may be a risk factor for the progression of glaucoma, especially normal tension glaucoma [2-8]. Several studies using scanning laser Doppler flowmetry and fluorescein angiography have been used to demonstrate the relationship between DH and hemodynamic changes in glaucomatous eyes [9,10]. However, there have been no reports of changes in blood flow over time in the optic nerve head (ONH) in glaucomatous eyes after DH.

To investigate changes in the ONH hemodynamics and vessel density after DH, we used laser speckle flowgraphy (LSFG) and optical coherence tomography angiography (OCTA).

Materials and Methods

Twenty-eight eyes of 14 patients with primary open angle glaucoma (POAG) (5 males and 9 females; mean age, 64.7 years) with unilateral DH were included in this study between June 2015 and August 2017 in the Department of Ophthalmology, Osaka Medical College, Japan. The patients had been using a topical therapy with prostaglandin analogue solutions (6 patients using 0.005% latanoprost, 3 patients using 0.0015% tafluprost, 3 patients using 0.03% bimatoprost, and 2 patients using 0.004% travoprost) in both eyes for more than 6 months. The exclusion criteria included smoking, severe cataract, retinal or optic nerve diseases other than glaucoma, glaucoma of advanced stage, high myopia (refractive error worse than -6.00 D), and any systemic medication able to alter ocular blood flow, such as calcium channel blockers. All studies were conducted according to the tenets of the Declaration of Helsinki. This study protocol was reviewed and approved by the Institutional Review Board/Ethics Committee of Osaka Medical College. All participants provided informed consent to participate after the nature and possible consequences of the study were explained.

The topical therapy with prostaglandin analogue solutions were continued after DH occurred. Intraocular pressure (IOP), mean deviation (MD) on Humphrey visual field test, ONH blood flow, and ONH vessel density were measured when DH was detected, and at 6 and 12 months after the first measurement.

The patients were instructed not to drink coffee or alcohol for one day prior to each measurement. IOP was measured by using a Goldmann applanation tonometer. Mydriasis was induced with 1- 2 drops of topical 0.5% tropicamide (Mydrin-M ophthalmic solution; Santen Pharmaceutical Co., Ltd.) for ONH blood flow measurements, which was measured while the patient was in a sitting position. Each measurement was repeated three times using laser speckle flowgraphy (LSFG-NAVI; Softcare Co., Ltd., Fukuoka, Japan). At the same time, microvascular density indices were obtained using OCTA.

The principles of the methods used for determining ONH blood flow via LSFG have been previously described [11]. In the current study, the mean blur rate (MBR) was used as an indicator of blood flow [12]. The MBRs in the tissue and vascular areas of the ONH (MBR-T and MBR-V, respectively) were automatically calculated using the LSFG Analyzer software (Ver. 7.0.26.0, Softcare, Ltd.). As stated above, MBR-T and MBR-V were measured three times at each time point. The average of these three measurements was used in data analyses, and the eye that showed DH was masked during the data analysis.

The principles of OCTA and its applications to glaucoma have been previously described [13-17]. The commercially available RS 3000 Advance (Nidek, Tokyo, Japan) OCTA instrument was used. The images were obtained using a SD-OCT device with a central wavelength of 880 nm, an acquisition speed of 53,000 A-scans/sec, and an axial and transversal resolution of 7 and 20 μm in tissue. Scans were taken from 3 × 3 mm cubes, with each cube consisting of 256 clusters of four repeated B-scans centered on the ONH. Based on these default settings, the radial peripapillary capillary plexus (RPCP) extended from the top of the internal limiting membrane (ILM) to 104 μm below it, the outer layer of the retina extended from 109 μm below the top of the ILM to the retinal pigment epithelium (RPE), the choroid extended from 4 to 125 μm below the RPE, and the deep capillary network at the lamina cribrosa extended from 63 to 376 μm below the ILM. The axial adjustment was performed using the software equipped with this device. Three vessel density indices (VDIs) were calculated for each layer (2 mm diameter), and the means of them were used for the current study.

Results

There were no significant differences in IOP, MD, MBR-T, MBR-V, and vascular density indices when DH occurred between DH and non-DH eyes (Table 1 and table 2).

	DH eyes	Non-DH eyes	P value
IOP (mmHg)	14.2 ± 2.1	14.8 ± 1.8	0.69
MD (dB)	-4.5 ± 3.3	-8.8 ± 7.0	0.24
MBR-T	11.2 ± 2.3	10.8 ± 2.0	0.77
MBR-V	38.9 ± 5.0	40.1 ± 4.7	0.52

Table 1: *Intraocular pressure (IOP), mean deviation (MD), mean blur rate in the tissue area of the optic nerve head (MBR-T), and mean blur rate in the vascular area of the optic nerve head (MBR-V) in each eye of patients with primary open angle glaucoma (n = 14) when disc hemorrhage (DH) occurred.*

Data are presented as means ± standard deviations. P values were calculated by using the Mann-Whitney U-test.

	DH eyes	Non-DH eyes	P value
RPCP	16.6 ± 3.0	16.6 ± 4.9	0.93
Outer layers of retina	29.3 ± 4.0	29.5 ± 7.5	0.68
Choroid	17.1 ± 7.7	15.0 ± 8.3	0.33
Lamina cribrosa	26.2 ± 5.0	26.0 ± 8.0	0.68

Table 2: *Optic nerve head vessel density indices in various layers obtained by optical coherence tomography angiography in each eye of patients with primary open angle glaucoma (n = 14) when disc hemorrhage (DH) occurred. Data are presented as means ± standard deviations. P values were calculated by using the Mann-Whitney U-test. RPCP: Radial Peripapillary Capillary Plexus.*

Figures 1 and 2 show changes in MBR-T and MBR-V in DH and non-DH eyes after DH was detected. MBR-T decreased significantly 12 months after DH detection only in DH eyes (Figure 1). However, there were no significant changes in MBR-V in DH and non-DH eyes for a year after DH was detected (Figure 2).

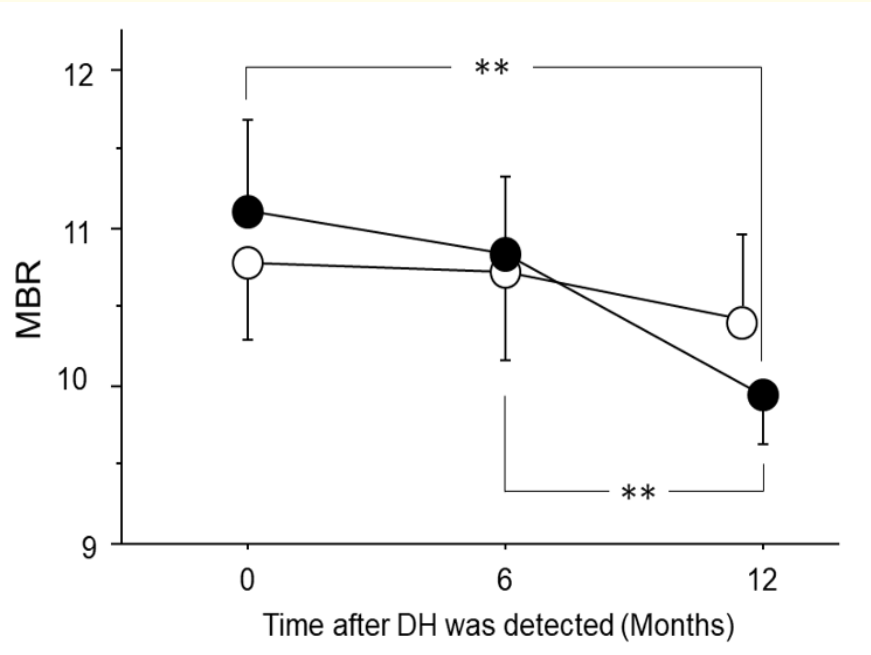

Figure 1: *Changes in the blood flow in the optic nerve head tissue (MBR-T, mean ± standard error) after disc hemorrhage (DH) in DH eyes (closed circles) and non-DH eyes (open circles). **p < 0.01 (Bonferroni test).*

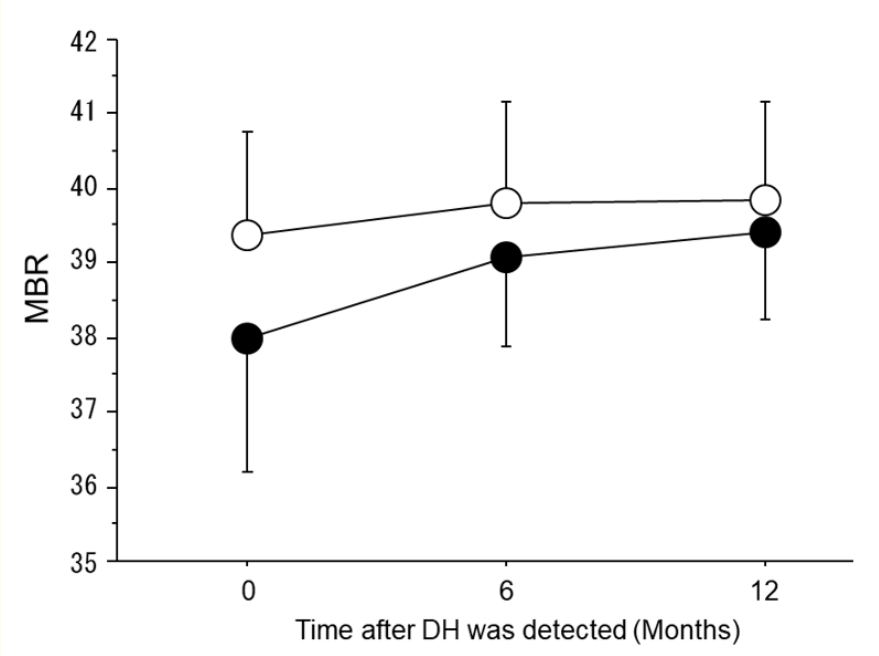

Figure 2: *Changes in the vascular blood flow in the optic nerve (MBR-V, mean ± standard error) after disc hemorrhage (DH) in DH eyes (closed circles) and non-DH eyes (open circles). No significant difference was found in any comparisons between the values at each time-point for both eyes (p > 0.1, Bonferroni test).*

No significant changes were found in the ONH vessel density indices in DH eyes (Table 3) as well as non-DH eyes (data not shown). There were also no significant changes in IOP and MD in both DH and non-DH eyes (data not shown).

	First measurement	6 months	12 months
RPCP	16.6 ± 3.0	17.0 ± 3.9	16.6 ± 3.2
Outer layers of retina	29.3 ± 4.0	30.4 ± 5.5	29.9 ± 6.9
Choroid	17.1 ± 7.7	15.6 ± 8.4	15.1 ± 9.2
Lamina cribrosa	26.2 ± 5.0	26.6 ± 6.4	25.7 ± 7.7

Table 3: *Changes in the optic nerve head vessel density indices obtained by optical coherence tomography angiography in Disc Hemorrhage (DH) eyes (n = 14). Data are presented as means ± standard deviations. One-way ANOVA indicated no statistical difference among three time-point values. RPCP: Radial Peripapillary Capillary Plexus.*

Changes in MBR-T and those of MD following an occurrence of DH were not significantly correlated with each other (simple regression analysis, data not shown).

Discussion

To the best of our knowledge, this is the first longitudinal report on the changes in the ONH blood flow of glaucomatous eyes after DH. We detected a significant decrease in blood flow in the tissue area of the ONH by LSFG. However, no significant changes in blood flow were found in the vascular area of the ONH when measured by LSFG and vessel density when measured by OCTA.

The decrease in MBR-T without any significant change in MBR-V after DH in glaucoma patients agree with previous reports on the MBR-T decrease in accordance with the progression of glaucoma [18] and on the DH as a risk factor for the progression of glaucoma [4,6,8]. Although we evaluated the changes in blood flow in patients on the topical therapy with prostaglandin analogue solutions, the comparison was performed between both eyes with the same therapy; the effects of the topical therapy on the ONH blood flow in both eyes were probably similar in this study.

Furthermore, no significant long-term changes in the ONH vessel density after DH were observed, which was consistent with the previous study reporting that the ONH vessel density was similar in POAG eyes with and without DH [19]. However, if the peripapillary vessel density was evaluated, the results might differ from those in the current study.

In the current study, the association between changes in the ONH tissue blood flow and those in the visual field test could not be detected. However, an evaluation period of 12 months for visual field changes might be short. Whether visual field changes for a longer period are associated with changes in ONH blood flow after DH should be investigated in future studies.

It should be noted that the present study has several limitations. First, we were unable to determine the blood flow level before DH occurred in our patients. Therefore, our data do not indicate the differences compared to the levels before DH occurrence. Second, we did not evaluate short-term changes after DH occurrence. In other words, we might have missed the changes at earlier stages after DH occurrence.

Conclusion

The present study demonstrated that there was a significant decrease in the blood flow of ONH tissue when measured by LSFG, although no significant change was detected in the ONH vessel density when measured by OCTA, 12 months after DH occurred.

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Conflict of Interest

The authors state that the manuscript has not been published previously, and they have no conflict of interest.

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