Comparison of flow velocity of ophthalmic artery between primary open angle glaucoma and normal tension glaucoma

Yoshio Yamazaki, Fukuko Hayamizu

Abstract
Aims—This study describes an investigation of the relation between the change of intraocular circular dynamics and visual field defect between primary open angle glaucoma (POAG) and normal tension glaucoma (NTG).
Methods—The method was to determine the blood flow velocity of the ophthalmic artery using colour Doppler imaging and quantitative peak systolic flow velocity, mean envelope velocity, end diastolic velocity, and Pourcelot resistivity index (RI) were determined. The visual field was examined using program 30–2 of the Humphrey field analyser: the mean deviation (MD) and corrected pattern standard deviation (CPD) were calculated as indices for visual field defects. There were 25 patients with POAG and 25 patients with NTG.
Results—There were no significant differences in all the four indices of the ophthalmic arterial flow and in both of visual field indices between patients with POAG and those with NTG. However, NTG patients alone showed a statistically significant correlation between RI and MD.
Conclusion—The results suggest the vascular resistance of the ophthalmic artery may be associated with the development of visual field defect in NTG patients.


The impairment mechanism of visual function in glaucoma is still unclear. It has been said that an elevated intraocular pressure (IOP) alone caused the optic nerve damage. However, vascular factors, with or without an elevated IOP, have been also implicated in the development of glaucomatous optic nerve damage. Many vascular diseases have been attributed to glaucoma including diabetes,1 hypertension,2 and migraine.3 Spasms of peripheral vessels were found to be more common in patients with normal tension glaucoma (NTG) than in normals.4 Disc haemorrhage, which is thought to be an ocular vasospastic sign, has a higher prevalence in patients with NTG than in those with primary open angle glaucoma (POAG), suggesting that circulatory disturbances may play a role in the development of glaucomatous damage.5 However, it is difficult to study the ocular circulatory dynamics in human eyes owing to the limitation of the evaluation methods.

Coloured Doppler imaging (CDI) is a recent advance in diagnostic imaging for the study of vascular disorders.6–10 CDI enables us to evaluate blood flow at specific locations by simultaneous B-mode imaging. The technique has been developed to investigate orbital arterial blood supply in the eye and orbit by identifying waveforms from specific sites. Recently, several authors demonstrated that patients with glaucoma showed a significant reduction of the ophthalmic arterial flow velocity compared with the normals.11,12

In this study, we compared the blood flow velocity of the ophthalmic artery in patients with POAG with those with NTG and examined the pathophysiology of the progression of visual field defect.

Subjects and methods

We studied 50 subjects comprising of 25 patients with POAG and 25 patients with NTG. Diagnostic criteria for POAG were characteristic visual field defects and glaucomatous optic disc change with elevated IOP over 21 mm Hg in multiple readings. Diagnostic criteria for NTG were IOP consistently lower than 21 mm Hg including diurnal variation, and the characteristic glaucomatous optic disc cupping with visual field defects. Patients with a history of intraocular surgery, cardiovascular disease, systemic hypertension or hypotension, diabetes mellitus, and collagen or vascular disease were excluded from this study. IOP in POAG and NTG had been controlled at below 21 mm Hg with topical medication: 13 eyes in patients with POAG had been treated with β blockers and 12 eyes with β blockers plus pilocarpine; 20 eyes in those with NTG had been treated with β blockers and five eyes with β blockers plus pilocarpine.

METHODS

This study was approved by the ethics committee of the Nihon University School of Medicine. Informed, written consent was obtained from each subject after the procedure had been fully explained. The flow velocity of the ophthalmic artery was determined using a CDI scanner (SSA-160A, Toshiba, Tokyo) with 5-0 MHz sector phased transducer (PVT-50FT, Toshiba, Tokyo). The estimated peak temporal intensity at 3-5 cm depth in the spectrum analysis mode was approximately 93 mW/cm². This intensity exceeds the guideline limit for ophthalmic application by the current Japanese industrial
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Table 1 Clinical characteristics of patients with primary open angle glaucoma (POAG) and with normal tension glaucoma (NTG)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>POAG (n=25)</th>
<th>NTG (n=25)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>59.7 (7.7)</td>
<td>58.8 (11.0)</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>127.3 (14.5)</td>
<td>125.6 (12.1)</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>74.4 (10.6)</td>
<td>71.4 (7.4)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>77.1 (8.9)</td>
<td>81.1 (8.5)</td>
</tr>
<tr>
<td>IOP (mm Hg)</td>
<td>14.2 (2.4)</td>
<td>13.6 (2.0)</td>
</tr>
<tr>
<td>MD (dB)</td>
<td>-9.2 (7.6)</td>
<td>-9.6 (6.1)</td>
</tr>
<tr>
<td>CPSD (dB)</td>
<td>7.5 (4.3)</td>
<td>9.4 (4.6)</td>
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BP=blood pressure; IOP=intraocular pressure; MD=mean deviation; CPSD=corrected pattern standard deviation.

standard, but the Doppler power during the measurement was set at 15% of the peak power.

Colour Doppler examinations were performed by an observer who was masked as to the clinical diagnosis of the subjects. Velocimetric readings were obtained within the branch of the ophthalmic artery that entered the ethmoid sinus adjacent to the medial orbital wall which is approximately 15 mm posterior to the globe.

The peak systolic flow velocity (peak), the mean envelope velocity (mean E), and end diastolic flow velocity (diastolic) were determined, and the Pourcelot resistivity index (RI) was calculated according to the following formula:

$$RI = \frac{\text{peak} - \text{diastolic}}{\text{peak}}$$

We compared one randomly selected eye of 25 patients with POAG and 25 patients with NTG for each of the four indices. Systemic blood pressure, heart rate, and intraocular pressure were also recorded before the CDI examination. The visual field was examined using program 30-2 of the Humphrey field analyser (Allergan-Humphrey, San Leandro, CA, USA). Using a statistical analysis package (STATXACT, Allergan-Humphrey, San Leandro, CA, USA), we calculated the mean deviation (MD) and the corrected pattern standard deviation (CPSD) as indices for visual field defects.

Student’s t test was used for statistical evaluation.

Results

The clinical background of patients with POAG or NTG is shown in Table 1. There were no statistically significant differences in age, systolic or diastolic blood pressure, heart rate, and intraocular pressure between the two groups at the time of examination. The visual field defect in both groups showed a similar pattern, and there were no statistically significant differences in MD and CPSD between the two groups.

Table 2 Ophthalmic flow velocities in patients with primary open angle glaucoma (POAG) and normal tension glaucoma (NTG)

<table>
<thead>
<tr>
<th>Flow Velocity (cm/s)</th>
<th>POAG (n=25)</th>
<th>NTG (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak velocity (cm/s)</td>
<td>30.4 (14.0)</td>
<td>34.9 (11.5)</td>
</tr>
<tr>
<td>Mean E velocity (cm/s)</td>
<td>19.0 (12.3)</td>
<td>21.2 (10.1)</td>
</tr>
<tr>
<td>Diastolic velocity (cm/s)</td>
<td>7.1 (5.5)</td>
<td>7.7 (4.4)</td>
</tr>
<tr>
<td>Resistivity index</td>
<td>0.78 (0.09)</td>
<td>0.77 (0.08)</td>
</tr>
</tbody>
</table>

Table 2 demonstrates the results of the four indices between patients with POAG and NTG. There were no statistically significant differences in peak, mean E, diastolic velocity, and RI between patients with POAG and those with NTG. The relations among indices for blood flow indices and indices for visual field were examined in both groups using the linear regression technique. The linear regression between RI and MD was highly statistically significant in patients with NTG (Fig 1), but not in those with POAG (Fig 2). Values for peak, mean E, and diastolic velocity did not show significant correlation with MD and CPSD in either group.

Discussion

The pathogenesis of glaucomatous optic nerve damage is not yet fully understood. Two main mechanisms have been proposed. One suggests mechanical damage directly to the axons or small vessels by structural alterations at the lamina cribrosa. The other suggests a primary problem in the blood circulation of the optic nerve as the result of localised organic changes with or without a low perfusion pressure. It is likely that both have an influence on the glaucomatous process either separately or together.

The advent of Doppler ultrasonometry, which enables a reliable non-invasive measurement of the blood flow velocity in the ophthalmic artery, was the impetus for comparing the flow velocity of the ophthalmic artery between patients with POAG and those with NTG. Although a previous study reported that there was a statistically significant difference in mean E velocity between patients with POAG and those with NTG, we found no difference in all four indices for flow velocity between the two groups matched in similar visual field defects and mean age. There are two possible interpretations of the present results. One is that there is no real difference in blood flow velocities in the ophthalmic artery between eyes with POAG and those with NTG. The other is that confounding factors, such as medications or IOP, might have a hidden significance.

Recently, it has been reported that topical timolol has been shown to lead to constriction...
of the retinal arterial vasculature. Baxter et al investigated the effects of the instillation of timolol 0.5% on the orbital blood flow velocities of healthy volunteers with CDI.17

The authors concluded that timolol does not affect the blood flow at the ophthalmic artery. Additionally, it has been shown that there is no difference in flow velocities in the ophthalmic artery between the NTG patients who were on topical antiglaucoma medication with or without systemic antihypertensive agents and those who were not on any medication.16 In the present study, colour encoded blood flow of the ophthalmic artery was identified with a B-scan grey scale image as a larger calibre pulsatile vessel adjacent to the medial orbital wall so the topical medication is not likely to be responsible for these results.

This study demonstrated a significant correlation between RI and MD in patients with NTG, but not in patients with POAG. The influence of IOP on blood flow to the eyes is a potentially important factor in the development of glaucomatous optic nerve damage. Pathologically, there is a decrease in vascularity of the optic disc in glaucomatous eyes. Despite the vascular resistance either by vascular kinking or by direct compression blood flow in the retina and optic nerve of experimental animals is little affected by elevated IOP.18-21 This is evidence that autoregulatory relaxation of muscle tone exists at some other point along the arteriovenous pathway to compensate for the pressure induced constriction. This coincides with the clinical experience that many patients with ocular hypertension do not produce a detectable functional loss.22 Nevertheless, there are a number of clinical observations that suggest that poor vascular function may contribute to glaucomatous optic nerve damage.

Patients with generalised vasospastic disorder manifested by migraine headaches and Raynaud’s phenomenon, who also develop typical glaucomatous optic nerve damage and visual field defect, may represent a subtype of NTG. Gasser and Flammer23 reported that the occurrence of readily measured vasospasm in the nailfold capillaries and simultaneous visual field defect, may play a role in introducing this type of optic nerve damage. A paper by Drance et al24 reported on blood flow measurements in fingers of NTG patients and controls; the mean baseline flow and the mean flow after exposure to cold water were lower in those patients with NTG. Those findings indicate a subtype of patients with NTG has a generalised vasospastic disorder and that vasospasm may contribute to optic nerve damage.

One of the fundamental outstanding questions is whether blood flow changes are the result of the optic nerve damage or are a cause of this. Although the results of the present study do not reflect the general vascular function of the optic disc directly, it may be concluded that the vascular resistance of the ophthalmic artery is associated with the development of visual field defect in patients with NTG. Further research to elucidate the difference in circulatory dynamics between NTG and POAG and to determine methods of improving ocular blood flow may be helpful in the treatment of glaucoma.