SCIENTIFIC REPORT

Retrobulbar haemodynamics in non-arteritic anterior ischaemic optic neuropathy

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Br J Ophthalmol 2006;90:1350–1353. doi: 10.1136/bjo.2006.093559

Aim: To compare retrobulbar haemodynamics in patients with acute non-arteritic anterior ischaemic optic neuropathy (NAION) and age-matched controls by colour Doppler imaging (CDI).

Methods: 25 patients with acute NAION and 35 age-matched controls participated in this study. By means of CDI, the blood flow velocities of the ophthalmic artery, central retinal artery (CRA), and nasal and temporal short posterior ciliary arteries (PCAs) were measured. Peak-systolic velocity (PSV) and end-diastolic velocity (EDV) and Pourcelot's resistive index were determined.

Results: In the ophthalmic artery, no marked differences between patients with NAION and controls were detected. PSV and EDV of the CRA ($p < 0.001$, $p = 0.002$) and PSV of the nasal PCA ($p < 0.05$) were significantly decreased in patients with NAION compared with healthy controls. No marked differences between patients and controls were detectable for temporal PCAs.

Conclusion: Blood flow velocities of the nasal PCA and the CRA are considerably reduced in patients with acute NAION compared with controls. Patients with NAION in part showed markedly different retrobulbar haemodynamics.

The aetiology of non-arteritic anterior ischaemic optic neuropathy (NAION) is believed to be multifactorial, resulting in acute hypoperfusion of the short posterior ciliary arteries (PCAs).^{1–2} The pathogenic mechanisms encompass various risk factors together with an acute incident of hypoperfusion—for example, nocturnal arterial hypotension.³

Several studies investigated circulatory abnormalities in patients with NAION. Using fluorescein angiography, Bertram *et al*⁴ found an increased retinal arteriovenous passage time. Arnold and Hepler⁵ disclosed markedly delayed filling of optic nerve head capillaries in patients with NAION. Furthermore, patients with NAION showed decreased velocities of blood cells in the capillaries of the optic nerve head measured by laser Doppler velocimetry.⁶

The retrobulbar haemodynamics of patients with NAION have been studied previously by means of colour Doppler imaging (CDI).^{7–9} CDI is an ultrasound technique with a simultaneous B-mode image using colour to represent intravascular movement on the basis of Doppler frequency shifts.¹⁰ Blood-flow velocities of the ophthalmic artery, the central retinal artery (CRA) and the short posterior ciliary arteries (PCAs) can be measured using CDI. A previously published study evaluated the peak-systolic velocities (PSVs) and Gosling's pulsatility indices of retrobulbar vessels in progressive NAION before and after optic nerve sheath decompression.⁷ Preoperatively, eyes with NAION showed considerably lower PSVs in the CRA and the PCAs than the contralateral eye. Postoperatively, eyes with NAION showed a

remarkable increase in blood flow velocities in the ophthalmic artery and CRA, and a marked decrease in vascular resistance in the PCAs. The presented case series showed normal velocities in the PCAs (in one patient with acute NAION,⁸ and in three of four patients with NAION⁹).

The present study is, to our knowledge, the first of its kind to compare the retrobulbar haemodynamics of patients with acute NAION with healthy age-matched controls in a larger cohort.

PATIENTS

Twenty-five patients (mean age 68 years) with unilateral NAION were enrolled in the retrospective study. Patients were included if they presented with pathogenic acute painless visual field loss (mean latency 7 days) and optic disc oedema without evidence of other neurological, systemic or ocular disease. Patients with a high erythrocyte sedimentation rate or a positive history for clinical features of giant cell arteritis were excluded from this study. The control group consisted of 35 age-matched subjects (mean age 64 years) who had never had any eye disease other than mild refractive errors (<4 dioptres). Among the participants, 13 controls and 12 patients had a history of arterial hypertension, and 2 controls and 5 patients had a history of diabetes mellitus. Table 1 summarises the demographic and clinical data.

METHODS

All patients and controls had a detailed ophthalmological examination, visual field testing with the Goldmann perimeter or the Humphrey Field Analyzer (Model 750, Humphrey–Zeiss, San Leandro, California, USA) using a white-on-white 24-2 programme and CDI.

Retrobulbar blood flow velocities of the ophthalmic artery, CRA and temporal and nasal PCAs were measured by CDI prospectively by an experienced operator (MK).¹⁰ A 7.5 MHz

Table 1 Demographic and clinical data of the patients and controls (mean (standard deviation))

	NAION	Controls	p Value
Age (years)	68 (9)	65 (8)	0.92
IOP (mm Hg)	16 (3)	15 (3)	0.64
Systolic BP (mm Hg)	157 (29)	142 (23)	0.03
Diastolic BP (mm Hg)	82 (14)	78 (11)	0.13
Heart rate (per min)	73 (10)	72 (12)	0.85
Mean arterial pressure (mm Hg)	107 (17)	99 (13)	0.04
OPP (mm Hg)	55 (12)	50 (10)	0.06

BP, blood pressure; IOP, intraocular pressure; NAION, non-arteritic anterior ischaemic optic neuropathy; OPP, ocular perfusion pressure.

Abbreviations: CDI, colour Doppler imaging; CRA, central retinal artery; EDV, end-diastolic velocity; IOP, intraocular pressure; NAION, non-arteritic anterior ischaemic optic neuropathy; OPP, ocular perfusion pressure; PCA, posterior ciliary arteries; PSV, peak-systolic velocity

linear probe (Sonoline Sienna Siemens, München, Germany) was applied to a closed eyelid using a coupling gel. Samples of pulsed-Doppler signal from within a 1.2×1.2 mm sample volume were analysed to calculate blood velocities. The Doppler-shifted spectral waveforms of each vessel were recorded over a period of >5 s. Over that period, constant samples were required before velocities were measured. In each vessel, peak-systolic velocity (PSV) and end-diastolic velocity (EDV) were determined from the Doppler-shifted spectral waveform. In addition, Pourcelot's resistive index (RI), a measure of peripheral vascular resistance, was calculated as follows:

$$RI = (PSV - EDV) / PSV.$$

The ophthalmic artery was examined approximately 25 mm behind the globe at the straighter portion of the vessel in the nasal orbit to obtain the most reliable results.¹¹ The CRA was measured approximately 10 mm behind the optic nerve head in the retrolaminar portion of the optic nerve. The PCAs were detected 10–20 mm behind the nasal globe, and temporal to the optic nerve where they begin as trunks before forming multiple branches surrounding the optic nerve in its retrobulbar portion.¹⁰

Heart rate and blood pressure (BP) were determined by sphygmomanometry (Poet Te Plus, Criticare Systems, Wisconsin, USA) in a sitting position after a rest of 5 min. Intraocular pressure (IOP) was measured before CDI examination using Goldmann applanation tonometry. Ocular perfusion pressure (OPP) was calculated from the mean arterial blood pressure and IOP data ($OPP = 2/3(\text{diastolic BP} + 1/3(\text{systolic BP} - \text{diastolic BP})) - IOP$).¹²

Statistical methods

For the statistical analysis of this study, an unpaired non-parametric test (Mann–Whitney rank test) was applied for comparisons between patients with NAION and controls. In all analyses, $p < 0.05$ was regarded as significant.

RESULTS

Table 2 summarises the blood flow velocities and resistive indices. The ophthalmic artery showed no significant differences in haemodynamics between patients with NAION and controls. The PSV ($p < 0.001$) and EDV ($p = 0.002$) of the CRA were significantly decreased in patients with NAION compared with healthy controls. (figs 1, 2). The PCAs showed significantly reduced PSVs of the nasal PCA in NAION ($p < 0.05$, fig 3) and no differences between patients and controls for temporal PCA. No significant differences were found for the resistive indices of all retrobulbar vessels.

Figure 1 Box plots of the peak-systolic velocities of the central retinal artery in patients with non-arteritic anterior ischaemic optic neuropathy and controls (centiles 10, 25, 50, 75 and 90 are assigned).

Figure 2 Box plots of the end-diastolic velocities of the central retinal artery in patients with non-arteritic anterior ischaemic optic neuropathy and controls (centiles 10, 25, 50, 75 and 90 are assigned).

IOP, calculated OPP and heart rate were not different between patients and controls, but the mean arterial pressure was significantly higher in patients with NAION ($p < 0.05$; table 1).

DISCUSSION

In this study, the retrobulbar haemodynamics in patients with acute NAION were examined by CDI and compared with healthy controls. Blood flow velocities of the nasal PCA and the CRA were considerably reduced in NAION. The pathogenic concept of an acute NAION is due to acute hypoperfusion of the optic nerve head including the PCAs.^{1, 2} A decrease in velocities can be interpreted as either a decrease in blood flow or a compensatory vasodilatation after temporary vasoconstriction. Hayreh¹³ has argued for the occurrence of a temporary occlusion of the PCAs in NAION. Our examinations of the retrobulbar vessels were carried out when the patients visited our clinic for the first time, a few days after onset of symptoms. At this time, the PCAs might be re-perfused as shown by Williamson,⁸ which may explain why the measured blood flow velocities of PCAs only partly showed marked differences from controls. Further studies by Hayreh¹⁴ showed that NAION may be due to defective circulation in only one PCA. There may have been partial occlusion of the posterior ciliary circulation, and we measured the trunk of the temporal PCA with preserved

Figure 3 Box plots of the peak-systolic velocities of the nasal posterior ciliary artery in patients with non-arteritic anterior ischaemic optic neuropathy and controls (centiles 10, 25, 50, 75 and 90 are assigned).

Table 2 Blood flow velocities (peak-systolic and end-diastolic velocities) and resistive indices of the retrobulbar vessels (ophthalmic artery, central retinal artery and nasal and temporal posterior ciliary arteries) in patients with non-arteritic anterior ischaemic optic neuropathy and controls (mean (standard deviation))

	NAION	Controls	p Value
OA PSV (cm/s)	33.5 (11.5)	32.9 (9.2)	0.72
OA EDV (cm/s)	6.6 (2.6)	7.1 (3.5)	0.91
OA RI	0.8 (0.06)	0.79 (0.06)	0.71
CRA PSV (cm/s)	7.6 (2.2)	9.6 (1.7)	<0.001
CRA EDV (cm/s)	2.1 (0.6)	2.7 (0.7)	0.002
CRA RI	0.72 (0.07)	0.71 (0.06)	0.96
NPCA PSV (cm/s)	7.0 (1.7)	8.1 (2.1)	0.04
NPCA EDV (cm/s)	2.4 (0.6)	2.6 (0.6)	0.18
NPCA RI	0.65(0.06)	0.67 (0.07)	0.57
TPCA PSV (cm/s)	7.2 (1.7)	7.7 (2.1)	0.33
TPCA EDV (cm/s)	2.4 (0.7)	2.7 (0.6)	0.07
TPCA RI	0.66 (0.07)	0.65 (0.72)	0.54

CRA, central retinal artery; EDV, end-diastolic velocity; NAION, non-arteritic anterior ischaemic optic neuropathy; NPCA, nasal posterior ciliary artery; OA, ophthalmic artery; PSV, peak-systolic velocity; RI, resistive indices; TPCA, temporal posterior ciliary artery

circulation, as the temporal part of the optic nerve head is more vascularised than the nasal part, as shown in healthy eyes by Hayreh.¹⁵

Our study showed considerably reduced blood flow velocities in the CRA and the nasal PCA in patients with NAION compared with age-matched healthy controls. The previously published study that evaluated the retrobulbar haemodynamics in NAION before and after optic nerve sheath decompression also showed preoperatively lower PSVs in the CRA and the mean PCAs, but they compared the data with the contralateral eye and only 60% of the patients had a clinically normal fellow eye.⁷ Flaharty *et al* showed no data of the EDVs that may be influenced by the downstream resistance of the vessels. Furthermore, they determined the Gosling's pulsatility indices, developed for high-resistance vessels such as the main arteries of the lower limb,¹⁶ and not the Pourcelot's resistive index to measure vascular resistance in smaller vessels.

Collignon-Robe *et al*⁶ showed decreased velocities of blood cells in the capillaries of the optic nerve head in patients with NAION, as measured by laser Doppler velocimetry. The authors pointed out that they measured the capillaries of the prelaminar region of the optic nerve head, which are supplied by the PCAs. The decreased blood flow in the capillaries might be due to reduced PSVs of the PCAs, as we measured in our study. Leiba *et al*¹⁷ found similar results of the optic nerve head capillaries in patients with NAION by scanning laser Doppler flowmetry. Their technique measures blood flow velocities on the surface of the optic nerve.¹⁸ These capillaries in the nerve fibre layer are supplied by the CRA. The findings of Leiba agree with our results regarding the decreased blood flow velocities in CRA in patients with NAION.

Recently, the morphological study of a reconstructed optic nerve infarction showed that the pathogenesis of NAION might be due to a form of compartment syndrome that causes tissue ischaemia.¹⁹ Tesser *et al* found that the loss was at its greatest extent in the superior part of the nerve encircling the CRA.

The prelaminar, laminar and retrolaminar regions of the optic nerve head are supplied by the circulation of the posterior ciliary arteries.²⁰ Hayreh found that the CRA may rarely supply a minor branch to the retrolaminar region and mainly supplies only the surface layer of the nerve fibre layer. Despite the minor role of the CRA in the blood supply of the optic nerve head, we found reduced blood flow velocities for

the CRA in NAION. Simultaneous reductions in the PSV and EDV of the CRA may be interpreted as reduced volumetric flow in this vessel as shown by Spencer *et al*.²¹ It remains unclear whether the reduced blood flow of the CRA is a primary or secondary phenomenon in NAION. It might be secondary due to the oedema of the optic nerve surrounding the CRA.

The reduced retrobulbar blood flow velocities in our study reflected the acute circulatory disorder of the optic nerve head in NAION. In normal tension glaucoma, the pathomechanism is caused by a chronic hypoperfusion of the optic nerve head.²² CDI measurements of patients with normal tension glaucoma also showed reduced blood flow velocities and higher resistive indices in retrobulbar vessels than in controls.^{23–25} Thus, CDI may detect chronic perfusion deficits of retrobulbar vessels in normal tension glaucoma, as well as acute circulatory abnormalities in NAION, as shown in our study. By contrast, optic atrophy itself does not lead to altered retrobulbar blood flow velocities as in non-vascular and non-glaucomatous optic neuropathy.²⁶

In conclusion, this study showed reduced blood flow velocities of the nasal short posterior ciliary artery and the CRA in patients with NAION compared with controls. An improvement of the retrobulbar circulation might be beneficial in the treatment of NAION.

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Competing interests: None.

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Accepted 2 July 2006

Published Online First 6 July 2006

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