·Brief Report·

Analysis of optic disc damage by optical coherence tomography in terms of therapy in non–arteritic anterior ischemic optic neuropathy

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Abstract

• **This study aimed to assess the relationship between the rate of nerve fiber loss in non –arteritic anterior ischemic optic neuropathy (NAION) and time delay before therapy. Total 24 patients received the same treatment within or after 2wk (early and late groups). There were significantly lower level of destruction of nerve fibers (P=0.0014) and significantly better visual field sensitivity (P=0.039) in early group. The results indicate that therapy should be started within 2wk. The degree of ischemic damage due to NAION correlates well with retinal nerve fiber layer thickness and the ischemia–induced decrease in visual field sensitivity.**

• **KEYWORDS:** non-arteritic anterior ischemic optic neuropathy; optical coherence tomography; perimetry; retinal nerve fiber layer

INTRODUCTION

Anterior ischemic optic neuropathy (AION) is the acute ischemia of the optic nerve head due to insufficient blood supply by the short posterior ciliary arteries. Generally divided into two types. The rare arteritic anterior ischemic optic neuropathy (AAION) is associated with giant cell arteritis. The non-arteritic anterior ischemic optic neuropathy (NAION) is more common and is mainly related to the blood flow defect of the short posterior ciliary arteries[1].

Blood supply to the optic nerve is uniquely complex containing several collaterals. Due to the presence of several collateral branches and a wide inter-individual variability the degree of ischemic damage may vary considerably from patient to patient[2].

In our study, we evaluated optic disc damage and morphological changes during the procession of NAION. The aim of this study was to assess the relationship between the values of retinal nerve fiber layer (RNFL) and visual field sensitivity, and the time delay before starting therapy.

SUBJECTS AND METHODS

All patients gave oral informed consent before enrolment. The study was approved by the Ethical Committee of the University of Debrecen. To exclude AAION, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were determined. CRP levels above 0.5 mmol/L and ESR values above 33 mm/h were taken to indicate vasculitis. Enrolment was based on a review of our clinical patient records to identify cases from the last 16y. Total 48 invitations have been send out for a control examination. Of these cases, 5 patients died, 8 patients moved away and were not able to reach, 6 patients did not want to participate in this study, 3 patients had glaucoma and 2 patients had increased CRP levels.

At last 28 NAION eyes of 24 patients (15 men and 9 women), who recieved the same therapy, were enrolled in the study. The rest fellow eyes served as control.

After optic atrophy developed (min: 4y, average: 8.5y, SD: 3.99y) thorough ophthalmological examination, optical coherence tomography (OCT; OCT3, Stratus, Zeiss Meditech, Dublin, CA, USA) and visual field examinations (Humphrey FDT perimeter, Zeiss Meditech, Dublin, CA, USA) were performed.

The initiation of therapy depended on time when patients presented at our department and not on randomization. Based on this time our patients were divided into two groups. The first group (early group) consisted of patients who had received treatment within 2wk after NAION development

(range: 1-13d, average: 6.57d, SD: 4.38d). The other group (late group) comprised patients who had presented at our clinic 2wk or later after NAION symptoms (range: 21-196d, average: 76d, SD: 67.36d).

The two-group approach is part of the design for the sake of clarity of presentation and description, while the analysis itself is based on handling treatment delay as a continuous variable in linear regression.

In the study, each patient underwent the same treatment for 5d: daily administration of 500 mg 6% hydroxyethyl starch infusion, 2×400 mg pentoxifylline infusion, 500 mg vitamin C infusion, subcutaneous 50 IU/kg low-molecular-weight heparin (LMWH), *per os* 250 mg acetazolamide and *per os* 100 mg aspirin.

For statistical analysis we used the RNFL average thickness index and central retinal thickness (CRT) by OCT examination, the decreased sensitivity (mean deviation, MD) from visual field examination, and best corrected visual acuity (BCVA, logMAR).

RESULTS

The mean age of the 24 patients (15 men and 9 women) was 66.6y (SD: 11.06y). No significant difference in age was found between the early and the late groups (68.21±10.35y *vs* 64.19±12.06y, P=0.45). The average follow-up period was 8.5±3.99y. During the follow-up period, 4 patients developed bilateral NAION.

We evaluated the changes in visual acuity between the first and the last examinations. Similarly to the Ischemic Optic Neuropathy Decompression Trial (IONDT), a decrease of 0.3 logMAR corresponded to three lines better on the ETDRS chart. At the first examination the average BCVA was 0.78 logMAR (0.73 logMAR in early group; 0.82 logMAR in late group) (Table 1).

In both NAION groups RNFL showed significant decrease compared to the control eyes (P=0.0004, and P <0.0001). We detected significantly higher nerve fiber destruction in the late group comparing to the early group (P=0.0014) (Table 2). Analyzing the effect of duration of treatment as a continuous variable and adjusted for age, gender, and cardiovascular risk score, with each unit increase in log-transformed number of days (*i.e.* a 2.718-fold increase in number of days), the RNFL parameter was estimated to decrease by 5.812 μm (95%CI: 3.09 to 8.53, P<0.0001) (Figure 1).

MD values associated with the decrease in visual field sensitivity showed a significant difference compared to the fellow eyes (P<0.001) and also between the two groups (P=0.039). Adjusted for age, gender and cardiovascular risk score, a visual field sensitivity reduction of 2.01 (95% CI: 0.29 to 3.74; P=0.0217) units was associated with each unit increase in log-day of treatment onset.

Regarding CRT, no significant difference was found either compared to the control group (P=0.451), between the

Table 1 Changes in visual acuity between first and last examination in the early and late group %

Patients	≥3 lines better	Little change	≥3 lines worse
Early group	42.9	42.9	14.2
Late group	21.4	57.2	21.4

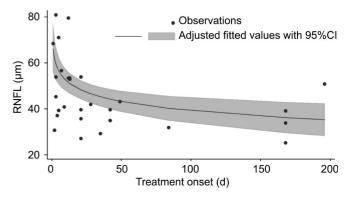Decrease of 0.3 logMAR corresonded to three lines better on the ETDRS chart.

Figure 1 Post−treatment RNFL thickness plotted against the number of days before treatment onset Linear regression adjusted for age and gender; line fitted at average age and gender. CI: Confidence interval.

treated groups (P=0.519), or in relation to quantified treatment delay (P=0.399).

In visual acuity (logMAR) analysis, significant deviations were observed compared to control eyes (0.06±0.23) in the early group (0.57±0.59) and in the late group (0.74±0.54) (P=0.007, 0.0002, respectively). However, the difference between the two treatment groups was not significant (P=0.31), and neither was the adjusted effect of treatment delay (P=0.550).

Comparing the unaffected fellow-eyes of patients in early and late groups RNFL, CRT, visual field sensitivity and visual acuity showed normal and very closely similar values. P-values were between 0.87 and 0.95.

CONCLUSION

Due to complex circulatory conditions, the destruction of the optic nerve fibers does not occur immediately in NAION. The correction of microcirculation disturbances at an early stage can minimize the degree of nerve fiber loss[2]. Ischemic axoplasmic damage plays an important role in the pathogenesis of NAION. The swelling may compromise capillaries; the increased vessel permeability due to the stasis enhances the edema, which further reduces axoplasmic flow, leading to a vicious cycle[3].

Numerous treatments have been investigated, although the exact therapy still remains unclear [4]. We designed our therapy based on our experiences with NAION patiens and considering the results of international studies.

In our study, OCT and visual field deviations demonstrated a significant difference between early and late groups (Table 2). We used statistical modeling to determine the relationship

Table 2 RNFL, CRT, average decrease of visual field sensitivity, BCVA in NAION eyes treated at different times, and in unaffected fellow eyes

Patients	RNFL (μm)	CRT (μm)	Visual field sensitivity (MD)	BCVA (logMAR)
Early group	54.5±15.6	203±33.6	-20.17±10.2	0.59±0.6
Late group	37.54±8.2	195.7±17.7	-26.8±4.5	0.74±0.54
Fellow eyes	78.39±24.7	204.9±26.2	-7.61±8.4	0.018±0.41
[a]P (all NAION vs fellow eyes)	<0.0001	0.254	<0.0001	0.0002
[b]P (early vs late group)	0.0014	0.519	0.039	0.31

[a]All NAION vs fellow eyes; [b]Early vs late group; Values of $P<0.05$ are considered to be significant.

between the extent of fiber destruction and the quantitatively handled amount of time elapsing before treatment onset (Figure 1). The statistically highly significant 5.8 μm difference associated with each log-day increase is a finding of strong clinical importance. These results suggest that treatment for improving blood circulation is recommended as early as possible.

Regarding visual field defects, we carried out a similar analysis and found that the later the treatment started, the greater the sensitivity reduction in the visual field was: the parameter decreased by 2.01 units with each log-day. This identifies an important functional domain where early intervention potentially translates to improved clinical outcomes.

Visual loss showed no significant difference between the two groups. Our results correlated well with those by Hayreh and Zimmerman[5], demonstrating that good visual acuity does not preclude NAION diagnosis and gives no information about visual field defects, which are of a greater diagnostic value.

It is well documented that RNFL thickness decreases with age [6]. In our study the patients in both groups were of nearly the same age (68.21 vs 64.19y, P =0.45), so age is not likely to have affected the differences in RNFL values between the groups. Comparing the fellow eyes of both groups, all parameter (RNFL, CRT, visual field sensitivity and BCVA) showed normal and very closely similar. Jonas et al [7] and Budenz et al [8] analized the optic disc C/D ratio and RNFL in normal eyes. There were no statistically significant relationships between the side of eye. These findings and our results support the assumption that the decreased parameter values of NAION eyes are not random but really the consequence of ischemic damage.

We have investigated the degree of fiber loss in NAION in relation to the onset time of therapy. The earliest possible restoration of blood supply in ischemic events is fundamental in terms of the later outcome of the disease. Our study demonstrates that conservative therapy started as early as possible (within two weeks) can significantly reduce the degree of optical nerve fiber loss and the visual field sensitivity deficit. The applied circulatory improving therapy can be effective in NAION. We are the first to demonstrate that optimal timing of the first line therapy is within two weeks, as late-initiated therapy cannot effectively prevent and stop the destruction of the optical nerve.

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