ORIGINAL RESEARCH

Prognostic determination using optical coherence tomography compared with visual functions in optic neuritis

Kitthisak Kitthaweesin, Plern Sutra

Department of ophthalmology, Faculty of Medicine, Khon Kaen university, Khon Kaen, Thailand

Correspondence: Kitthisak Kitthaweesin. Address: Department of Ophthalmology, Faculty of Medicine, Khon Kaen University, Khon Kaen, 40002, Thailand. E-mail: Kitthisak@hotmail.com

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Abstract

Background: The majority of optic neuritis patients often notice improvement and gain stability of their visual functions, however, evidences of ongoing retinal nerve fiber layer (RNFL) thinning have been reported.

Purposes: To investigate the correlation between RNFL thickness measured with Optical coherence tomography (OCT) and visual function tests and to determine the utility of OCT in visual prognostic assessment of optic neuritis.

Method: A prospective study was performed in 12 patients with acute isolated optic neuritis. Best corrected visual acuity (BCVA), Swedish interactive threshold algorithms (SITA) 30-2 strategy on Humphrey field analyzer, and fast RNFL thickness analysis were performed on both affected and fellow eyes at baseline, 1.5, three and six months.

Results: Mean BCVA and average mean deviation (MD) of the affected eye were significantly different from the fellow eyes at baseline. Affected eyes had significant thinner of RNFL at baseline, 1.5, three, and six months. Significant correlations between (i) mean RNFL thickness and BCVA at 1.5 ($r = 0.707$, $p = .010$), (ii) mean RNFL thickness and MD at 1.5 months ($r = 0.674$, $p = .016$) and six months($r = 0.710$, $p = .032$), (iii) mean RNFL thickness at 1.5 months and MD at six months ($r = 0.782$, $p = .013$).

Conclusion: A correlation between RNFL thickness and visual function tests indicates that OCT might have roles in detection and prediction of RNFL damage in Optic neuritis (ON) patients despite no evidence of MS.

Key words

Optic neuritis, Optic neuropathy, Optical coherence tomography, Retinal nerve fiber layer, Visual field, Visual loss

1 Introduction

Optic neuritis (ON) is an inflammatory disease of the optic nerve. Patients usually present as subacute monocular visual loss within days to weeks, periorbital pain with eye movement, visual field defect, and red color vision deficit [1, 2]. Practically, ON is a clinical diagnosis, but usually visual evoked potentials (VEP) and MRI are done in these patients to investigate if it is not only ON but if it is a MS [1, 2]. Optic Neuritis Treatment Trial (ONTT) indicated intravenous methylprednisolone as the standard treatment of ON, which speed recovery of visual functions and reduced risk for

development of clinically definite multiple sclerosis (CDMS). The majority of patients often notice improvement of their visual functions within three weeks, and gain optimal stability for visual field and visual acuity within three months and one year, respectively [1]. However, evidences of ongoing retinal nerve fiber layer (RNFL) thinning have been reported [3-5]. To date, ophthalmologists often use subjective tests to monitor patients, which probably provide insufficient determination for visual prognosis in ON. Optical coherence tomography (OCT) is a noninvasive technique which creates an image according to the histological layers of the retina in real time with high resolution, accuracy, and reproducibility [6-8].

The purposes of the present study were to investigate the correlation between RNFL thickness measured with OCT and visual function tests; including visual acuity and visual field, and to determine the utility of OCT in visual prognostic assessment of ON.

2 Material and method

Patients diagnosed as having ON with the eligibility criteria; including (i) clinical of typical ON(1), (ii) unilateral involvement with asymptomatic fellow eye, (iii) no previous episodes of ON in an affected eye. Exclusion criteria were patients with (i) other ocular diseases those might interfere with vision; including glaucoma, dense cataract, retinal detachment, and (ii) denial to comply with a follow-up program. After informed consent, all eligible patients underwent VEP, cerebral MRI and intravenous administration of methylprednisolone. Patients' anonymity was carefully protected thorough the study. Besides testing for best corrected visual acuity (BCVA), intraocular pressure, biomicroscopic and funduscopic examinations, Swedish interactive threshold algorithms (SITA) 30-2 strategies on a Humphrey field analyzer 750 (Zeiss/Humphrey Systems, Dublin, CA, USA), and fast RNFL thickness analysis with Stratus OCT model 3,000 (Carl Zeiss Meditec, Dublin, CA, USA) were performed three times each on both affected and fellow eyes at baseline, 1.5, three and six months by a certified technician who was masked with the diagnosis. Three parameters including: BCVA according to the Snellen chart which converted to the logarithm of minimum angle of resolution (logMAR), mean deviation (MD) of perimetry (decibel, dB), and RNFL thickness (micron) around optic disc in four aspects, were recorded. After pupillary dilation with 1% tropicamide (Alcon, Thailand), each eye was circularly scanned three times 3.4 mm around the optic nerve with acceptable pupillary size and signal strength (5 mm and 7, respectively). Statistical analysis was performed with SPSS version using Wilcoxon signed rank test for comparison of affected and fellow eyes and using Spearman's rho for correlations of three parameters.

3 Results

Twelve patients (nine males and three females) were enrolled ranging between 31 and 54 years of age (average, 44), who had been diagnosed with isolated ON (see Table 1). All patients presented with subacute visual loss in seven left eyes and five right eyes. The mean duration of symptoms was 14.9 days (range seven days-36 days). Seven (58%) patients noticed pain with eye movement, while five (41%) showed optic disc swelling. All patients had normal cerebral MRI but had delayed P100 component in an affected eye. Intravenous methylprednisolone (250 mg every six hour) for three days, followed by 1mg/kg/day) of oral prednisolone for 11 days were prescribed.

Mean baseline BCVA of the affected eye (0.96 ± 0.78) was different from the fellow eyes (0.02 ± 0.01, $p < .001$). However, no statistically significant difference was revealed at 1.5, three, or six months. The most frequent abnormal perimetry was a generalized defect (50%). Altitudinal and cecocentral defects were revealed in four (33%), and one (0.8%) cases, however, one had normal perimetry. Average MD of the affected eyes was -24.22 ± 11.22 dB, but that of the fellow eyes was -6.83 ± 8.39 ($p < .001$). Despite significant differences of mean MD in the affected eyes compared to the fellow eyes at baseline ($p < .001$) and 1.5 months ($p < .01$), no statistically significant difference was shown at three, and six months.

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Table 1. Demographic and baseline characteristics

Patient	Sex	Age (years)	Affected eye	Underlying disease	Onset (day)	Visual acuity	Visual field defect	Mean deviation	Optic disc
1	F	52	L	-	7	0.691	normal	-1.74	normal
2	F	51	L	migraine	7	0.025	cecocentral	-5.37	normal
3	M	28	L	-	4	0.101	diffuse	-31.15	swelling
4	F	51	L	DM, HT	13	1	altitudinal	-26.18	normal
5	F	54	R	DM, HT	14	0.602	altitudinal	-13.98	swelling
6	F	31	L	-	7	1.9	diffuse	-33.59	swelling
7	F	40	R	-	7	0.151	altitudinal	-28.95	swelling
8	F	41	L	-	36	2.0	diffuse	-31.8	normal
9	F	49	R	-	30	1.9	diffuse	-32.59	normal
10	F	45	L	DM, HT	14	1	diffuse	-27.5	normal
11	M	30	R	-	30	1.9	diffuse	-35.00	normal
12	M	51	R	-	10	0.301	altitudinal	-22.89	swelling

Table 2. RNFL thickness at each visit

	RNFL (Mean ± *SD*) (μm)			
	Baseline	**1.5 months**	**three months**	**six months**
Affectd eyes	113.0 ± 24.2	96.6 ± 12.2	90.9 ± 9.7	87.5 ± 13.1
Fellow eyes	121.0 ± 20.4	107.1 ± 13.0	99.4 ± 14.6	98.6 ± 17.6
p value	.001	.000	.003	.000

Table 3. Correlations of retinal nerve fiber layer thickness and visual acuity

Parameters		VA baseline	VA 1.5 months	VA three months	VA six months
RNFL baseline	Correlation coefficient	0.312	0.357	0.250	0.194
	p value	.324	.254	.434	.545
RNFL 1.5 months	Correlation coefficient	0.523	0.707	0.574	0.491
	p value	.081	.010	.051	.105
RNFL three months	Correlation coefficient	0.459	0.634	0.501	0.390
	p value	.133	.027	.097	.210
RNFL six months	Correlation coefficient	0.379	0.545	0.435	0.327
	p value	.224	.067	.158	.299

Table 4. Correlations of retinal nerve fiber layer thickness and visual field

Parameters		VF baseline	VF 1.5 months	VF three months	VF six months
RNFL baseline	Correlation coefficient	0.033	0.401	0.340	0.563
	p value	.920	.196	.280	.114
RNFL 1.5 months	Correlation coefficient	0.399	0.674	0.487	0.782
	p value	.199	.016	.109	.013
RNFL three months	Correlation coefficient	0.340	0.322	0.283	0.557
	p value	.280	.307	.372	.119
RNFL six months	Correlation coefficient	0.365	0.293	0.318	0.710
	p value	.244	.356	.314	.032

The present study demonstrated significant thinning of the mean RNFL thickness, which calculated from RNFL thickness in the superior, inferior, nasal and temporal aspects, of the affected eyes at baseline, 1.5, three, and six months (see Table 2). Although significant correlations between mean RNFL thickness at 1.5 months and BCVA of the affected eyes at 1.5 (r = 0.707, p = .010) was detected, the correlation between mean RNFL thickness at 1.5 month and BCVA at three (r = 0.574, p .051), six months (r = 0.491, p = .105) were not significant (see Table 3). RNFL thickness at 1.5 months had significant correlations with MD of the affected eyes at 1.5 months (r = 0.674, p = .016) and six months(r = 0.782, p = .013).

Moreover, mean RNFL thickness at six months also correlated significantly with MD at six months (r = 0.710, p = .032) (see Table 4).

4 Discussion

The present study revealed rapid improvement of mean BCVA but perimetry improved significantly at three months, which were comparable to ONTT [1, 2]. The authors noticed correlations between RNFL thickness and visual function tests, particularly perimetry. Moreover, correlation between RNFL thickness at 1.5 months and MD at six months might indicate the role of OCT in monitoring axonal loss and in providing long-term perimetric outcome in ON [9]. However, correlation between RNFL thickness at 1.5 months and BCVA at six months was statistically insignificant. Correlations between RNFL thickness and BCVA, perimetry have been described in patients with ON with [10-12] and without [13] multiple sclerosis.

Petzold A *et al*. [14] meta-analyzed 12 studies regarding RNFL in eyes with multiple sclerosis optic neuritis (MS ON) [12, 15-24]. They observed significant average RNFL loss -20.38 μm in MSON eyes (95% CI, -22.86 to -17.91). RNFL thickness in eyes affected by ON 59.79 μm-85 μm and in fellow eyes 82.73 μm-99 μm [12, 21, 25-26]. In ON without evidence of MS, Costello *et al.* [5] demonstrated RNFL thickness in affected and fellow eyes were 77.5 μm and 99.88 μm, respectively. They noticed that the greatest proportion of the patients developed reduction between three and six months after the episode of ON and stabilized thereafter [27]. ON is not a risk factor for progressive axonal loss after six months without relapses [28]. The present study detected thinner RNFL in affected eyes compared to those of asymptomatic fellow eyes (p < .001) since diagnosis and throughout follow-up program. These indicate roles of OCT in the detection and prediction of RNFL damage in ON patients despite no evidence of MS.

The limitation of the present study is the small sample size, hence the findings have to be reproduced in future larger sample sizes. However, the authors observe the capacity of OCT in RNFL defect detection, which is a promising marker for permanent axonal damage after ON. Furthermore, correlations between RNFL thickness and visual function tests, particularly perimetry, indicated that OCT might have potential to monitor as well as to predict the visual prognostic outcome in ON.

Conflict of interests

After approval by the institutional review board, this prospective study was conducted at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand from August 2009 to April 2011. The authors had no conflict of interest that might influence the outcome or conclusion of the present study.

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