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Scanning Laser Polarimetry in Patients with Acute Attack of Primary Angle Closure

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Purpose: To compare the retinal nerve fiber layer measurements of attacked eyes with their fellow eyes after a single unilateral attack of acute primary angle closure (APAC).

Methods: Patients with a single episode of APAC in 1 eye, successfully treated with laser peripheral iridotomy, were recruited. Eyes with persistently raised intraocular pressure (IOP) after resolution of the acute attack were excluded. Scanning laser polarimetry was carried out at 6 months after remission of the acute attack. The various parameters between the attacked and the fellow eyes were compared using the Student *t*-test.

Results: Twenty-six patients (24 female and 2 male, mean age 66.9 ± 8.1 years) were recruited. The duration of the APAC ranged from 5 to 98 hours (mean, 36.3 hours). The mean presenting IOP during the acute attack was 62.0 ± 9.4 mm Hg. Only the mean inferior ratio and the ellipse modulation showed a statistically significant difference between the attacked and the fellow eyes among the 12 standard scanning laser polarimetry measurement parameters.

Conclusion: No severe retinal nerve fiber layer damage was documented in eyes that suffered a single episode of APAC with duration of attack up to 48 hours. With duration of attack longer than 48 hours, retinal nerve fiber layer damage was detected. **Jpn J Ophthalmol 2003;47:543–547** © 2003 Japanese Ophthalmological Society

Key Words: Acute angle-closure glaucoma, retinal nerve fiber layer, scanning laser polarimetry.

Introduction

Acute primary angle closure (APAC) is an acute, symptomatic ocular hypertension caused by the abrupt closure of the drainage angle secondary to pupillary blockade.[1] The high intraocular pressure (IOP) causes pain, decrease in vision, headache, nausea and vomiting, corneal edema, ciliary flush, and a fixed, semi-dilated pupil. Prolonged increase in the IOP may lead to irreversible damage to the optic nerve and other ocular tissues. With the immediate application of laser peripheral iridoplasty, the IOP can be lowered much more rapidly.[2,3] However, a substantial proportion of patients consult an ophthalmologist more than 24 hours after the onset of attack.[1] It is not known if noticeable optic nerve damage occurs during this period of time. Conventionally, perimetry has been used for documentation of retinal nerve fiber damage. In general, APAC patients belong to the elderly group and most of them have noticeable cataract. Visual field test during and after remission of the attack is often difficult and unreliable.

The Nerve Fiber Analyzer (NFA) is a confocal scanning laser ophthalmoscope with an integrated polarimeter that evaluates the thickness of the retinal nerve fiber layer (RNFL) objectively by using the birefringent properties of the nerve fibers. It has been used for quantitative

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measurement of the RNFL thickness in patients with ocular hypertension and primary open-angle glaucoma.[4–7] As the measurement procedure is fast and objective, it is ideal for elderly patients who find the visual field test difficult.

This study was conducted to evaluate the sensitivity of the NFA in the detection of high IOP-induced subclinical optic neuropathy after a single attack of APAC. The various parameters were compared between the attacked and the nonattacked fellow eyes. Automated perimetry of the attacked and fellow eyes was also performed at the same time for comparison.

Materials and Methods

Study subjects were recruited from patients with a first episode of unilateral APAC presenting to the United Christian Hospital and Prince of Wales Hospital between July 2000 and September 2001. The definition of APAC in this study was: (1) the presence of at least two of the following symptoms: ocular pain, blurred vision, headache, nausea ± vomiting; (2) corneal edema, semidilated unreactive pupil, injected conjunctiva; (3) IOP > 40 mm Hg by Goldmann applanation tonometer; (4) gonioscopic finding of a closed angle. The exclusion criteria were (1) bilateral attack; (2) secondary angle closure; (3) IOP ≥ 21 mm Hg 2 hours after initiation of treatment; (4) progression to chronic angle closure glaucoma characterised by IOP ≥ 21 mm Hg with persistent angle closure and increased cupping; (5) repeat APAC of the studied eyes during follow-up; (6) APAC of the fellow eye in the past or during the premeasurement follow-up; (7) refraction of > ± 5.00 dioptre sphere and/or ± 3.00 dioptre cylinder; (8) persistent corneal edema; (9) other ocular surgery or laser before NFA measurement; and (10) other ocular disease or degeneration that may result in abnormal RNFL thickness.

At presentation, all patients had their IOP lowered initially by medication or laser peripheral iridoplasty, and subsequently received laser peripheral iridotomy to both the attacked and the fellow eyes after remission of the acute attack. Data including the duration of attack, visual acuity, IOP profile, gonioscopic finding and cup-to-disc ratio before and after treatment were documented.

At 6 months after the acute attack, the RNFL thickness of both eyes was measured using the NFA (GDx, Laser Diagnostics Technologies, San Diego, CA, USA). The optic disc images of both eyes of each subject were captured by an experienced operator. The quality of each optic disc image was assessed by an image checklist of the NFA software, and parameters assessed included image intensity, image vignetting, image illumination, contrast and centrality of optic disc. At least three sets of the image of each optic disc judged to have ''pass'' quality by the software checklist were stored and compared by the operator. Only the one with the highest quality was chosen for further analysis. An ellipse was placed around the optic disc margin. Another concentric measuring ellipse of 10 pixel thickness and at 1.75 disc diameter from center of optic disc was generated. The RNFL under this measuring band was analysed in four different quadrants, namely superior and inferior segments of 120º each, a temporal segment of 50º, and a nasal segment of 70º. A series of GDx parameters, including symmetry, superior ratio, inferior ratio, superior/nasal ratio, maximum modulation, the GDx number, ellipse modulation, average thickness, ellipse average, superior average, inferior average and superior integral, were generated and printed in a formatted report. A detailed description of the GDx parameters is available as an appendix (page 105) to the GDx Nerve Fiber Analyzer System Manual, available from Laser Diagnostic Technologies.

Automated perimetry of both eyes using the Humphrey Field Analyzer (HFA 750, Humphrey Instruments, Dublin, CA, USA) C 30(2) full threshold program was performed on the same day. Unreliable results, defined as fixation loss >20% and/or false positive and/or false negative >30%, were excluded from visual field test analysis. The Student *t*-test was used to analyse the difference in the mean GDx standard parameters and the pattern standard deviation (PSD) between the attacked and the fellow eyes. A P value of $<.05$ was considered statistically significant.

Results

In the period between July 2000 and September 2001, a total of 37 eyes with acute angle closure were treated at the United Christian Hospital and the Prince of Wales Hospital. Eleven eyes were excluded from the study for the following reasons: 8 eyes had developed chronic angle-closure glaucoma; 2 eyes had cataract extraction done within 6 months after the acute attack; 1 patient was demented and the NFA measurement failed. The remaining 26 APAC eyes of 26 patients (24 women and 2 men) with a mean age of 66.9 ± 8.1 years were compared to their 26 fellow eyes. Among the APAC eyes, there were 10 right eyes (38.5%) and 16 left eyes (61.5%) in this series. The mean duration of the APAC attack, defined as the onset of at least two of the following symptoms, ocular pain, blurred vision, headache, nausea with or without vomiting; to the time when IOP was ≤21 mm Hg after treatment, was 36.3 ± 26.5 hours (range, 5–98 hours). The mean presenting IOP during the

Table 1. Characteristics of the Attacked and Fellow Control Eyes 6 Months After Remission of the Acute Primary Angle-closure Attack

	Visual Acuity (Range)	Mean Intraocular Pressure ± SD (mm Hg)	Mean Cup-to-disc Ratio ± SD	Mean Refraction (Spherical Equivalence)/ Dioptre	Mean Pupil Size (mm)
Attacked eyes (n = 26)	0.4–0.7 ≤0.5 (65.4%) >0.5 (34.6%)	13.4 ± 3.7	0.38 ± 0.12	−4.25 to +2.25	3.6 ± 0.9
Nonattacked fellow eyes (n = 26)	0.4–1.0 ≤0.5 (53.8%) >0.5 (46.2%)	12.9 ± 3.3	0.32 ± 0.08	−4.00 to +3.00	2.8 ± 0.7
P-value*		.591	.056		<.001*

**P*-value < .05, statistically significant.

acute attack was 62.0 ± 9.4 mm Hg. Nineteen of the studied patients received argon laser peripheral iridoplasty and 7 patients received antiglaucoma medications as the immediate treatment for the acute attack. All patients had their IOP lowered to ≤21 mm Hg within 2 hours after treatment. All patients had laser peripheral iridotomy performed to the attacked and the fellow eye within 48 hours after remission of the acute attack. The characteristics of the attacked and fellow eyes 6 months after remission of the APAC attack are shown in Table 1. There was no statistically significant difference in the mean IOP and cup/disc ratio between the attacked and the fellow eyes at the time of the NFA measurement. However, the mean pupil size of the attacked eyes (3.6 ± 0.9 mm) was significantly larger than that of the fellow eyes (2.9 ± 0.7 mm) ($P<.001$). Details of the RNFL measurement parameters and the automated perimetry are shown in Table 2. Among the 12 standard GDx parameters, only the mean inferior ratio and the ellipse modulation showed a statistically significant difference between the attacked and the fellow eyes. Fourteen patients (53.8%) had unreliable perimetry results and their PSD values were excluded from analyses. There was no statistically significant difference in the PSD between the attacked and the fellow eyes ($P = .439$).

A subgroup analysis on the association between the duration of attack and the RNFL damage was performed. The studied eyes were divided into two groups: (1) duration of attack <48 hours (15 eyes) and (2) duration of attack >48 hours (11 eyes). In the group with duration of attack <48 hours, none of the eyes showed a statistically significant difference in the NFL measurements between the attacked and the fellow eyes (Table 3). In the group with duration of attack >48 hours, the inferior

Table 2. Comparison of the GDx Parameters and the Pattern Standard Deviation Between the Attacked and the Fellow Eyes (All Cases)

Parameters (Mean ± SD)	Attacked Eyes (n = 26)	Fellow Eyes (n = 26)	*P*-value*
Inferior ratio	1.74 ± 0.36	1.99 ± 0.44	.027*
Ellipse modulation	1.71 ± 0.53	2.15 ± 0.68	.013*
Symmetry	0.94 ± 0.17	0.95 ± 0.15	.717
Superior ratio	1.64 ± 0.50	1.90 ± 0.50	.064
Superior/nasal ratio	1.60 ± 0.35	1.63 ± 0.43	.826
Maximum modulation	0.97 ± 0.36	1.14 ± 0.42	.116
GDx number†	62.58 ± 26.30	49.04 ± 27.21	.074
Average thickness	56.35 ± 10.46	58.54 ± 10.72	.459
Ellipse average	57.31 ± 10.56	60.81 ± 11.06	.249
Superior average	60.73 ± 14.02	64.88 ± 14.98	.307
Inferior average	65.08 ± 13.18	69.96 ± 12.77	.181
Superior integral	0.19 ± 0.05	0.20 ± 0.05	.560
PSD‡	4.30 ± 2.95	3.70 ± 2.11	.439

**P* < .05, statistically significant.
†GDx number: a figure ranging from 0 (normal) to 100 (glaucoma).
‡PSD: pattern standard deviation.

Table 3. Comparison of the GDx Parameters and the Pattern Standard Deviation Between the Attacked and the Fellow Eyes (Duration of Attack <48 Hours)

Parameters (Mean ± SD)	Attacked Eyes* (n = 15)	Fellow Eyes (n = 15)	*P*-value†
Inferior ratio	1.69 ± 0.41	1.86 ± 0.41	.292
Ellipse modulation	1.67 ± 0.62	2.00 ± 0.70	.182
Symmetry	0.98 ± 0.15	0.96 ± 0.17	.687
Superior ratio	1.68 ± 0.53	1.80 ± 0.56	.547
Superior/nasal ratio	1.60 ± 0.33	1.62 ± 0.43	.920
Maximum modulation	0.91 ± 0.36	1.05 ± 0.44	.344
GDx® number‡	67.73 ± 27.25	59.20 ± 27.55	.401
Average thickness	56.35 ± 10.46	58.54 ± 10.72	.459
Ellipse average	55.40 ± 11.70	59.20 ± 13.42	501
Superior average	60.73 ± 14.02	64.88 ± 14.98	.307
Inferior average	62.07 ± 13.17	67.53 ± 14.99	.298
Superior integral	0.20 ± 0.05	0.20 ± 0.06	.947
PSD§	5.39 ± 3.10	4.33 ± 2.38	.300

*Mean duration of attack 18.1 ± 11.9 hours. Mean presenting intraocular pressure: 63.9 ± 9.0 mm Hg.
†$P < .05$, statistically significant.
‡GDx number: a figure ranging from 0 (normal) to 100 (glaucoma).
§PSD: pattern standard deviation.

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ratio, ellipse modulation, superior ratio, and GDx number showed statistically significant differences between the attacked eyes and the fellow eyes ($P < .05$) (Table 4).

Discussion

The high IOP during APAC may cause permanent damage to the optic nerve especially if the attack is prolonged. Various reports on the post-APAC visual field defects revealed different results.[8–10] The inconsistency in the results may be partly explained by the fact that perimetry is technically demanding, especially in elderly patients with slow sensory-motor co-ordination. Other factors that might have influenced the visual field test included post-APAC cataract and mydriasis.[11,12] Therefore, post-APAC visual field defect may not accurately reflect the true extent of IOP-induced optic neuropathy. In the current study, 53.8% of the patients failed to produce a reliable automated perimetry result despite clear and repeated instructions. It would be difficult to rely on visual field tests to identify early glaucomatous change in these patients.

Scanning laser polarimetry measurement, on the other hand, does not require the patient's sensory-motor co-ordination. Unfortunately, the two factors, cataract and mydriasis, that affect the visual field test may also interfere with the RNFL thickness measurement by scanning laser polarimetry. In this series, patients who had developed significant cataract were scheduled for cataract operation and were excluded from the study. This would minimize the error in the RNFL thickness measurement due to the presence of cataract. However, the attacked eyes had significantly larger pupil size then the fellow eyes. With a dilated pupil, the laser beam may enter the eye through the peripheral cornea resulting in retardation exceeding the range of the anterior segment compensating device. Hoh et al found no significant change in the RNFL thickness measured by the scanning laser polarimetry in eyes under pharmacological mydriasis (mean pupil size, 7.3 mm).[13] In our series, the mean pupil size of the attacked eyes was only 3.6 mm. The effect on retardation should have been minimal.

Table 4. Comparison of the GDx Parameters and the Pattern Standard Deviation Between the Attacked and the Fellow Eyes (Duration of Attack >48 hours)

Parameters (Mean ± SD)	Attacked Eyes* (n = 11)	Fellow Eyes (n = 11)	*P*-value†
Inferior ratio	1.79 ± 0.28	2.16 ± 0.35	.014
Ellipse modulation	1.76 ± 0.40	2.35 ± 0.63	.017
Superior ratio	1.58 ± 0.45	2.04 ± 0.42	.023
GDx number‡	55.55 ± 24.43	35.18 ± 20.54	.047
Symmetry	0.87 ± 0.175	0.94 ± 0.13	.287
Superior/nasal ratio	1.60 ± 0.39	1.64 ± 0.44	.837
Maximum modulation	1.04 ± 0.38	1.26 ± 0.37	.185
Average thickness	57.64 ± 8.77	59.64 ± 6.67	.554
Ellipse average	59.00 ± 9.03	63.00 ± 6.65	.251
Superior average	60.00 ± 10.74	66.09 ± 10.10	.186
Inferior average	69.18 ± 12.62	73.27 ± 8.47	.383
Superior integral	0.18 ± 0.04	0.20 ± 0.04	.315
PSD§	3.20 ± 2.11	3.97 ± 2.70	.469

*Mean duration of attack: 61.1 ± 19.8 hours. Mean presenting intraocular pressure: 59.5 ± 9.8 mm Hg.

†$P < .05$, statistically significant.

‡GDx number: a figure ranging from 0 (normal) to 100 (glaucoma).

§PSD: pattern standard deviation.

Comparison of the attacked eye against the fellow eye of the same patient has the advantage of minimizing the impact of individual variations in ocular anatomical parameters. The attacked and the control samples are of the same age and sex. The attacked and the control eyes have similar refractive error and media clarity and both have received laser peripheral iridotomy. The major difference is the size of the pupil during RNFL measurement. The inter-patient variability in perimetry examination is also minimized.

This study shows that a single attack of APAC, with duration of ocular hypertension up to 48 hours, does not cause statistically significant difference in the GDx parameters as measured by NFA. However, in eyes with duration of ocular hypertension longer than 48 hours during the acute APAC, NFA measurement parameters including the inferior ratio, ellipse modulation, superior ratio and GDx number showed statistically significant differences between the attacked and the fellow eyes ($P < .05$). The results have indicated that the severity of the NFL damage is likely to depend on the duration of the attack.

The inferior ratio is the ratio of the average of the 1500 thickest pixels in the inferior quadrant over the average of the 1500 median pixels in the temporal quadrant. In other words, it reflects the thickness of the inferior quadrant relative to that of the temporal quadrant. It is interesting to note that there are no statistically significant differences, between the attacked and the fellow eyes, in the 'inferior average' and the 'average thickness' parameters (Table 2). The clinical relevance of a difference in the inferior ratio, while the inferior average and the average thickness parameters remain statistically equivalent, is not known. This could be due to the small sample size, or could represent early glaucomatous damage in APAC eyes.

The ellipse modulation is an indication of the difference between the thickest parts of the nerve fiber layer and the thinnest parts. Rather than using all the points in the image, ellipse modulation uses the pixels covered by

the ellipse surrounding the optic nerve. Ellipse modulation is calculated by taking the thickest pixel beneath the ellipse, subtracting the thinnest pixel beneath the ellipse, and dividing the total by the value of the thinnest pixel. The clinical relevance of a difference in this parameter, while the majority of the other parameters remain statistically equivalent, is again unknown.

It should be noted that in all the thickness parameters, the mean values of the attacked eyes are smaller than those of the nonattacked fellow eyes. These differences have, however, not reached statistical significance. If a much larger sample size had been used, these differences may have reached statistical significance. The same also applies to the statistically insignificant difference in the pattern standard deviation, as measured by automated perimetry. A sample size calculation based on results of this study shows that the number of eyes required to reach a statistical significant result is 40 (90% power at 5% significance level). Despite this shortcoming of the study, the authors feel it is still reasonable to conclude that after one single attack of APAC, with ocular hypertension lasting up to 48 hours, there is no severe and obvious RNFL damage or loss, as measured by NFA or automated perimetry. However, when the high IOP persists for longer than 48 hours, damage in the RNFL is detectable in some of the NFA measurements.

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