Correlation between Clinical Grading and Quantification by Neutral Density Filter of Relative Afferent Pupillary Defect (RAPD)

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***Objective**: To investigate the correlation between clinical grading in plus scale and quantified relative afferent pupillary defect (RAPD) using the neutral density filter bar.*

***Material and Method:** This was a prospective analytical cross sectional study. Sixty-nine patients of any ocular disease with relative afferent pupillary defects were prospectively examined. The RAPD was graded twice in each patient by the clinical grading plus scale (grade 1+ to 4+) and then by using a neutral density filter (NDF) bar. Patients with an abnormal pupil or had been dilated with medication were excluded. Both clinical grading of RAPD and quantified RAPD by the NDF bar were performed by the same physician. All patients were tested by the same technique. Statistical analysis was done to compare the results of both methods.*

***Results:** The RAPD grading by the clinical plus scale correlated significantly with the grading by the neutral density filter bar, ($p < 0.05$). The four clinical grades had corresponding values in the neutral density log unit: grade1+ $\leq$ 0.6 log unit (94.7%), grade 2+ = 0.6-0.9 log unit (85%), grade 3+ = 1.2-1.5 log unit (88.3%), grade 4+ $\geq$ 1.8 log unit (84.6%).*

***Conclusion:** The results of the two methods of grading RAPD using the plus scale and the neutral density filter bar are comparable. Each grade had a corresponding value in log units. In a clinical setting where neutral density filter bars are not available, the authors can grade RAPD using the plus scale.*

***Keywords:** Relative pupillary defect, Pupillary light reaction, Neutral density filter, Swinging flashlight test, RAPD grading*

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Relative Afferent Pupillary Defect (RAPD) is an important diagnostic test evaluating abnormalities along the optic nerve. By comparing functions between both optic nerves, RAPD reveals positive results not only in cases of unilateral optic nerve dysfunction or asymmetrical bilateral optic nerve dysfunction, but also conditions with decreased ganglion cell input such as macular or extensive retinal diseases, in which the degree of RAPD and the quantity of abnormal nerve fibers correlate correspondingly[1,2].

RAPD testing can be achieved by various techniques, such as the swinging flashlight test, automated swinging flashlight test, or pupillography. The swinging flashlight test is the most common technique in practice. RAPD can be graded clinically or objectively quantified with a neutral density filter, which involves placing an increasingly dense filter in front of the sound eye and reading the last measurement at which RAPD disappears. The latter technique has been proven to be more precise[3] and more useful in grading severity in certain disorders (*e.g.*, central retinal vein occlusion[4] and traumatic optic neuropathy[5]). It also correlates better with automated visual field defects[6,7]. Despite such advantages, the neutral density filter is not popular in Thailand where clinical grading of 1+ to 4+ still prevails. Interchangeable values between the two systems have yet to exist, raising uncertainties and much confusion in communication and especially at times of medical transferal.

In the present study, the authors aimed to find a correlation between the clinical grading of RAPD and the results measured with a neutral density filter. Bell et al reported validity and reproducibility between the two techniques and concluded that they were correlated[8], but the clinical grading used in that study

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was different from the clinical plus scale being used in Thailand.

Material and Method

The present study is a prospective, analytical cross-sectional study. The protocol of the study adhered to the provisions of the Declaration of Helsinki and was approved by the Medical Ethics Committee of Songklanagarind Hospital. Informed consent was obtained from all patients. Inclusion criteria included a positive result on RAPD testing. Exclusion criteria included patients treated with mydriatics/miotics, patients with pupil abnormality, corneal opacity, CN III palsy with pupillary involvement, and Horner's syndrome. In patients that were deemed eligible, the data collected included best corrected visual acuity (BCVA) as measured with an Early Treatment Diabetic Retinopathy Study (ETDRS) chart in log MAR unit, color vision tested with Ishihara plates, biomicroscopy examination and causative disease. RAPD was tested with the swinging flashlight technique with the patient in a dark or dimly light examination room with his/her sight focused at 6 meters and then alternately a swinging bright light from a 6.5V indirect ophthalmoscope which was placed 30 cm from the eyes and between both eyes with equal duration (3 seconds in each eye). The procedures were repeated 3 times.

Clinical grading of RAPD was graded from 1+ to 4+[9,10]. Grading 1+ means initial constriction and early re-dilatation. Grading 2+ is no initial constriction (initial stall) then dilatation. Grading 3+ is immediate dilatation while grading 4+ is fixed amaurotic pupil. Then RAPD was graded with the neutral density filter[3]. The neutral density filter was placed in front of the sound eye, and the density was increased at 0.3 log unit increments until RAPD became negative, at which point the density was further increased 0.3 log unit more to confirm its disappearance. The neutral density filter bar used in the present study had 6 levels of density, ranging from 0.3 to 1.8 log unit (as illustrated). If 1.8 log unit density was reached and RAPD had not become negative, a measurement of above 1.8 log unit was read.

Both clinical and neutral density grading were done by the same investigator and the results were randomly confirmed by a neuro-ophthalmologist.

Statistical Analysis

Data were collected with the EpiData program and a statistical analysis was performed with SPSS. The Pearson Chi-square test was used to identify the correlation between the two grading systems. A p-value of less than 0.05 was considered statistical significant.

Results

Sixty-nine patients were included in the present study, 43 (62.3%) were male and 26 (37.7%) were female. The mean age (± SD) was 39.54 (± 19.35) years, ranging from 10 to 80 years (Table 1). Causative diseases were 15 (21.74%) optic neuritis, 14 (20.29%) traumatic optic neuropathy, 9 (13.04%) non-arteritic anterior ischemic optic neuropathy, 5 (7.25%) sellar/parasellar mass, 3 (4.35%) optic nerve sheath meningioma, 3 (4.35%) glaucoma, 3 (4.35%) pachymeningitis, 3 (4.35%) cavernous sinus fistula, 3 (4.35%) non-specific orbital inflammation, 8 (11.59%) retinal diseases and 3 (4.35%) others.

The mean VA in eyes with RAPD was 1.2 logMAR (± 0.99), with VA ranging from 0 to 3 log MAR.

Clinical grading revealed 19 patients with grade 1+ (27.5%), 20 patients with grade 2+ (29%), 17 patients with grade 3+ (24.6%) and 13 patients with grade 4+ (18.8%).

A correlation was found between the two grading systems at all levels, with grade 1+ and ≤ 0.6 log unit (94.7%), grade 2+ and 0.6-0.9 log unit (85%), grade 3+ and 1.2-1.5 log unit and grade 4+ and ≥1.8 log unit (Fig. 1, Table 2).

Discussion

The present study aimed to find a correlation between clinical and neutral density filter grading of RAPD and interchangeable values from both grading systems. The authors found a statistically significant

Table 1. Patients' data (n = 69)

Characteristics	n (%)
Gender	
Male	43 (62.3%)
Female	26 (37.7%)
Age (years)	
mean (± SD)	39.54 (± 19.35)
range	10-80
VA (log Mar)	
mean (± SD)	1.20 (± 0.99)
range	0.00-3.00
Group	
RAPD 1+	19 (27.5%)
RAPD 2+	20 (29%)
RAPD 3+	17 (24.6%)
RAPD 4+	13 (18.8%)

RAPD = Relative Afferent papillary Defect

Table2. Correlation between clinical grading and neutral density filter

RAPD	NDF (log unit), n (%)							Total	p*
	0.3	0.6	0.9	1.2	1.5	1.8	>1.8		
1+	13(68.4)	5(26.3)	1(5.3)	-	-	-	-	19(100)	< 0.05
2+	1(5)	7(35)	10(50)	2(10)	-	-	-	20(100)	< 0.05
3+	-	-	1(5.9)	8(47.1)	7(41.2)	1(5.9)	-	17(100)	< 0.05
4+	-	-	-	-	2(15.4)	7(53.8)	4(30.8)	13(100)	< 0.05
Total	14	12	12	10	9	8	4	69	

* p-value, p < 0.05 (Pearson Chi-square), RAPD = Relative afferent pupillary defect, NDF = Neutral density filter

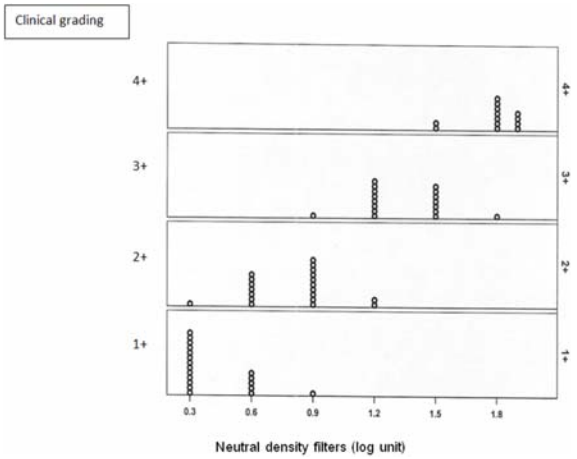

Fig. 1 Correlation between clinical grading and neutral density filter

correlation between the two systems with clinical grade 1+ equal to ≤ 0.6 log unit, grade 2+ equal to 0.6-0.9, grade 3+ equal to 1.2-1.5 log unit and grade 4+ equal to ≥1.8 log unit.

Compared with to the Bell et al study, the authors found that the results agreed in a similar trend; grade I was equal to 0.4 log unit, grade II was equal to 0.7 log unit, grade III was equal to 1.1 log unit, grade IV was equal to 2.0 log unit and grade V was equal to infinity[8]. But in that study, clinical grade IV and V were defined differently. The present assumed grade IV and V to be equal to grade 4+.

The present study has limitations. The wide range of the age group provided a wide range of pupillary size, which in turn affected the detection of RAPD. In young patients with large pupils it might be overestimated and in older patients with small pupils it might be underestimated[3].

Both grading systems were done by the same investigator without blinding. This could pose a measurement bias. The authors have tried to reduce this by having a random confirmation by a neuro-ophthalmologist.

A neutral density filter has a maximal density at 1.8 log unit, hence any larger RAPD than 1.8 log unit cannot be quantified accordingly. A high density neutral density filter also made it difficult to evaluate pupillary reaction, especially in dark-iris subjects.

Clinical grading or neutral density filter grading of RAPD is important in monitoring disease progression and treatment response. Clinicians who do not have the neutral density filter can still use the clinical grading system and compare it with the RAPD measured with the neutral density filter because there is a correlation between both methods.

Conclusion

Both RAPD grading systems are correlated and interchangeable. In the absence of a neutral density filter, clinical grading can be converted into a log unit so to communicate better among medical professionals.

Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างการประเมินผลระดับความผิดปกติในการตอบสนองต่อแสงของรูม่านตาแบบแบ่งเกรดกับการใช้แผ่นฟิล์มกรองแสง

ปาริดา โยธารักษ์, นิพัฒน์ เอื้ออารี

วัตถุประสงค์*: เพื่อหาความสัมพันธ์ระหว่างระดับความผิดปกติในการตอบสนองของรูม่านตาต่อแสง (Relative afferent pupillary defect, RAPD) แบบแบ่งเกรดกับวิธีใช้แผ่นฟิล์มกรองแสง (neutral density filters bar)*

วัสดุและวิธีการ*: การวิจัยเชิงวิเคราะห์แบบศึกษาไปข้างหน้า (prospective cross section analysis) ศึกษาจากผู้ป่วยที่มาตรวจที่คลินิกตาโรงพยาบาลสงขลานครินทร์ระหว่างเดือนกรกฎาคม พ.ศ. 2552 – สิงหาคม พ.ศ. 2553 โดยเลือกผู้ป่วยที่ตรวจพบ RAPD จากโรคต่างๆ และมีรูม่านตาที่ผิดปกติ โดยเกณฑ์คัดออกคือผู้ป่วยที่ม่านตาผิดปกติไม่สามารถประเมินรูม่านตาได้หรือผู้ป่วยที่ได้รับยาขยายม่านตาหรือหดม่านตามาก่อน มีผู้เข้าร่วมการศึกษา 69 คน ทุกคนได้รับการตรวจ RAPD และประเมินระดับความผิดปกติ 2 แบบ โดยแบบแบ่งเกรด(เกรด 1+ ถึง 4+)ก่อนจากนั้นโดยวิธีใช้แผ่นฟิล์มกรองแสง ผู้ป่วยทุกคนได้รับการตรวจโดยวิธีการและอุปกรณ์แบบเดียวกัน นำผลระดับผิดปกติทั้งสองแบบมาวิเคราะห์ทางสถิติ*

ผลการศึกษา*: ระดับความผิดปกติ RAPD แบบแบ่งเกรดสัมพันธ์กับระดับความผิดปกติโดยใช้แผ่นฟิล์มกรองแสง (NDF) มีอย่างมีนัยสำคัญทางสถิติ (P<0.05) ทั้ง 4 เกรด มีค่าที่ไปด้วยกันกับค่าความผิดปกติแบบ log unit โดยเกรด 1+ ≤0.6 log unit (ร้อยละ 94.7) , เกรด 2+ = 0.6-0.9 log unit (ร้อยละ 85), เกรด3+ = 1.2-1.5 log unit (ร้อยละ 88.3),เกรด 4+ ≥1.8 log unit (ร้อยละ 84.6)*

สรุป*: ผลการศึกษาระดับความผิดปกติ RAPD ทั้งสองแบบสัมพันธ์กัน สามารถเปรียบเทียบค่าโดยประมาณได้ โดยในสถานที่ที่ไม่มีแผ่นแถบฟิล์มกรองแสงซึ่งสามารถตรวจได้ค่าที่แม่นยำกว่า เราสามารถใช้การตรวจแบบแบ่งเกรดและประเมินระดับความผิดปกติได้*