Comprehensive Study of Relative Afferent Pupillary Defect in Kanyakumari Medical College, Tamil Nadu

Beena R.[1], Anuradha T.R.[2]

[1, 2] Department of Ophthalmology, Kanyakumari Government Medical College, Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

ABSTRACT

BACKGROUND

Relative afferent pupillary defect (RAPD) or Marcus Gunn pupil is a highly sensitive and significant objective clinical finding in eye examination. It can be detected by swinging flashlight test. Its presence indicates unilateral afferent sensory abnormality or an asymmetric bilateral disease. However, it can be determined even in an unconscious patient, requires no complicated gadgets, relies on clinical observation but can be a manifestation of a myriad of disorders affecting the eye or the brain. The goal of our study was to identify the aetiology of relative afferent pupillary defect and ascertain whether the grade of relative afferent pupillary defect correlated with the visual prognosis.

METHODS

This was a prospective observational hospital-based study. 25 consecutive patients who presented with a clinical diagnosis of relative afferent pupillary defect to the Ophthalmology Department of Kanyakumari Government Medical College in Tamil Nadu from February 2019 to January 2021 were included in the study. The patients were evaluated based on visual acuity, refraction, colour vision, slit lamp, fundus examination, intra ocular pressure (IOP) measurements & fields. Statistical analysis was done by trial version of statistical package for social sciences (SSPS) software.

RESULTS

Of the 25 cases analysed, 60 % (15) were male, 36 % (9) were females and 4 % (1) children. An analysis of the aetiology revealed that the optic nerve pathology was the predominant aetiology accounting for 60 % (15) of cases, followed by glaucoma 24 % (6) and retinal pathology in 16 % (4). Glaucoma though a bilateral disease has an asymmetrical presentation which led to RAPD. Grade of RAPD correlated well with the visual prognosis.

CONCLUSIONS

RAPD is a good and valuable clinical tool for any clinician, it is also a useful guide for assessing the management and response to treatment.

KEYWORDS

Relative Afferent Pupillary Defect, Optic Neuropathy, Retinal Detachment, Glaucomatous Optic Atrophy

Corresponding Author:
Dr. Anuradha Thanjavur Rajagopal,
M-18/C, Geetanjali Complex,
15th Avenve, Ashok Nagar,
Chennai - 600083, Tamil Nadu, India.
E-mail: dranuophthal@gmail.com

DOI: 10.18410/jebmh/2021/569

How to Cite This Article:
Beena R, Anuradha TR. Comprehensive study of relative afferent pupillary defect in Kanyakumari Medical College, Tamil Nadu. J Evid Based Med Healthc 2021;8(33):3128-3133. DOI: 10.18410/jebmh/2021/569

Submission 02-03-2021,
Peer Review 10-03-2021,
Acceptance 28-06-2021,
Published 16-08-2021.

BACKGROUND

The pupil is central to any neuro ophthalmological examination. Pupillary abnormalities by themselves are capable of pinpointing the aetiology on several occasions. Marcus Gunn pupil, Holmes Adie pupil, Horner's syndrome, Argyll Robertson pupil to name a few. Marcus Gunn pupil is an important pupillary sign which is also known as relative afferent pupillary defect. Named after Robert Marcus Gunn, the Scottish ophthalmologist, relative afferent pupillary defect is the hallmark of a unilateral lesion or a bilateral asymmetric disease of the anterior visual pathway. It is never bilateral because it compares the optic nerve conduction of one relative to another.

A relative afferent pupillary defect is one of the most reliable and sensitive indicator of optic nerve dysfunction that is asymmertrical.[1] It has been found to be very valuable tool which can be applied as a rapid test in a clinical setting. This test can be graded using the swinging flashlight test and neutral density filter test which are relatively easier to perform without the requirement of complicated gadgets but nonetheless provide you with information and offer a clue to the aetiology. In an unconscious patient, a relative afferent pupillary defect may be the only sign signalling a graver pathology. In a patient with traumatic optic neuropathy, poor initial visual acuity and a higher grade of relative afferent pupillary defect usually reflects a very grave visual prognosis. RAPD is usually picked up by the swinging flashlight test with or without neutral density filters and graded accordingly.

The grades of RAPD are as follows
1 +: Initial pupillary constriction followed by escape
2 +: No initial pupillary constriction then dilatation
3 +: Immediate pupillary redilatation
4 +: Amaurotic pupil[2]

Grades using neutral density filters are
1 + < 0.6 log units
2 + = 0.6 – 0.9 log units
3 + = 1.2 – 1.5 log units
4 + > 1.8 log units[3]

At least 25% retinal nerve fibre layer (RNFL) loss is required for significant RAPD.[4]

Objective

- To analyse the various aetiological factors of RAPD
- To assess the significance of association between the grade of RAPD and visual prognosis.
- To identify the correct aetiological factor for management and also for educating, motivating the patient for proper follow up.

METHODS

This study was a prospective, observational, hospital-based study. 25 consecutive patients presenting with relative afferent pupillary defect (RAPD) to the Department of the Ophthalmology at Kanyakumari Government Medical College Hospital from Feb 2019 to Jan 2021 were included in the study. After obtaining Institutional Ethical committee clearance and necessary informed consent from patients, the following evaluation were done in patients with relative afferent pupillary defect. A complete ocular history was taken along with detailed past history of previous surgeries, trauma, glaucoma, diabetes mellitus, hypertension etc. Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) were recorded using Snellen's chart.

Swinging flashlight test was done and the grade of the RAPD determined. This was done under ambient lighting conditions, with the patient fixing at a distance using the bright light of a torch light as light source. The light source was rapidly moved between the two eyes allowing the light to rest 3 seconds in each eye and pausing for 2 seconds in between. This was done on an average 5 times as a single alternation alone is not ideal. The test was quantified by using the neutral density filters, increasing in steps of 0.3 log units placed in front of the normal eye until there was no relative afferent pupillary defect. The patient was asked to fix at a distance to negate the effects of miosis due to near reflex and a very bright source was avoided as it was likely to cause false negative results. Detailed slit lamp examination was done with special emphasis on the corneal oedema, keratic precipitates, iris angle/iris neovascularisation, pseudo exfoliation, cataract grading etc. The eyes were dilated using tropicamide and phenylephrine eye drops and fundus examination using slit lamp with 90 Diopter lens and indirect ophthalmoscope with 20 Diopter lens was done.

Intra ocular pressure was measured using Applanation tonometer. Color vision was checked using Ishihara's pseudo isochromatic charts. Fields were done by automated perimetry Humphrey field analyser (HFA) where possible depending on the vision.

Inclusion Criteria

All patients with RAPD with defective vision.
All age groups and both sexes were included.

Exclusion Criteria

Anatomically abnormal pupil.

Statistical Analysis

Statistical analysis was done using trial version of SPSS software.

RESULTS

	Optic N Pathology	Glaucoma	Retina
Male	11	3	1
Female	3	3	3
Children	1		
Total	**15**	**6**	**4**

Table 1. Distribution of Subjects by Pathology and Gender

Looking into the details of optic nerve pathology, we find that optic neuritis and optic atrophies were more common. While optic neuritis and traumatic optic neuropathies have a sudden onset, compressive optic neuropathy usually has a gradual onset.

Grades	Optic Neuritis	Traumatic ON	Compressive ON	AION	POA	SOA	COA
1+	2	1					
2+	2	1			3		1
3+	1		1	1		1	
4+		1					

Table 2. Association of RAPD Grades with Optic Nerve Pathology

Among the grades of RAPD, Gr 1 + RAPD was present in 3 patients, Gr 2 + RAPD in 12 patients, Gr 3 + RAPD in 7 and Gr 4 + in 3 patients.

Grade	Male	Female	Children
1+	1	1	1
2+	8	4	-
3+	4	3	-
4+	2	1	-
Total	**15**	**9**	**1**

Table 3. Gender Wise Distribution of RAPD Grades

An analysis of visual acuity showed grade 4 + RAPD with poor vision, grade 1 + RAPD with relatively better vision grade 2 + and grade 3 + in between. The prevalence rate of Gr 1 + RAPD was 12 %, Gr 2 + 48 %, Gr 3 + 28 %, Gr 4 + 12 %.

Grade	6/9-6/24	6/36-6/60	5/60-1/60	CFCF-	HM	PL	No PL
1+	3						
2+		8	2	2			
3+			4	2		1	
4+						1	2

Table 4. Significance of Association of Grades of RAPD with Visual Acuity

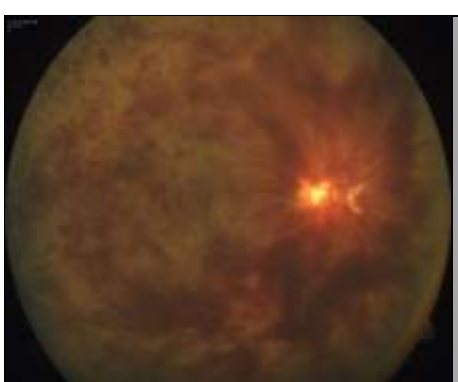

Figure 1a. Central Retinal Vein Occlusion (CRVO)

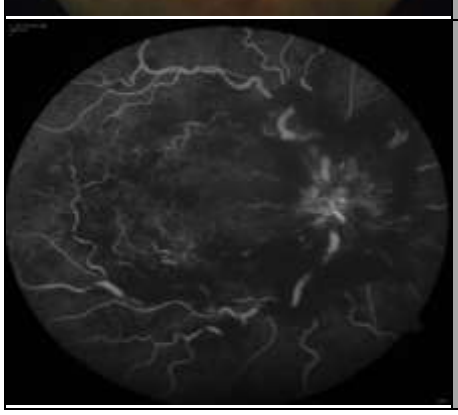

Figure 1b. CRVO- FFA

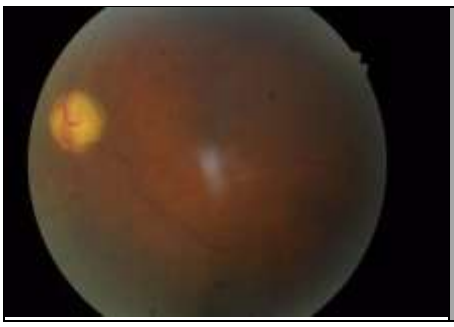

Figure 2. Glaucomatous Optic Atrophy

Figure 3. Papillitis

The decimal equivalent of visual acuity was plotted against the log units of relative afferent pupillary defect grades and a negative correlation was obtained with a correlation coefficient of -0.7164. This suggests a strong correlation that increasing grades of RAPD are associated with a poorer visual prognosis.

Of the twenty-five patients with RAPD who were analysed, 60 % (15) were males, 36 % (9) were females and 4 % (1) children. The predominant cause for RAPD was optic nerve pathology which was seen in 60 % (15) patients. Glaucoma in 24 % (6) patients and retinal pathology in 16 % (4) patients. Optic nerve disease is usually the most common cause for RAPD.[5]

DISCUSSION

In our study, 25 consecutive patients with defective vision and relative afferent pupillary defect on examination, were subjected to relevant investigations and the aetiology was determined. Grading of RAPD was done to find out if it correlated with the visual prognosis. A relative afferent pupillary defect is usually picked up with a swinging flashlight test and if present indicates the possibility of a greater pathology which could be due to optic nerve pathology, glaucoma, or retinal pathology. In our study more males 60 % (15) were affected than females 36 % (9) which correlates with the study by Eulogio Beseda et al.[6] However no gender difference was noted in the study by Lada Kalabhoukhova et al. where glaucoma and healthy subjects were considered.[7]

Optic neuritis is common in females when compared to males and the typical age group for presentation is 20 - 45 years. When it occurs with paralysis due to transverse or ascending myelitis, it is called as neuro myelitis optica (NMO). Neuromyelitis optica has a tendency to affect the paediatric age group, is bilateral and has a predilection for both Asian and African races.[8] In asymmetric optic nerve disease, RAPD can be used for quantifying the loss of

neuronal function. The nasal visual field is smaller than the temporal visual field. So, patients with complete homonymous hemianopia can have a RAPD in the eye contralateral to the side of complete optic tract lesion.

A relative afferent pupillary defect can be seen predominantly in lesions of optic nerve like optic neuritis. Optic nerve pathologies (60 %) were the predominant cause of RAPD in our study, followed by glaucoma (24 %) and retina (16 %) which is different from other studies where glaucoma was the predominant cause for RAPD. Of the optic nerve pathologies, optic neuritis and optic atrophy accounted for five cases each (20 %). Of the optic neuritis 2 were retrobulbar neuritis, 2 papillitis and one neuroretinitis. Magnetic resonance imaging (MRI) done for 4 cases of optic neuritis was normal. Fields revealed central scotoma and centro caecal scotoma. Traumatic optic neuropathy with 12 % (3) cases was the next commonest. This could be due to the fact that in our centre we used to get cross referrals from neurology and also see a greater number of trauma cases.

Traumatic optic neuropathy following orbital trauma is one of the important causes for vision loss in young patients. It can be due to either direct or indirect injury. Direct traumatic optic neuropathy is due to direct injury to optic nerve whereas indirect injury is due to the shearing forces which act on the optic nerve as it is relatively anchored in the optic canal due to fusion of the dural sheath to the canal. Direct decompression is indicated if there is a dislocated bony fragment, fractured or narrowed optic canal or foramen impinging directly on the optic nerve. Optic nerve sheath decompression can be done if ultrasonography demonstrates a fluid filled sheath.

Indirect traumatic optic neuropathy remains more common than the direct optic nerve trauma and its prevalence in closed head trauma varies from 0.5 % - 5 %.[9] The site of injury is usually the forehead or supra orbital rim. Even trivial trauma in this region can lead to indirect optic nerve injury. If there is deterioration of the initial visual acuity/field at presentation following trauma, it most probably indicates a compression of optic nerve or its vascular supply. However, till date the treatment of indirect optic nerve injury remains controversial. As per the second national acute spinal cord injury study protocols (NASCIS 2), intravenous loading dose of methyl prednisolone 30 mg/kg followed by 15 mg/kg 2 hours after the initial dose, followed by 15 mg/kg every hour has been tried with favourable results.

In patients with RAPD < 2.1 log units, moderate doses of steroids are given like optic neuritis treatment trial (ONTT).[10] 1 gm IV methyl prednisolone for three days followed by oral methyl prednisolone 1 mg/kg body weight for eleven days is given. In our traumatic optic neuropathy cases, moderate steroid therapy based on the individual case analysis did provide good results as was seen in the study by Menezes Valerie.[11] In patients with traumatic optic neuropathy, initial visual acuity when poor and higher grades of RAPD usually reflect a very grave visual prognosis. Pallor with significant cupping can occur in the end stage of anterior ischaemic optic neuropathy. This can be confused with glaucomatous disc cupping. Neuro retinal rim pallor usually helps us in distinguishing non glaucomatous disc cupping from glaucomatous cupping. In open angle glaucoma, the remaining rim usually remains pink and does not show any pallor.[12] Grade 2+ RAPD (48 %) was significantly more which correlated with study by Amjad A Younis et al. where 86 % of patients had an RAPD less than or equal to 0.6 log units.[13]

Lesions of pretectum produce relative afferent pupillary defect (RAPD) in the contra lateral eye due to the pupillomotor input asymmetry extending from the optic tract to pre-tectal nucleus. Here the relative afferent pupillary defect is usually not accompanied by visual loss, loss of color vision or visual field. An optic tract lesion would produce RAPD in the contra lateral eye which is associated with temporal field loss as each tract contains more crossed fibres than uncrossed fibres.

In glaucoma, the incidence of relative afferent pupillary defect is slightly less hovering around 23 % in cases with primary open angle glaucoma. Relative afferent pupillary defect has been tried as a screening test for glaucoma. It is usually present on the side with greater field loss.[14] It is also commonly found in patients with open angle glaucoma and elevated intra ocular pressures compare to those with Normo tensive glaucoma.[15] In our study, primary open angle glaucoma (POAG) was the biggest contributor on the glaucoma front with 16 % (4), secondary open angle glaucoma (SOAG) 4 % (1) and neovascular glaucoma (NVG) 4 % (1). Fields revealed generalized depression and arcuate defects in 2 glaucoma patients. RAPD has been tried as a screening test for glaucoma. Since it was found that RAPD was more common in patients with open angle glaucoma and elevated intra ocular pressure when compared to those with normal tension glaucoma, relative afferent pupillary defect can be considered as an important parameter for estimating the loss of neuronal function in asymmetric optic nerve disease.

The Marcus Gunn pupil can be taken as a sign of early asymmetric glaucoma and can present even before visual field defects are seen on perimetry. Swinging flashlight for relative afferent pupillary defect had been tried as a screening test for glaucoma. It was found to be moderately sensitive and strongly specific for glaucoma.[16] However, in a large study based on South Indian population, it did not prove to be that reliable.[17] In a study by Anna Bruckmann et al. there was a high correlation between relative afferent pupillary defect and visual field loss in patients with glaucomatous optic neuropathy. Patients who presented with a relative afferent pupillary defect usually had a significant difference in the visual fields of both eyes, compared to patients who did not have relative afferent pupillary defect.

RAPD reflects a reduction in the retinal nerve fibre layer and hence in usually more in cases with advanced losses of retinal nerve fibre layer when compared to the other eye in asymmetrical glaucoma. Our study did not correlate with the study by Dara Lankaranian et al. which showed presence of RAPD even before significant optic N and visual field defect because probably our patients presented late in the course of diseases. Cases like central retinal vein occlusion especially of the ischaemic variety present with typical

relative afferent pupillary defect in close to 90 % of cases and in retinal detachment involving the macula approximately half of the cases usually manifest a Marcus Gunn pupil.

Of the retinal diseases, there were 2 retinal detachments with involvement of macula and 1 total retinal detachment 12 % (3) and central retinal vein occlusion (CRVO) in 4 % (1). Patients with ischaemic CRVO had higher grades of RAPD compared to patients with non-ischaemic CRVO. Relative afferent pupillary defect is seen in retinal detachment but is likely to return to normal with successful surgery, which is able to restore the anatomy. The size of relative afferent pupillary defect usually reflects the extent of retinal detachment. It is significant if more quadrants or macula is involved.

The degree of RAPD is usually a reflection of the number of fibres affected. Hence, even a relatively smaller lesion of the optic nerve can affect a large number of fibres and result in a large RAPD. However, a retinal lesion should be substantially bigger for producing a higher grade of RAPD.

A RAPD with normal field, colour vision and normal visual acuity would usually point to a pretectal lesion. Such are the nuances that by watching out, fine tuning one's clinical skills to pick up RAPD and corroborating it with other clinical and diagnostic evidence such as colour vision, fields one can arrive at the proper aetiology and conclusion regarding further management and visual prognosis.

Glaucoma even though it affects bilaterally has an asymmetrical presentation which explains the RAPD. Retinal pathology however has to be extensive usually involving macular area to present with RAPD.

CONCLUSIONS

RAPD is a very good example of a clinical skill. If mastered, becomes a game changer as the aetiology is varied. It not only helps us to arrive at the expected visual prognosis but also helps us assess disease progression by its appearance or disappearance. Swinging flashlight test has been found to be a valuable tool which can be applied as a rapid test in a clinical setting. Detecting a relative afferent pupillary defect is of utmost importance and has to be over emphasized because it may be the only objective sign of an organic problem in the visual system.

Limitations

This study was based on subjective assessment and neutral density filter grading of RAPD. A more objective reproducible method like pupillometer or optical coherence tomography (OCT) would have been better. Our sample size was 25. A larger sample size would have been definitely better.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Newman SA, Arnold AC, Friedman DI. Basic and clinical science course. Chap - 3. The patient with decreased vision evaluation. Sec – 5. Neuro ophthalmology pupillary testing. USA: American Academy of Ophthalmology 2004: p. 83.
[2] Campbell WW, Barohn RJ. De Jong's The neurologic examination. Chap - 14. Ocular motor nerves. 8th edn. Philadelphia: Wolters & Kluwer 2020: p. 416.
[3] Yotharak P, Aui-Aree N. Correlation between clinical grading and quantification by neutral density filter of relative afferent pupillary defect (RAPD). Journal of Medical Association of Thailand 2012;95(Suppl 4):S92-S95.
[4] Nakanishi Y, Nakamura M, Tatsumi Y, et al. Quantification of retinal nerve fibre layer thickness reduction associated with relative afferent pupillary defect. Graefe's Arch Clin Exp Ophthalmol 2006;244(11):1480-1484.
[5] Broadway DC. How to test for a relative afferent pupillary defect (RAPD). Community Eye Health 2012;25(79-80):58-59.
[6] Besada E, Frauens BJ, Makhlouf R, et al. More sensitive correlation of afferent pupillary defect with ganglion cell complex. J Optom 2018;11(2):75-85.
[7] Kalaboukhova L, Fridhammar V, Lindblom B. Relative afferent pupillary defect in glaucoma: a pupillometric study. Acta Ophthalmol Scand 2007;85(5):519-525.
[8] Nakashima I, Fujihara K, Miyazawa I, et al. Clinical and MRI features of Japanese patients with multiple sclerosis positive for NMO-IgG. Journal of Neurology, Neurosurgery & Psychiatry 2006;77(9):1073-1075.
[9] Jang SY. Traumatic optic neuropathy. Korean J Neurotrauma 2018;14(1):1-5.
[10] Newman NJ. The optic neuritis treatment trial. Ophthalmology 2020;127(Suppl 4):S172-S173.
[11] Valerie M, Ugam U, Ramona M. Visual outcome in patients of indirect traumatic optic neuropathy treated with steroids. D J O 2020;30:27-31.
[12] Danesh-Meyer HV, Boland MV, Savino PJ, et al. Optic disc morphology in open-angle glaucoma compared with anterior ischemic optic neuropathies. Invest Ophthalmol Vis Sci 2010;51(4):2003-2010.
[13] Younis AA, Eggenberger ER. Correlation of Relative afferent pupillary defect and Retinal nerve fibre layer loss in unilateral or asymmetric demyelinating optic neuropathy. Investigative Ophthalmology and Visual Science 2010;51(8):4013-4016.
[14] Bruckmann A, Gäßler C, Dietzsch J, et al. High correlation between relative afferent pupillary defect (rapd) and visual field loss in patients with glaucomatous optic neuropathy. Invest Ophthalmol Vis Sci 2011;52(14):5513.
[15] Lawlor M, Quartilhao A, Bunce C, et al. Patients with normal tension glaucoma have relative sparing of the relative afferent pupillary defect compared to those with open angle glaucoma and elevated intraocular pressure.

Ivestigative Ophthalmology & Visual Science 2017;58(12):5237-5241.
[16] Charalel RA, Lin HS, Singh K. Glaucoma screening using relative afferent pupillary defect. Journal of Glaucoma 2014;23(3):169-173.
[17] Hennessy AL, Katz J, Ramakrishnan R, et al. The utility of relative afferent pupillary defect as a screening tool for glaucoma: prospective examination of a large population based study in a south Indian population. The British Journal of Ophthalmology 2011;95(9):1203-1206.