Original Article

Acquired color vision deficiency in Vietnamese patients with primary open angle glaucoma

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Abstract

Aim: *To study acquired color vision deficiency (ACVD) in Vietnamese patients with primary open angle glaucoma (POAG).*

Methods: *Cross-sectional descriptive study on 51 eyes of 27 patients with POAG presenting to the Vietnam National Institute of Ophthalmology. Color vision defects were assessed using Farnsworth-Munsell 100 Hue Test. Data were matched to visual field defects on the Humphrey Visual Analyzer (HVFA) and optic nerve analysis on optical coherence tomography (OCT).*

Results: *48/51 eyes had color vision defects, with average total error score (TES) of 128.78 ± 117.93. Of these44 of 48 eyes manifested a tritan color vision defect. We found an inverse correlation between TES and mean deviation (MD) on the HVFA (Spearman's Rho Testing, $r = -0.238$, $p < 0.05$). The severity of color vision deficiency was correlated to average retinal nerve fiber layer (RNFL) thickness on OCT. There was a high degree of interocular correlation in TES at the FM100Hue; however, asymmetry was noted in patients having different clinical stages of glaucoma between eyes. (Wilcoxon signed-rank test, $z = -2.667$, $p < 0.01$). 19.6% of eyes had ACVD without manifest visual field defect on the HVFA and 7.6% eyes had ACVD without decreased RNFL thickness on OCT.*

Conclusion: *We found a high prevalence of acquired color vision deficiency in our cohort of patients with POAG, suggesting ACVD may be an important finding in POAG.*

Keywords*: Acquired color vision deficiency (ACVD), primary open angle glaucoma (POAG).*

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Introduction

Human color vision is trichromatic: every perceivable color can be matched using three judiciously chosen primary color, provided that color subtraction is permitted. Individuals with normal color vision have three types of specialized cells, known as cones, in retina to perceive red, green and blue colors.[1] The first steps of chromatic discrimination occur in the retina: the three classes of cone possess different but overlapping spectral sensitivities. The neural apparatus of vision compares the rates of quantal catches between the classes of cone to derive color vision.[2] Color vision deficiency is one of the commonest disorders of vision and can be divided into congenital and acquired forms.[3] The primary difference between congenital and acquired CVDs is that genetic deficiencies present bilaterally at birth with congenital CVD, whereas acquired CVD can be unilateral, asymmetric or even transient.[4] Traditionally, acquired color vision deficiency is considered a separate entity from congenital color vision deficiency, although emerging clinical and molecular genetic data would suggest a degree of overlap. Acquired color vision deficiency (ACVD) may be classified by the site of pathology or by its clinical characteristics.[5] ACVD can occur at any step in the process of visual formation: photoreceptors, optic nerve, optic tract, lateral geniculate nucleus of thalamus, optic radiation and visual cortex or systemic disease.[6] Acquired CVD due to ocular disease, neurological disease or drug toxicity.[7] Bull (1883) provided one of the earliest descriptions of ACVD in patients with glaucoma[8] and more recent studies suggest that ACVD may occur in early glaucoma.[8-11] This study aims to access acquired color vision deficiency in Vietnamese patients with POAG, which may contribute to be an inexpensive test for national glaucoma control program.

Methods

Twenty-seven (27) patients were randomly selected amongst those with treated POAG and controlled intraocular pressure (IOP) at Glaucoma Department, Vietnam National Institute of Ophthalmology (VNIO) from 2/2016 to 9/2016.

Inclusion criteria

- Visual Acuity (VA) > 20/200.
- Approve the consent form.

Exclusion criteria

- Normal tension glaucoma (NTG)
- Any opacification of ocular media e.g. cataract, corneal disease, vitreo-retinal diseases.
- Optic nerve disorders and cortical visual impairment.
- History of using tuberculosis drugs or any other medication known to be associated with ACVD.
- Patients with congenital color vision deficiency were excluded by Seohan Computerized 85-Hue Test.[12-13]

In addition to taking a medical and ophthalmic history, we performed an ophthalmic examination, including best corrected visual acuity (BCVA), Ishihara Test, IOP, visual field (Humphrey® Field Analyzer 24-2 SITA test, Carl Zeiss Meditec, Inc, Dublin, CA), slit-lamp examination, posterior segment examination and imaging by Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA)

FM100 Hue Color vision test was assessed unilaterally without mydriasis under standardized conditions 1000 lux (specify the daylight simulator). We assessed severity of color vision deficiency using the total error score (TES) and computed a confusion axis using the method described by Vingrys and King-Smith.[14]

For the purposed of analysis, color vision deficiency severity was classified thus:

- TES ≤ 40: None CVD
- 40 < TES ≤ 100: Slight CVD
- 100 < TES ≤ 180: Moderate CVD
- TES > 180: Severe CVD

In order to categorize the state of glaucoma, we used the glaucoma severity staging system (GSSs) proposed by Mills which is comprised of six ordered stages and is on the basis of the Humphrey visual field, as previously described.[15]

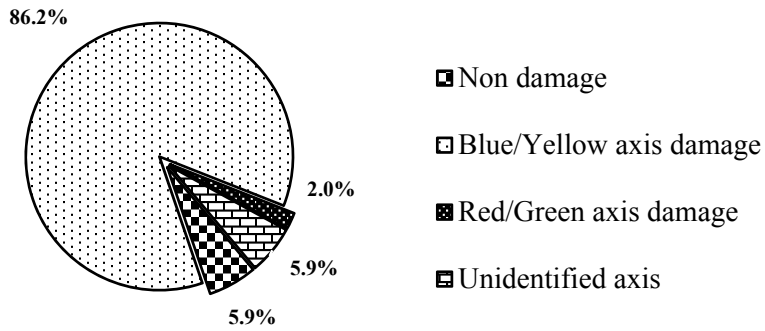
This research has been approved by the scientific and technical council of the Vietnam National Institute of Ophthalmology and the Hanoi Medical University. The diagnosis and treatment is for scientific and patients' health purposes only. There is no other purpose. Patients and families will be counseled, explain the purpose of the study, be informed results during the study. The study was conducted only in voluntary patients.

I hereby declare that this study is my own original work, except where acknowledgment is made below and where due reference is made in the text. All the examinations included in this study were performed in the Glaucoma Department-Vietnam National Institute of Ophthalmology in 2016.

Results

The study was performed on 51 eyes of 27 patients (18 females and 9 males). The mean age of patients was 44.3 yrs (range 11-63 yrs). 48/51 eyes had a color vision defect, (TES 128.78 ± 117.93), amongst which 86.2% (44/51 eyes) manifested color vision defect on blue/yellow axis (Figure 1).

Figure 1. Acquired color vision defect profiles



Total Error Score (TES) was recorded and graphed according to visual field defect phases and glaucoma stages and showed a statistically significant difference (Table 1). Also, ACVD were similar between two eyes of a specific patient at the same stage of the disease (Figure 2). Further, the Wilcoxon signed-rank test showed the statistically significant difference of TES between two eyes of a patient at different stage disease (Figure 3).

Table 1. ACVD according to visual field defect phases and glaucoma stages

Classification	**Total Error Score (TES)**					***p****
	Ocular Hypertension (Earliest Glaucoma)	Early Glaucoma	Moderate Glaucoma	Advanced Glaucoma	Severe Glaucoma	
Visual field defect phases	93.2±33.2	103.6±43.9	60 ± 35.4	132.7±118.7	206.8±168.4	*< 0.05*
Glaucoma stages	100±43.2	88.7±28.3	89.8±52.5	97.1±82.3	198.4±166.7	*= 0.05*

(*) Kruskal - Wallis Test

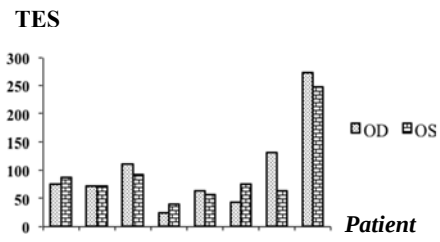


Figure 2. ACVD of two eyes in a specific patient with two eyes at the equivalent stages

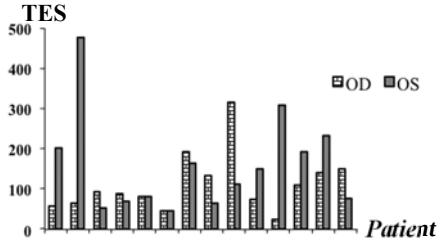


Figure 3. ACVD of two eyes in a specific patient with two eyes at different stages

Correlation between ACVD and visual field defect/ glaucoma stages was shown in Table 2 and 3. Patients with visual field defect and advanced glaucoma were more likely deficient in color perception. However, 19.6% eyes had signs of ACVD without visual field defect. And 7.9% eyes had signs of ACVD without optic nerve abnormalities on OCT.

Table 2. ACVD severity and visual field defect **(**VFD**)** phases

ACVD severities / **VFD phases**	**Normal**	**Mild**	**Advanced**	**Severe**	***Total***	***p*(*)**
Ocular hypertension		***8 (15.7%)***	***2 (3.9%)***		***10 (19.6%)***	
Early		5 (9.8%)	3 (5.9%)	1 (2%)	9 (17.6%)	
Moderate	2 (3.9%)	7 (13.7%)	1 (2%)		10 (19.6%)	*< 0.05*
Advanced	1 (2%)	2 (3.9%)	1 (2%)	2 (3.9%)	6 (11.8%)	
Severe		5 (9.8%)	3 (5.9%)	8 (15.7%)	16 (31.4%)	

(*) *Phi and Cramer's V test*

Table 3. ACVD severity and glaucoma stages

ACVD severities / **Glaucoma stages**	**Normal**	**Mild**	**Advanced**	**Severe**	***Total***	***p*(*)**
Ocular hypertension		***3 (5.9%)***	***1 (2%)***		***4 (7.9%)***	
Early		5 (9.8%)	1 (2%)		6 (11.8%)	
Moderate	2 (3.9%)	5 (9.8%)	2 (3.9%)	1 (2%)	10 (19.6%)	*< 0.05*
Advanced	1 (2%)	8 (15.7%)	3 (5.9%)	2 (3.9%)	14 (27.4%)	
Severe		6 (11.8%)	3 (5.9%)	8 (15.7%)	17 (33.3%)	

(*) *Phi and Cramer's V test*

Table 4 showed the correlation between ACVD with MD value in Humphrey visual test and with retinal nerve fiber layer (RNFL) thickness in OCT.

Table 4. Relationship between ACVD and MD in visual field test, RNFL thickness

ACVD Types of impairment	Normal or Mild	Moderate	Severe	$p^{(*)}$
MD $\left(\overline{x} \pm s\right)$	-9.99 ± 9.7	-13.05 ± 10.95	-22.41 ± 7.92	< *0.05*
RNFL $\left(\overline{x} \pm s\right)$	76.97 ± 18.4	75.7 ± 21.8	59.73 ± 18.6	< *0.05*

(*)*Kruskal -Wallis Test*

Discussion

This was the first study on Vietnamese patients, which showed similar results as the previous papers.[16-18] The study targeted young aged patients with glaucoma to eliminate cataract that can compromise color perception.[19] In the primate visual system, retinal ganglion cells projected to magnocellular, parvocellular, and koniocellular layers in geniculate nucleus, which responded preferentially to motion, red/green color, and blue/yellow stimuli, respectively.[20] Recent studies showed that blue/yellow perception was early altered because of specific features of Koniocellular pathway: low physiological storage, little cross-linking and large sized axon.[6, 9, 21, 22]

In this study, the average age of patients was relatively young (44.3 years old) and concentrated mostly in middle age. This was explained by the process of selecting study subjects, all factors could affect the ability to recognize colors especially cataract, were minimized. This study has shown that mean TES increased according to visual field defect phases and glaucoma stages, which can be clearly observed in patients with advanced disease. However, TES score in moderate stage was lower than ocular hypertension (earliest glaucoma) and early ones (Table 1). This abnormal reduction was due to the small sample size of this research, additionally, two patients had no ACVD at advanced stages (accounting for 1/5 of all eyes at this stage) made the average TES reduced. This required to be further investigated in a larger cohort study. Previous studies also revealed that about 25% of cases had no ACVD despite severe damage on visual field and RNFL thickness, leading to the hypothesis that two or more mechanisms could be involved in glaucoma pathogenesis.[17, 23]

A five-year prospective study of Flammer et al (1984) exploring glaucoma suspects and patients with early questionable field defects, has shown the progression of visual field defect in patients with early ACVD and the relationship between TES and MD on the Octopus perimetry.[24] More recently, Misiuk-Hojlo (2004) evaluated the clinical benefits of color vision test in the early diagnosis of glaucoma also demonstrated a linear correlation between TES and MD on visual field testing.[17] Our study showed inverse correlation between TES and MD. ACVD was found to be present even at the earliest glaucoma stage without trace of visual field defect.

We also observed that that ACVD occurred even when RNFL thickness was still within the normal range (Table 3). And decreased RNFL exacerbated ACVD (Table 4). Previous studies have found an association between ACVD RNFL loss.[25,26] Moreover, Polo et al. (1999) also found a correlation between visual field indexes (MD) with RNFL defect.[27]

Conclusion

In summary, our results suggest that ACVD may be an early biomarker of glaucomatous optic neuropathy. Given that the assessment of ACVD is comparatively cost-effective compared to perimetry, we suggest that

the assessment of color vision may be a suitable assessment tool in settings in which perimetry cannot be undertaken.

Conflict of interest disclosure

A.T. VU, None conflict of interest; H.D. PHAM, None; T.V. PHAM, None; H.P. NGO, None.

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