Effect of Panretinal Photocoagulation on Color Vision in Diabetic Retinopathy

Fatrin Patrycia, Rova Virgana

Ophthalmology Departement Padjadjaran University

Cicendo Eye Hospital National Eye Center

Abstract

Background: Panretinal photocoagulation (PRP) which aims at reducing disease progression in proliferative diabetic retinopathy (PDR) and severe non-proliferative diabetic retinopathy (NPDR), can also lead to cone cell photoreceptor destruction that leads to diminished color vision.

Method: Eyes diagnosed with severe NPDR and PDR with or without diabetic macular edema, after completion of single session PRP lasers (Yellow or Green) were followed up at 1 week to re-assess uncorrected visual acuity and color vision using Ishihara plates.

Result: Among 22 eligible eyes, 16 eyes of 14 patients completed the study. There were female predominance (90.9%) in yellow laser group, and male predominance (80%) in green laser group. Mean age was 54.14 years and 54.53 in yellow and green laser group, respectively. Incorrect readings of Ishihara plates compared to baseline was found in 31.2% of patients.

Conclusion: Colour vision assessment is essential among diabetic retinopathy subjects undergone laser photocoagulation intervention.

Keywords : panretinal photocoagulation, green laser, yellow laser, diabetic retinopathy, color vision

INTRODUCTION

Diabetic retinopathy is the most common microvascular complication of diabetes mellitus (DM) and the leading cause of blindness in individuals of working age (40-65 years). The prevalence rate for retinopathy for all adults with diabetes aged 40 and older worldwide is estimated at 34.6% (93 million people). For vision-threatening diabetic retinopathy (VTDR), the prevalence rate worldwide is estimated at 10.2% (28 million people).[1,2]

Diabetic retinopathy is broadly classified into nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). NPDR is characterized by retinal microvascular changes that are limited to the retina, whereas PDR shows growth of new vessels from the retinal surface into the vitreous space.[3,4]

Panretinal laser treatment considerably improves the visual prognosis, especially in PDR. Although clinically effective, retinal laser photocoagulation leads to collateral damage and side effects including pain, reduced color vision and night vision, macular and peripheral scotoma, exacerbation of macular edema and disruption of the retinal anatomy through scarring.[4,5]

A new paradigm of diabetic retinopathy management is developing. The ultimate goal should not be merely to prevent blindness but to help patients maintain their visual function and prevent progressive vision loss, especially because the age group mainly affected are productive age group. Most of the tasks on real-world performance or specific occupations may concern good color discrimination. This is why the primary aim of this study is to evaluate the effect of single session PRP on color vision alteration.[4,5]

MATERIAL AND METHOD

Subjects in this study were taken from a prospective observational descriptive study conducted on 22 eyes of 20 patients attending Vitreoretina Unit of Cicendo National Eye Hospital, Bandung, Indonesia between July 10th to August 16th 2018. History regarding age, duration of diabetes and the treatment, other medical and surgical history were recorded. Several laboratory tests were examined, such as fasting and post prandial blood sugar, HbA1C, lipid profile and renal function test. Pre and post PRP laser examination were visual acuity by Snellen's chart, intraocular pressure by applanation tonometer, color vision test by Ishihara's test, anterior segment by slit lamp biomicroscopy, and fundus evaluation by indirect ophthalmoscopy and +20D lens examination.

Inclusion Criteria

After undergone aforementioned examinations, patients above 18 years old, with type 1 and type 2 DM and newly diagnosed severe NPDR or PDR with or without diabetic macular edema (DME) based on ETDRS Criteria that underwent PRP laser were selected.

Exclusion criteria

Patients with congenital color vision defect, abnormal optic nerve head or retinal abnormalities aside form

Diabetic Retinopathy, Uncorrected Visual Acuity (UCVA) less than 6/60, severe cataract that could affect color vision and precise laser treatment, vitreous hemorrhage severe enough to preclude retinal laser photocoagulation, patients with prior retinal laser treatment or anti-VEGF treatment were excluded from the study.

Laser therapy intervention

In both treatment arms, laser burn intensity was determined based on grade II-III DRS definition to make white to light gray burns. Two laser systems were used in this study, green laser system (Carl Zeiss Meditec, Visulas 532s) and yellow laser system (Nidek, Multicolor Scan Laser Photocoagulator MC-500 Vixi). Laser intervention was done by the same Ophtalmologist, with randomization. Both systems provided 30-50 ms duration with up to 2200 mW of power and a spot size of 100-200 μm. Spacing between two burns were 1 burn width apart. The burns are placed from the vascular arcades to the equator, nasally 500μm apart from the optic disc and temporally 2 disc diameters temporal to the macular center (3,000 μm). All laser sessions were done by one ophtalmologist under topical anesthesia 0.5% tetracaine hydrochloride ophthalmic solution. After completion of single session PRP, patients were followed up at 1 week.

RESULTS

Among 22 eligible eyes, 6 were excluded due to inability to attend post-laser visit (5 eyes in green laser group and 1 in yellow laser group). In total, 16 eyes of 14 patients completed the study. There were only 1 (9.09%) male in yellow laser group, and 4 males (80%) in green laser group. In yellow laser group there were 10 (90.9%) females, and 1 female (20%) in green laser group.

Mean age (SD) of the patients in yellow laser group was 54.14 (3,64) years, and mean age (SD) in green laser group 54.53 (12,21) years (Table 1). Two patients had bilateral laser treatment and both were in yellow laser group. Of the 16 patients, all patients were type 2 DM. More than 45% patients in both laser groups had less than 5 years duration of diabetes (Table 1).

Seven eyes were diagnosed as severe NPDR with one patient DME in yellow laser group, whilst 3 eyes were severe NPDR in green laser group. There were 4 eyes diagnosed as PDR in yellow group, whilst 2 eyes were PDR with DME in green laser group (Table 1). Two patients who were PDR with DME had duration of Diabetes Mellitus for more than 10 years. Mean of HbA1C was 8,2±2,12 in yellow group and 7,95±1,24 in green group.

The laser parameters for each study group are shown in Table 2. The mean total burn (SD) of spots was 1618,27 (211,6) in yellow group and 1248 (357,2) in green group. Mean laser power (SD) of yellow group was 986,36 (118,5) mW and 796 mW (800,8) in green group.

Majority of patients in both group had visual acuity more than 6/18 (66.67% and 60% in yellow and green laser group, respectively). Only one patient had baseline visual acuity of 6/60 in yellow laser group (Table 3).

Color vision alteration was found in both group. Majority of patients in both group had more than 26 correct Ishihara plates (90,9% and 80% in

Table 1. Comparison of Subject Characteristics

	Yellow Laser (n=11) n (%)	**Green Laser (n=5) n(%)**	**Total (n= 16) n (%)**
Sex			
Men	1 (9,09)	4 (80)	5 (31,25)
Women	10 (90.9)	1 (20)	11 (68.75)
Mean age (SD)	54.14 (3,64)	54.53 (12,21)	
HbA1C			
Mean (SD)	8,2 (2,12)	7,95 (1,24)	
<6,5	1 (9.09)	1 (20)	2 (12.5)
>6,5	7 (63.63)	3 (60)	10 (62.5)
No data	3 (27.28)	1 (20)	4 (25)
Diabetes Mellitus Duration			
<5 years	5 (45,45)	3 (60)	8 (50)
5-10 years	3 (27,27)	0 (0)	3 (18,75)
10-15 years	2 (18,18)	2 (40)	4 (25)
>15 years	1 (9,09)	0 (0)	1 (6,25)
Diabetic Retinopathy Types			
Severe NPDR	6 (54,54)	3 (60)	9 (56,25)
Severe NPDR + DME	1 (9.09)	0 (0)	1 (6,25)
PDR	4 (36,36)	0 (0)	4 (25)
PDR + DME	0 (0)	2 (40)	2 (12,5)

yellow and green group, respectively) at baseline (table 4).

Table 2. Laser Parameters for Each Study Group

Laser Parameter	Yellow Laser (n=11)	Green Laser (n=5)
Total Burn		
Mean	1618,27	1248
SD	±211,6	±357,2
Range	1179-1850	706-1606
Power (mW)		
Mean	986,36	796
SD	±118,5	±800,8
Range	750-1150	240-2200
Duration (ms)		
Mean	36,4	50
SD	±9,3	0
Range	30-50	50

Table 3. Uncorrected Visual Acuity Pre and One Week Post PRP Laser

Uncorrected Visual Acuity (Snellen Chart)	Pre Yellow Laser (n=11)n(%)	Post Yellow Laser (n=11)n(%)	Pre Green Laser (n=5) n(%)	Post Green Laser (n=5) n(%)
>6/18	8 (66.67)	9 (75)	3 (60)	3 (60)
>6/18-6/60	3 (25)	2 (16.67)	2 (40)	1 (20)
6/60 – 3/60	1 (8.33)	1 (8.33)	0	1 (20)

Table 4. Color Vision Changes Pre and One Week Post PRP Laser

Number of Ishihara Plates Reading	Baseline		One week post PRP Laser	
	Yellow Laser (n=11) n(%)	Green Laser (n=5) n(%)	Yellow Laser (n=11) n(%)	Green Laser (n=5) n(%)
1-12	1 (9,09)	1 (20)	1 (9,09)	1 (20)
13 -25	0 (0)	0 (0)	1 (9,09)	0 (0)
26-38	10 (90,9)	4 (80)	9 (81,81)	4 (80)

Five out of 16 patients (31.2%) had incorrect 1-4 Ishihara plates readings one week after PRP laser compared to baseline, with 36.4% reduction in yellow group and 25% in green group. None of both group had more than 4 incorrect Ishihara plates readings (Table 5).

Table 5. Color Vision Reduction 1 week after PRP Laser

Incorrect Plates Reading	Yellow Laser (n=11) n (%)	Green Laser (n=5) n (%)	Total (n=16) n (%)
More than 4 plates	0 (0)	0(0)	0(0)
1-4 plates	4 (36.4)	1 (25)	5 (31.2)
No reduction	7 (63.6)	4 (75)	11(68.8)

DISCUSSION

Diabetic retinopathy is a microvascular complication of diabetes mellitus that presents at various stages involving the neuronal and glial retinal tissue with eventual development of severe macular edema and/or abnormal retinal or optic disc neovascularization leading to irreversible functional visual loss. Patients with type I DM have higher risk of severe ocular complications, but more cases are of type II DM, therefore it affects higher proportion of patients with visual impairment.[1,4]

Occasionally diabetic retinopathy is the initial sign of type 2 DM. From data in table 5, most patients in both laser groups had less than 5 years duration of diabetes. Studies have shown that when

the diagnosis of type 2 DM is made, up to 15% already have diabetic retinopathy.[2,4,5]

Mean age of the patients in both laser group was 54-55 years. This finding is consistent with data from Riskesdas 2013 which states the highest prevalence of diabetes in the age group 45-64 years.[6]

Laser treatment of diabetic retinopathy is still the gold standard of treatment for PDR. When properly treated, the 5-year risk of blindness is reduced by 90% in patients with PDR and the risk of visual loss from macular edema is reduced by 50%. All patients in this study were type 2 DM. In type 2 diabetic patients, 50–80% have diabetic retinopathy after 20 years and 10–30% have PDR. A clinically significant macular edema is found in 25% of type 2 diabetic patients after 15 years. In this study, 2 patients who were PDR with DME had more than 10 years duration of DM.[2,7]

The laser treatment recommendations for diabetic retinopathy are based on the results of two randomized clinical trials of laser photocoagulation, the Diabetic Retinopathy Study (DRS) and the ETDRS. Therapeutic effect of the laser occurs through absorption of the laser energy in the retinal pigment epithelium. Various mechanisms by which PRP helps in the management of DR include decreased production of vasoproliferative substance by converting hypoxic retina into anoxic retina, upregulation the antiangiogenic factors from retinal pigment epithelium and by thinning the retina allow increased diffusion of oxygen from choroid.[1,2,7]

Currently, green lasers (521 - 532 nm wavelength) are most commonly utilized for performing PRP in clinical practice. Yellow lasers (577 nm wavelength) have been of recent interest in treating diabetic macular edema, but have not been extensively studied in PRP for diabetic retinopathy. Compared to shorter wavelength laser, yellow laser comports high transmission through dense ocular media and less light scattering than shorter wavelengths which minimizes spot size and reduces thermal spread. The limited literature comparing green and yellow laser for PRP in diabetic retinopathy has shown that yellow laser

requires less power to achieve a retinal burn.[5,8]

In this study, the mean total laser burn in yellow group was higher than the green group. Reduction of color vision reading by 1-4 Ishihara plates one week after PRP was slightly higher in yellow group than in green group (36.4% vs 25% reduction). However this finding is not ideally comparable due to small samples and uneven sample sizes between two groups. Nikhah et al considered the fewer number of laser burns would induce less retinal destructive effect. Birch et al found that long-duration (0.5 s) burns produce permanent tritanopia and reduced hue-discrimination while short-duration (0.05 s) burns produce transient colour vision deterioration. The direct correlation between laser parameters and color vision alteration has not been investigated before.[1,7]

Patients who were in the category of mild vision impairment (>6/18) did not show differences before and one week after the laser. In yellow laser group, there was an alteration in moderate visual impairment category from 25% to 16.67%. One patient in green laser group had alteration from moderate visual impairment (>6/18-6/60) to severe visual impairment category (<6/60-3/60). This patient already had DME at baseline.

Various studies showed the reduction of visual acuity post PRP laser in PDR patients were due to chronic macular edema (ETDRS no 9, Seiberth et al, McDOnald et al). Zweng et al reported visual loss one week after PRP laser in 140 eyes due to vitreous hemorrhage.

Diabetes Mellitus causes photoreceptor degeneration. Within 24 weeks of diabetes there is a reduction in the thickness of the nuclear outer layer and photoreceptor apoptosis. Cho's study showed dead cone cells obtained selectively by S cone (short wavelength / blue cones) cause tritan color blindness in diabetic retinopathy. Humans only have 9% of sensitive blue cone cells, therefore it can cause a larger loss percentage compared to L cone (long wavelength / red cones) or M cone (medium wavelength / green cones). Gella et al (2015) had found impairment of color vision even in diabetic subjects without retinopathy, which suggest an early indicator of neurodegenerative changes in the

retina and may be of non-vascular etiology.[9,10,11]

Photoreceptors are the most numerous and metabolically active cells in the retina. PRP laser for PDR involves the purposeful destruction of a significant fraction of photoreceptors, resulting in permanent retinal scarring and decreased peripheral, color, and night vision.[5,12]

In this study, 5 out of 16 eyes (31.2%) showed reduction in color vision 1 week post PRP. This finding is far less than Perwez Khan et al (2014) which found 81.82% patients had reduced color vision at the same one-week follow up. Matilda et al also found 100% impaired color vision to Tritanopia one week after PRP laser in PDR patients using Farnsworth-Munsell 100 hue test. Ishihara's color testing chart is less sensitive for detecting minor color vision error since it detects red-green color defect and laser PRP mainly cause tritanopic color defect.[1,13]

In the ETDRS, eyes with more severe retinopathy and macular edema who had early photocoagulation and eyes assigned to deferral had no significant differences in hue discrimination using Farnsworth-Munsell100-Hue test. For eyes with macular edema and less severe retinopathy assigned to immediate focal and early full scatter photocoagulation, there was less color vision loss at the 4-year visit (P <0.001).[4,5]

Canning's study compared PRP with three different wavelengths (blue-green 488/514 nm, dye yellow 577 nm, and dye orange 595 nm). The study showed eyes treated with blue-green color showed decreased hue discrimination. Birch and Hamilton also noted decreased hue discrimination following xenon and argon PRP. Their studies concluded that all examined eyes were tritanopic following PRP and did not recover to pre-PRP level during follow up period of 3 and 12 months. [1,12,13]

CONCLUSION

This study re-emphasizes the importance of colour vision assessment among diabetic retinopathy subjects undergone laser photocoagulation intervention. Using Ishihara chart for detecting color vision impairment in diabetic patients is less sensitive due to

inability to elicit tritanopic color defect. The main limitation of this study was a short-term study period that leads to short follow-up time and small uneven sample sizes. Further research is needed to follow up the examination of color blindness after PRP laser in a larger population, larger number of samples, and longer study time.

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