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THE DIFFERENCE OF VISUAL FIELD DEFECT ON DIABETIC RETINOPATHY PATIENTS TREATED WITH PANRETINAL LASER PHOTOCOAGULATION WITH 20-MILISECOND AND 100-MILISECOND DURATION

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ABSTRACT

***Introduction**: Panretinal laser photocoagulation (PRP) is a standard treatment for severe nonproliferative and proliferative diabetic retinopathy. Twenty-milisecond duration PRP show same effectiveness with 100-ms standard PRP in inhibit neovascularization progression. This shorter pulse tend to minimize retinal neuronal defect and visual field defect. This study aim to analyze the difference of visual field defect in diabetic retinopathy (DR) patients treated with 20-ms PRP compared with 100-ms PRP in Moh. Hoesin Hospital Palembang.*

***Methods**: A clinical trial with single blinding on severe-very severe NPDR and early PDR eyes treated with PRP between June and August 2016. Forty eyes (25 patients) were randomized into two groups. Twenty eyes were treated with 20-ms PRP, and other 20 eyes treated with 100-ms PRP. Visual field defect was evaluated using Humphrey Field Analyzer 30-2 SITA Standard at baseline and 2 weeks follow-up.*

***Result**: Unpaired t-test showed significant difference in mean deviation (MD) after laser on NPDR eyes (p=0.042, p<0.05), meanwhile there was no significant difference in early PDR eyes (p=0.17, p>0.05). In NPDR eyes, more MD improvement was found in 20-ms PRP group (0.79±0.93 dB) than in 100-ms group (-0.04±0.61 dB). In early PDR eyes, MD improvement was bigger (1.0±0.88 dB) in 20-ms PRP group than in 100-ms group (0.10±1.47 dB). There was no significant difference in pattern standard deviation (PSD) on both group at any DR grade (p=0.208; p=0.201; p>0.05).*

***Conclusion**: After 2 weeks, 20-ms PRP caused more improvement and lesser visual field defect (p=0.042, p<0.05) on NPDR eyes. There was no significant difference in PSD on both groups.*

Keywords: diabetic retinopathy, panretinal laser photocoagulation, visual field defect.
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INTRODUCTION

Panretinal laser photocoagulation (PRP) remains the gold standard treatment to inhibit progression and reduce the risk of severe visual loss in proliferative diabetic retinopahy (PDR). The goal of PRP is to destroy ischemic retina and increase oxygen tension in the eye so it can regress the neovascularization.[1,2]

The thermal effect of the laser coagulates surrounding photoreceptors and retinal pigment epithelium (RPE) cells and immediately creates laser burns within outer retinal layer. After photocoagulation, the photoreceptors were shifting from adjacent areas into the lesion, mediated by Mueller cells, form glial matrix filling the lesion in the photoreceptors layer in 1 weeks, and reestablish synapses to neurons in the inner nuclear layer (INL). This process restore light sensitivity and local activation of the bipolar and ganglion cells in the former lesion.[3,4]

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The laser scar expansion in the retina may be associated with photoreceptor loss, RPE hyperthrophy, and visual field loss. Longer pulse durations and greater laser energy have caused collateral damage not only in the outer but also into the inner retina. Blankenship reported that laser-induced damage within retinal ganglion cells results in the loss of nerve fiber layer and thinning within peripapillary nerve fiber layer zones. Heijl and Henricsson (1994) reported visual field sensitivity was often depressed even before treatment with mean MD -4.3 (-1, -11.6) dB, but it significantly lower 2 weeks after PRP with mean MD -8.6 dB.[2,3]

Conventional photocoagulation using a single application of laser energy per shots is usually delivered as a 100-200 ms duration burns. Early Treatment Diabetic Retinopathy Study (ETDRS) recommends aplication of up to 2000 visible end-point burns on the retina. A new laser method of pattern scan laser (PASCAL) photocoagulation using a shorter pulse (10-20-ms) duration was introduced in 2005 to reduce collateral retinal injuries. The laser burns are localized in outer retina so that it reduce RNFL loss and minimize visual field defect after laser.[5,6]

The use of 1500 20-ms burns in a single session was shown to be a safe regimen in the Manchester Pattern Scan Laser Study (MAPASS) trial. This shorter pulse duration PRP resulted in similar regression of diabetic retinopathy compared to conventional PRP.[6]

This study aim to assess the difference of visual field defect in DR patients treated with 20-ms PRP compared with 100-ms PRP.

METHODS

A clinical trial study with single blinding was conducted. It included 40 eyes of 25 type 2 DM patients with DR who attended Vitreoretina Subdivision at Mohammad Hoesin Hospital between June and August 2016. Written informed consent was taken from all patients for the procedure. Information was collected on age, sex, involving eye, duration of diabetes (years), and gradation of DR.

Inclusion criteria were patients with type 2 DM who had severe-very severe NPDR, early PDR, who underwent laser PRP; normal intraocular pressure (10-21 mmHg), had ability to perform accurate Humphrey visual field test.

Exclusion criteria were posterior segment abnormality which is not severe-very severe NPDR and early PDR, previous laser or intravitreal injection, glaucoma, and eyes with media opacity that prevent fundus examination and PRP laser treatment.

PRP was done with argon laser from VISULAS 532s (Carl Zeiss Meditec), with spot size 200 µm and power was adjusted untill received grey-white burn according to ETDRS guidelines, with one half burn width apart. An average 1200 to 2000 burns were given. The study sample was randomized into two groups. Twenty eyes were treated with 20-ms duration PRP, and other 20 eyes treated with 100-ms duration PRP.

Visual field defect was evaluated using Humphrey Field Analyzer 30-2 SITA Standard at baseline and 2 weeks follow-up. We recorded visual acuity (VA), visual field index (VFI), mean deviation (MD), and pattern standard deviation (PSD) before and 2 weeks after PRP treatment.

We performed statistical analyses using SPSS version 21 with *t*-test, Wilcoxon and Mann Whitney test to analyze the difference of visual field among the two groups. The null hypothesis was rejected for *P*-values < 0.05.

RESULTS

A total of 40 eye samples obtained from 25 diabetic patients (mean age 51.76 years; range 39-63) were treated with PRP. In 20-ms PRP group, the mean age was 52.65±7.54 years and in 100-ms PRP group was 51.75±7.59 (p=0.709). All included 16 female (64%) and 9 male (36%) eye samples. The characteristics of the subjects are described in Table 1.

Table 1. **Characteristics of the subjects in the study**

Characteristics	Number (%)
Sex	
Male	9 (36)
Female	16 (64)
Age	
<40 years	1 (4)
40-49 years	8 (32)
50-59 years	10 (40)
≥ 60 years	6 (24)
Laterality	
Bilateral	15 (60)
Right eye	6 (24)
Left eye	4 (16)
Duration of DM (years)	
< 5 years	7 (28)
5-10 years	7 (28)
>10 years	11 (44)
DR gradation	
Severe NPDR	15 (37.5)
Very severe NPDR	2 (5)
Early PDR	23 (57.5)

The mean duration of diabetes was 9.24 years (range 3-15 years) with 11 (44%) subjects had diabetes for more than 10 years. Seven (28%) subjects had diabetes for 5-10 years and less than 5 years, respectively. The distribution of DR gradation were 23 (57.5%) early PDR eyes, 15 (37.5%) severe PDR, and 2 (5%) very severe PDR eyes. Fifteen (65.2%) of all early PDR eyes had diabetes for more than 5 years, and 13 (76.5%) of all NPDR eyes either. The relation of DR gradation with duration of DM are shown in Table 2.

In severe-very severe NPDR eyes, paired *t-test* show no significant difference in VA before and after PRP on both group with p=0.351 for 20-ms PRP and p=0.121 for 100-ms PRP group (p>0.05). The same results were obtained in early PDR eyes (p>0.05). There was no significant difference on both group at any DR gradation. See Table 3.

Table 2. **Relation of DR gradation with duration of DM**

Duration of DM	DR gradation		p*
	Severe-very severe NPDR	Early PDR	
< 5 years	4 (23.5%)	8 (34.8%)	
≥ 5 years	13 (76.5%)	15 (65.2%)	0.505
Total	17 (100%)	23 (100%)	

**chi square* test (p<0.05)

Table 3. **Comparison of visual acuity on both group to DR gradation**

DR gradation	PRP duration	Visual acuity (logMAR)			p^{*}	p^{**}
		Before	After	Improvement		
Severe-very severe NPDR	20-ms	0.48±0.34	0.44±0.24	-0.04±0.10	0.351	0.130
	100-ms	0.60±0.22	0.53±0.12	-0.07±0.10	0.121	
Early PDR	20-ms	0.74±0.27	0.68±0.24	-0.06±0.03	0.101	0.918
	100-ms	0.72±0.27	0.67±0.24	-0.05±0.03	0.135	

*paired *t-test* (p<0.05); **unpaired *t-test* (p<0.05)

Table 4. **Comparison of visual field index (VFI) on both group to DR gradation**

DR gradation	PRP duration	*Visual Field Index* (VFI)			p^{+}	p^{++}
		Before	After	Improvement		
Severe-very severe NPDR	20-ms	94.5 (77-99)	94 (90-99)	-0.05	1.000	0.074
	100-ms	92 (76-100)	92 (77-95)	0	0.592	
Early PDR	20-ms	84.5 (34-93)	87.5 (59-95)	3	0.037	0.853
	100-ms	88 (45-98)	88 (58-95)	0	0.574	

$^{+}$Wilcoxon test (p<0.05); $^{++}$Mann Whitney test (p<0.05)

Table 5. **Comparison of Mean Deviation (MD) on both group to DR gradation**

DR gradation	PRP duration	*Mean Deviation* (MD)			p*	p**
		Before	After	Improvement		
Severe-very severe NPDR	20-ms	-7.48±2.72	-6.69±1.79	0.79±0.93	0.560	0.042
	100-ms	-8.77±2.71	-8.81±2.10	-0.04±0.61	0.954	
Early PDR	20-ms	-11.25±4.48	-10.25±3.60	1.0±0.88	0.138	0.719
	100-ms	-10.86±4.51	-10.76±3.04	0.10±1.47	0.928	

*paired *t-test* (p<0.05); **unpaired *t-test* (p<0.05)

Table 6. **Comparison of Pattern Standard Deviation (PSD) on both group to DR gradation**

DR gradation	PRP duration	*Pattern Standard Deviation* (PSD)			p*	p**
		Before	After	Improvement		
Severe-very severe NPDR	20-ms	3.39±1.80	3.30±1.57	-0.09±0.23	0.953	0.208
	100-ms	4.45±2.54	4.30±1.93	-0.15±0.61	0.860	
Early PDR	20-ms	6.16±1.92	6.19±2.24	0.03±0.32	0.863	0.201
	100-ms	5.14±2.17	4.99±2.44	-0.15±0.27	0.650	

*paired *t-test* (p<0.05); **unpaired *t-test* (p<0.05)

Visual Field Index (VFI)

At 2 weeks after PRP, there was a significant VFI improvement in early PDR treated with 20-ms duration PRP (p=0.037), but not in 100-ms PRP group (p=0.574). However, the difference between both laser laser group was insignificant in NPDR and PDR group (p=0.074 and p=853, respectively). These comparison can be seen in Table 4.

Mean Deviation (MD)

Before the treatment, there was a significant difference in MD between DR gradation. The mean MD in early PDR (-11.06±4.40) was reduced more than in severe-very severe NPDR eyes (-8.16±2.71) with p=0.021 (p<0.05).

At NPDR eyes follow up, we found more MD improvement (0.79±0.93, p=0.560) in 20-ms PRP and less improvement in 100-ms PRP (-0.04±0.61, p=0.954). Unpaired *t-test* showed a significant difference between both group (p=0.042, p<0.05).

At early PDR eyes, we found less MD improvement both in 20-ms PRP and 100-ms PRP group (1.0±0.88 and 0.10±1.47, respectively) than in NPDR eyes. This result also showed no significant difference in between both group (p=0.719). These comparison are outlined in Table 5.

Pattern Standard Deviation

At baseline, there was a significant difference in PSD between DR gradation. The mean PSD in early PDR (5.68±2.06) was reduced more than in severe-very severe NPDR eyes (3.95±2.22) with p-value =0.016 (p<0.05).

Compared to the baseline, we found PSD difference was insignificant between 20-ms and 100-ms PRP in NPDR eyes (p=0.953 and 0.860) and PDR eyes (0.863 and 0.650). Unpaired *t-test* also found no significant difference between these laser group (p=0.208). The similar result was also found in PDR eyes follow up, with p=0.201 (p>0.05) between both laser group. See Table 6.

DISCUSSION

Diabetic retinopathy is one of the most prevalent cause of legal blindness in patients aged 20-64 years. With aging population, this prevalence is expected to rise. In our study, the mean age in 20-ms PRP and 100-ms PRP group was 52.65±7.54 years and 51.75±7.59 years, respectively. The highest prevalence was at age range 50-59 years (40%). These results were close to a study performed by Park (2012), which obtained mean age of DR patients were 55.3 years. Al-Amer (2008) found a mean age 57.8 years with highest prevalence at age range 56-65 years. Meanwhile, Boesoirie (2005) reported that highest prevalence of DR was at age range 41-50 years and 51-60 years (36.84%, equally). [7,8,9]

All patients included 16 (64%) female and 9 (36%) male eyes. Wang *et al* (2013) also reported that the prevalence of DR in female (64.5%) were more than male (35.5%). Meanwhile, Tajunisah *et al* (206) reported that prevalence of DR in male (57.4%) was bigger than female. These

differences could probably due to different size of sample, population characteristics, and duration of the study.[10,11]

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) reported that the duration of DM was directly associated with an increased prevalence of DR in both type 1 and type 2 DM.[1] Al-Amer (2008) reported that the chance to have DR increase 21% per year duration of DM.[8] Jee *et al* (2013) reported the prevalence of DR was 2.8% in new DM patients, increase to 33.2% in patients having DM for ≥ 10 years.[12] He *et al* (2012) the mean duration of DM was 8.05±6.71 years, with PDR group (10.58±6.98) was longer than NPDR group (6.99±6.29).[13] In our study, fifteen (65.2%) of all early PDR eyes had diabetes for more than 5 years, and 13 (76.5%) of all NPDR eyes either (Table 2). Most of our patients did not realize that they had diabetic, so they would go for examination only if they already had visual disturbance.

There was no significant difference in VA before and after PRP on both laser group at any DR gradation (p=0.130 for NPDR group and p=0.918 for early PDR group). Cho *et al* (2013) reported no significant difference in VA between before and after 20-ms PRP (0.09±0.24, p=0.18). The thickening of the subfoveal choroid may indicate choroidal effusion produced by a disruption of the choriocapillaris caused by laser photocoagulation. The damage to the choroid induced transudation in 59-90% eyes after PRP, with the associated ciliochoroidal effusion resolving completely in 7-14 days.[14]

At 2 weeks after PRP, there was a significant VFI improvement in early PDR treated with 20-ms duration PRP (p=0.037), but not in 100-ms PRP group (p=0.574) and both laser group NPDR gradation (Table 4). VFI has focused on central visual field. Therefore, the decrease in VFI can be detected if the visual field change were at central, not peripheral visual field. Marvasti *et al* (2013) revealed that VFI has linear correlation with retinal ganglion cell (RGC) numbers.[15] This fact gives us an early information that 20-ms PRP cause lesser damage in RGC more improvement than 100-ms PRP.

Mean deviation (MD) is the average elevation or depression of the patient's overall field compare to the normal reference field. A significant MD may indicate that the patient has an overall depression, or that there is significant loss in one part of the field and not in others. Before the treatment, the mean MD in early PDR (-11.06±4.40) was significantly reduced more than in severe-very severe NPDR eyes (-8.16±2.71) with p=0.021.

A similar result also found in pattern standard deviation (PSD). PSD is a measurement of the degree to which the shape of the patient's measured field departs from the normal, age-corrected reference field. PSD reflects irregularities in the field caused by localized defects. The mean PSD in early PDR (5.68±2.06) was significantly reduced more than in severe-very severe NPDR eyes (3.95±2.22) with p-value = 0.016 (p<0.05). Henricsonn and Heijl (1994) reported that there was no evidence of visual field loss in eyes with mild disease, but clear visual field defects in eyes with more advanced disease. Significantly reduced sensitivity was often correlated with retinal non-perfusion and it tend to be in the midperiphery than paracentrally.[16]

Kiss and Miller reported that shorter duration pulse are confined more to the outer retina with less energy spread laterally or in the direction of the choroid or nerve fiber layer.[5] This theory supports our study results. At NPDR eyes follow up, we found more MD improvement (0.79±0.93) in 20-ms PRP and less improvement in 100-ms PRP (-0.04±0.61). Unpaired *t-test* showed a significant difference between both group (p=0.042, p<0.05). An unsignificant difference was obtained in early PDR group between both laser group with p-value 0.719. However, MD improvement in 20-ms PRP (1.0±0.88) was bigger than 100-ms PRP (0.10±1.47) group. This results give us an early information that shorter pulse laser give more improvement effect to visual field defect.

In our study, the irregularities in the field caused by localized defects has not change yet at 2 weeks after PRP. At follow up, PSD difference was insignificant between 20-ms and 100-ms PRP in NPDR and PDR eyes. Unpaired *t-test* also found no significant difference between these laser group in both DR gradation. Wang *et al* (2013) reported PSD improvement from 3.26±1.56 dB to 2.84±1.38 dB after 12 weeks with 20-ms PRP treatment.[10] Sher (2013) and Paulus (2008) reported that laser scar was formed in 1 weeks and get complete resolution in 2-4 months.[4,17] The difference result is due to our shorter follow-up time and lesser sample size.

CONCLUSION

After 2 weeks, 20-ms PRP caused more improvement and lesser visual field defect (p=0.042) on NPDR eyes. Although statistically insignificant, the study reported that MD and PSD improvement were bigger in 20-ms PRP than 100-ms PRP. Further study with larger sample size and longer follow-up is needed to assess the visual field difference after treatment between these difference laser duration.

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