Original Article

Comparison of Laser Photocoagulation Using 810 nm with 20 ms and 100 ms Duration on the Progression of Neovascularization in Proliferative Diabetic Retinopathy

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ABSTRACT

Background: *The aim of this study was to compare the effectiveness of laser photocoagulation 810-nm with 20 ms and 100 ms duration to prevent the progression of proliferative diabetic retinopathy.*

Method: *This study was prospective double blind randomized clinical trial. Twenty-eight participants who met the inclusion criteria divided into two groups to undergo laser photocoagulation by using 810 nm lasers. One group received 100 ms duration and the other received 20 ms duration. Grade 3 burns with a 200 µm spot sized were placed with both parameters. The progression of PDR was evaluated in two months follow up by using seven fields' fundus photographs. Fluence, power and visual acuity were compared in this study.*

Result: *Twenty five subjects completed the two months follow up. The proportion of non-progressive PDR in 100 ms group was 75.0% and in 20 ms was 76.9% (p=1.000). The power in 20 ms group increased twice than 100 ms group (1000 vs. 500 mW; p=0.000). The median fluence in 20 ms group was less than 100 ms group (6.36 vs. 15.91 J/cm^2; p=0.000). Improvement of visual acuity in 20 ms and 100 ms was comparable (23.1% vs. 33,3%; p=1.000).*

Conclusion: *The 20 ms duration showed similar result in preventing the progression of PDR compared to 100 ms duration.*

Keywords: *Proliferative diabetic retinopathy, laser photocoagulation, diode 810 nm*

Diabeties mellitus (DM) is the most frequent chronic disease in the world.[1] The prevalence was 2.8% or 171 million people around the world in 2000. The prevalace was estimated to be increased 4,4% or 366 million people in 2030.[2] Indonesia was in fourth place as a nation with the most affected of diabetic mellitus after India, Cina and United States of America with 8.4 million in 2000 and will increase to 21.3 million in 2030.

Diabetic retinopathy (DR) is the microvascular complication of DM which caused blind. The study by Sya'baniyah et al[3] in Cipto Mangunkusumo hospital showed that DR was 24.5% in diabetic patients who was reffered to ophthalmology clinic.

Laser photocoagulation is a gold standard for treatment of proliferative diabetic retinopathy (PDR) and severe nonproliferative diabetic retinopathy (NPDR) based on Diabetic Retinopathy Study (DRS).[4] Infra-red laser 810 nm is a laser option commonly used for retinal laser photocoagulation. The advantages of

laser 810 nm compared to others wave length is unabsorbed by haemoglobin, less absorbed by xanthophylls and well penetrated through cataract lens.[5-6]

The effectiveness of conventional laser 810 nm is equal to the argon laser in reducing neovascularizarion in PDR. Regression of neovascularization by 810 nm lasers ranged from 76.2% to100%. [7-8] Retrospective study by Talu[9] in 10 years experience showed reggresion of neovascularization was 88.9%.

The degree of retinal damage after laser photocoagulation can be minimized. Mainster[10] explained the ways to reduce the retinal damage by using shorter duration of laser application. Several studies using laser 532 nm with 20 ms duration revealed the success rate of PDR regression from 75 to 96%. The study by Muqit et. al.[11] showed neovascular regression was 75% in PDR mild, 67% in moderate PDR and 43% in severe PDR. Neovascular regression was 90% was reported by Al Hussainy et al[12] and Nagpal et al[13] showed neovascular regression was 96%.

Tissue destruction caused by laser treatment was reduced by using short duration parameters. There was no study of using short duration 20 ms of 810 nm laser photocoagulation in PDR treatment. The aim of this study is to compare the effectiveness of laser photocoagulation 810 nm short duration 20 ms and conventional 100 ms duration in reducing the progression of neovascularization in PDR.

MATERIAL AND METHOD

This was randomized double blind clinical trial located in Cipto Mangunkusumo hospital. The study was held from July to November 2013. Ethical approval and informed consent were obtained.

The inclusion criteria were subjects who suffered DM type 1 and 2 with 18 years old or above and recently diagnosed as proliferative diabetic retinopathy and have not received laser treatment before, best corrected visual acuity (BCVA) was more than 35 to 85 letters (6/60 in Snellen chart) and maximal pupil dilatation to performed fundus photographs and laser photocoagulation.

The exclusion criteria were HbA1c ≥10.0 mg/dl, blood pressure ≥180/110 mmHg, history of chronic kidney disease, kidney transplantation or nephropathy diabetic, history of intraocular surgery or intravitreal injection, subject with rerinal detachment, glaucoma, history of Nd:YAG laser in the past 6 months, and active eyelid infection.

This was a preliminary study which evaluated the effectiveness retinal laser photo-coagulation with 810 nm lasers 20 ms and 100 ms duration in PDR patients. Twenty eight eyes were estimated in this study.[14]

The subjects were randomized into two groups with block randomization. Each subject underwent visual acuity examination by using ETDRS chart in logMAR and seven field's fundus photographs with Topcon 3D-OCT 2000 (Topcon, Paramus, New Jersey, USA). Proliferative diabetic retinopathy was classified into 3 degrees. Mild PDR defined if there was NVE or NVD size less than the standard Airlie House photograph 10A (SAH10A), moderate if the NVE size was bigger than ½ disc diameter and or NVD size larger than SAH10A, and severe if the NVE size larger than ½ DD, multiple, and or forward NVD, and or preretinal hemorrage, and or vitreous hemorrage, and or tractional retinal detachment.

After randomized into two groups, the laser was performed in dilated pupil with topical anesthesia by using Mainster contact lens (Ocular Instruments, Bellevue, WA, USA). Laser photocoagulation was perfomed by two retinal specialists with laser competency. Subjects in short duration group received 810 nm laser (Iris Medical OcuLight SLx, IRIDEX Corporation, Mountain View, CA, USA) with 20 ms duration, 200 µm spot size, and 1500 shots. Subjects in conventional group received 100 ms duration, 200 µm spot size, and 1500 shots. Power was adjusted to produce laser burn grade 3 L'esperance.

The primary outcome was to evaluate neovascular progression 2 months post laser. Non progressive was defined if there was diminished neovascular, partial regression, stable neovascularization, or fibrosis of neovascular without presentation of neovascular in other sites. Progression was established if

there was an enlargement of neovascular or presentation of new neovascular in other sites. Fundus photographs were evaluated by two retinal specialists with competency of reading fundus photographs. Secondary outcomes were BCVA and complication after laser treatment.

Statistical analysis was performed by using SPSS program version 16.0. Independent student t-test or Mann-Whitney U test was applied for 2 independent numeric samples. Pair student t-test or Wilcoxon signed-rank test were used for 2 related numeric samples. Pearson Chi-Square, Fisher's Exact and Kolmogorov-Smirnov were applied for ordinal data. Kappa staristic was used for inter-observer agreement. All tests were 2-sided with a significance level of 0.05.

RESULT

Twenty eight subjects were included in this study and 25 subjects were finished the 2 months period. Three subjects were lost to follow. There were 17 women (60.70%) with average of mean age was 52.25±7.35 year. The mean of DM duration was 6.36±4.78 year. The mean of HbA1c was 8.56±0.94%. The average of cholesterol level was 260.92±53.27 mg/dL. Sistolic and diactolic measurement were 147.86±2.08 mmHg and 80.18 ±7.26 mmHg. Proportion of subject with mild PDR was 9 (32.1%), 5 (17.90%) subjects with moderate PDR and 14 (50.00%) subjects with severe PDR. The Average of BCVA was 0.56±0.27 logMAR. There were no differences of baseline caharacteristic in two groups (table 1).

The power used in 20 ms group was twice higher than 100 ms group. (1000 mW vs 500 mW, p=0.000). *Fluence* in 20 ms group was half than 100 ms group. (6.36 vs 15.91 p=0.000) (table 2). Non progressive neovascular was observed 75.0% in 100 ms group and 76.9% in 20 ms group (p=1.000) (table 3).

There was no BCVA difference before and after laser between two groups. (p=0.458) (table 4) In this study, there were 5 subjects with pain during laser session. There were no ruptures of Bruch membrane or vitreous hemmorege (table 5). Inter observer agreement by using kappa statistic was 0,752 (p=0,000).

Table 1. Comparison of baseline characteristic between two groups

Characteristic	100 ms (n=14)	20 ms (n=14)	p
Age (year)			
Mean ± SD	52.29±6.55	52.21±8.31	0.980[a]
Sex			
Man	7	4	0.246[c]
Woman	7	10	
DM duration (year)			
Median (min, max)	8.50 (1;15)	4.0 (1;16)	0.144[b]
HbA1c (%)			
Mean ± SD	8.62±0.90	8.49±1.00	0.725[a]
Total cholesterol (mg/dl)			
Mean ± SD	268.31±50.25	253.54±57.06	0.474[a]
BCVA (logMar)			
Median (min, max)	0.46 (0.3;1.0)	0.52 (0.17;1.07)	0.691[b]
Sistolic (mmHg)			
Median (min, max)	150 (100;180)	150 (130;180)	0.725[b]
Diastolic (mmHg)			
Median (min, max)	80 (60;90)	80 (70;90)	0.293[b]
Cataract			
Grade 1	3	3	1.000[d]
Grade 2	8	7	
Grade 3	3	4	
PDR			
Mild	4	5	0.617[d]
Moderate	1	4	
Severe	9	5	

[a]*Independent t-test,* [b]*Mann-Whitbey U Test,* [c]*Chiq-square Test,* [d]*Kolmogorov-Smirnov*

Table 2. Comparison of laser parameters between two groups (n=25)

Laser parameter	Laser Group		p
	100 ms (n=12)	20 ms (n=13)	
Power (mW)			
Median (min, max)	500 (200;800)	1000 (800;2000)	0.000
Shoot			
Median (min, max)	1504 (600;1672)	1505 (1294;2613)	0.398
Fluence (J/cm^2)			
Median (min, max)	15.91 (6.36;25.45)	6.36 (5.09;12.73)	0.000

Mann-Whitney U Test

Table 3. Comparison of PDR progression between two groups (n=25)

PDR Progression (n%)	Laser Group		p
	100 ms (n=12)	20 ms (n=13)	
Progressive	3 (25.0)	3 (23.1)	1.000
Non progressive	9 (75.0)	10 (76.9)	

Fisher's Extact Test

Table 4. Comparison of BCVA between two groups (n=25)

	Laser Group		p
	100 ms (n=12)	20 ms (n=13)	
BCVA pre laser (logMar)			
Median (min, max)	0.46 (0.3;1.0)	0.52 (0.17;1.07)	0.690[a]
BCVA post laser (logMar)			
Median (min, max)	0.46 (0.22;1.77)	0.52 (0.06;1.77)	0.458[a]
	0.799[c]	0.600[c]	
BCVA changes n (%)			
Improve	4 (33.3)	3 (23.1)	1.000[b]
Stable	5 (41.7)	7 (53.8)	
Worsen	3 (25.0)	3 (23.1)	

[a]*Mann-Whitney U Test,* [b]*Kolmogorov-Smirnov,* [c]*Wilcoxon rank test*

DISCUSSION

In this study, we found several risk factors which were higher HbA1c, uncontrol blood pressure, and higher level of cholesterol. Primary outcome was neovascular progression. Both treatments have the same effectiveness in reducing neovascular progression. Study by Salman[15] and Muraly et al[16] comparing 532 nm lasers in conventional and *Pattern Scan Laser* (PASCAL) 20 ms duration showed the same effectiveness in reducing PDR progression.

This study revealed range of power in both groups. Two factors influencing the amount of power were RPE thickness. Study by Gopalakrishnan[17] showed that power needed to produce spesific laser burn depended on RPE thickness. In every 4 micron thickened of RPE, the power reduced to 25%. This study did not measure the RPE thickness.

Power in 20 ms group was twice than 100 ms group. It was in line with Arrhenius theory which expained tissue damage depends on temperature and duration. The correlation of power and duration showed exponensial curve in 532 nm.[18] Decresing duration one fifth followed by increasing power only twice.

Fluance in 20 ms group was one half of 100 ms group (15.91 vs 6.36 J/cm^2). Decreasing the laser duration will reduce the fluence. Nagpal et. al.[13] and Muqit et. al.[19] showed that 20 ms duration in 532 nm laser needed lower fluence to produce the same laser burn. Study by Alvarez-Verduzco et. al.[20] showed that the lower fluence will cause less pain. In this study, the pain was experienced by 4 subjects in 100 ms group and 1 subject in 20 ms group.

Secondary outcome in this sudy was BCVA and pain. There were no difference in BCVA post laser in both groups. The BCVA improved in 20% subject and stable in 50% subjects. This result was similar with the aim of laser photocoagulation in PDR to reduce severe visual loss more than 50%.[21]

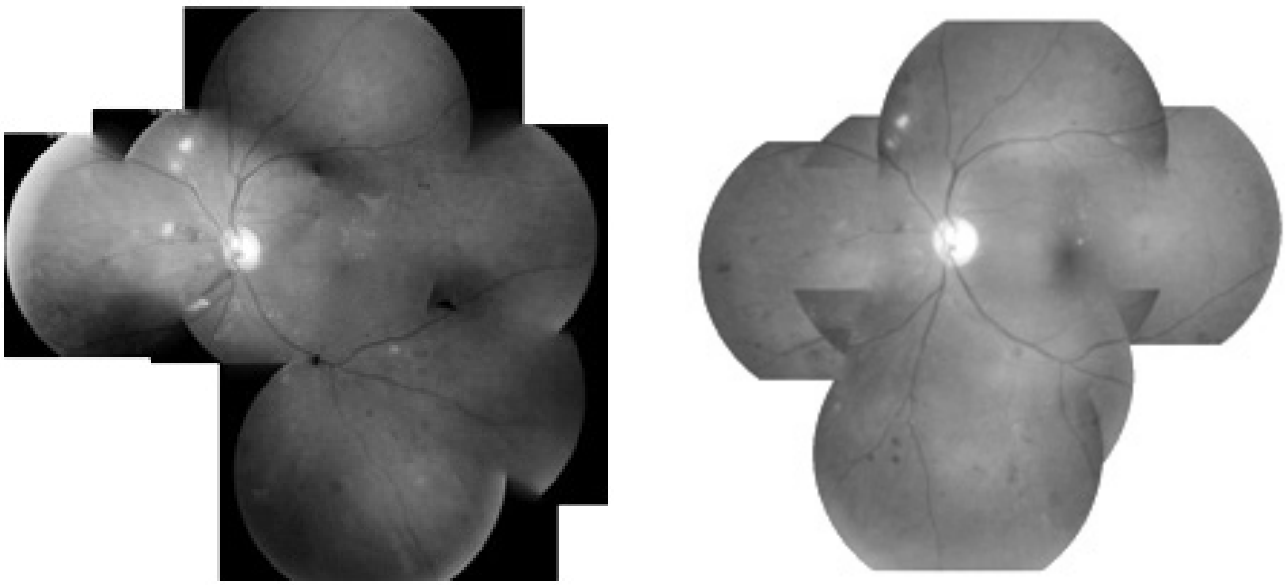

Fig 1. A) Before laser photocoagulation; B) Two months after laser. There was no PDR progression by using laser 810 nm with 20 ms duration

The 20 ms duration was safe. One subject in 20 ms group experienced pain during the laser session. There was no *Bruch* membrane rupture or vitreous hemorrhage. The subjects did not feel glare due to invisible light spectrum of 810 nm laser.

The strengthness of this study was the first randomized double blind clinical trial comparing short duration and conventional 810 nm laser. The limitations of this study were short period of follow up, small sample size and operator bias.

Table 5. Complication of laser photocoagulation in both groups (n=28)

Complication n (%)	100 ms	20 ms
Pain	4 (28.57)	1 (7.14)
Bruch membrane rupture	0	0
Vitreous hemmorage	0	0

CONCLUSION

Short duration 20 ms 810 nm laser photocoagulation was effective in preventing progression of neovascularization in PDR patients. The advantage of short duration laser was lower fluence than conventional one.

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