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The Open Ophthalmology Journal

Content list available at: www.benthamopen.com/TOOPHTJ/

DOI: 10.2174/1874364101812010308, 2018, *12*, 308-313

RESEARCH ARTICLE

Single-Session Low Duration Panretinal Photocoagulation Using Conventional Laser on Central Subfield Macular Thickness in Diabetic Retinopathy

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Received: June 10, 2018 Revised: October 25, 2018 Accepted: November 3, 2018

Abstract:

Objective:

To compare the change in central subfield macular thickness following single-session and multiple-session laser panretinal photocoagulation in subjects with diabetic retinopathy.

Methods:

A single-center, randomized controlled trial study was performed on 28 eyes of 16 patients with severe non-proliferative diabetic retinopathy or proliferative diabetic retinopathy. Eyes were randomly assigned for treatment with panretinal photocoagulation performed either in single-session or multiple-session divided into three sessions during two-week period. Central subfield macular thickness was quantified using spectral domain optical coherence tomography and changes at four weeks follow-up were compared to the baseline measurement.

Result:

Mean baseline central subfield macular thickness of 12 eyes underwent single-session and 16 eyes underwent multiple-session panretinal photocoagulation were 342.91±109.51 micrometers and 354±171.79 micrometers (p> .05), respectively. Mean post laser central subfield macular thickness in the single-session group was 305.83± 81.95 micrometers and 389.75 ± 229.51 micrometers in the multiple-session group (p > .05). Mean central subfield macular thickness changes four weeks post laser was 37.08 ± 94.21 micrometers for eyes treated with single-session and -35.75±123.62 micrometers for the multiple-session treated eyes (p = .101).

Conclusion:

There was no significant difference in change of central subfield macular thickness at four weeks post laser from treatment with single-session and multiple-session panretinal photocoagulation. Single-session panretinal photocoagulation can be used as effective multiple-session panretinal photocoagulation for the treatment of diabetic retinopathy.

Keywords: Diabetic retinopathy, Panretinal photocoagulation, Central subfield macular thickness, DRI, ETDRS, Conventional Laser.

1. INTRODUCTION

Diabetic Retinopathy (DR) is the most common blinding microvascular complication of diabetes mellitus. It is a growing problem as the number of people with diabetes increases. The use of laser photocoagulation in treating diabetic retinopathy has gained universal acceptance in ophthalmology practices since its introduction by Meyer-Schwikerath in

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the 1950s. The Early Treatment of Diabetic Retinopathy Study (ETDRS) and Diabetic Retinopathy Study (DRS), large multicenter randomized clinical trials for DR, demonstrated that panretinal (scatter) Photocoagulation (PRP) can reduce the risk of severe vision loss in patients with severe Non Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR) [1 - 5].

Standard conventional laser treatment is performed using single spot with spot size ranging from 100-500 micrometers, the pulse duration of 100-200 milliseconds (ms), and power adjusted to produce moderate-intensity burns. However, there are still debates among ophthalmologists whether to perform this procedure as a single-session PRP (S-PRP) or multiple-session PRP (M-PRP). The sessions are painful, costly, time-consuming, and require patient's compliance, which is tiring for both patients and doctors. In another hand, the single-session procedure has been associated with increased complications such as retinal detachment and vision-disabling macular edema [1, 5 - 7].

Advances in laser delivery systems have led to the use of a newer laser method, which can apply a uniform pattern of many laser spots at one time with shorter pulse duration and allows ophthalmologists to perform photocoagulation more rapidly with less pain than conventional lasers [8 - 11]. The overall safety of these pattern scan laser has been confirmed in large clinical trials. Several studies have demonstrated the use of PASCAL (pattern scanning laser photocoagulation) and shown beneficial of these methods performed in single sitting compared to the use of the conventional laser performed in multiple sittings [1, 2, 8 - 11]. However, this is an expensive machine and is not readily available in every medical facility, mainly in developing countries.

For that reason, we compare the change of the Central Subfield macular Thickness (CST) between low duration PRP performed in single-session and multiple-session using conventional multicolor pattern laser photocoagulator in DR.

2. METHOD

This is a single center, randomized controlled trial study on subjects newly diagnosed with severe NPDR and PDR recruited from vitreoretina department, Cicendo National Eye Hospital. The study protocol was approved by Universitas Padjadjaran Ethical Committee. After informed consent was obtained, eyes were randomized to receive either S-PRP or M-PRP divided into three sessions performed one week apart. The study inclusion criteria included the following: (1) patients age $\geq$ 18 years old, (2) newly diagnosed severe NPDR or PDR (3), no history or clinical evidence of prior PRP, (4) adequate pupil dilatation and clear media to perform laser photocoagulation, (5) follow-up for 4 weeks after treatment, (6) spectral domain Optical Coherence Tomography (OCT) performed before PRP and 4 weeks after the last treatment session. The exclusion criteria included the following: (1) other retinal disease such as retinal vein occlusion or uveitis, (2) history of cataract surgery within 12 months and any other intraocular surgeries including vitrectomy, (3) history of intraocular treatment such as intravitreal injection, (4) tractional retinal detachment, (5) presence of media opacities obscuring laser treatment and OCT imaging such as dense cataract and vitreous hemorrhage.

All patients underwent clinical ophthalmic examinations including posterior dilated indirect funduscopy examination, as well as OCT to document central macular thickness. The DR severity was determined from clinical findings by the treating physician based on International DR Severity Scale. Severe NPDR was diagnosed if four quadrants have retinal hemorrhage, two or more quadrants have venous beading, or one or more quadrant have Intraretinal Microvascular Abnormalities (IRMA), and PDR was diagnosed with the presence of neovascularization and/or vitreous or pre-retinal hemorrhage.

Macular thickness was performed using CIRRUS 5000 high-definition OCT (Carl Zeiss Meditec, Dublin, CA) based on macular cube 512x128 imaging before PRP and four weeks after the last treatment session. The CST was described as a central 1 millimeter (mm) area thickness of the ETDRS grid over the 6x6 mm cube on OCT image. Good quality images were considered in images with signal strength above 6. Patients were seen in follow up four weeks after the end of the session.

2.1. Laser photocoagulation technique

Laser procedure was performed with Multicolor Scan Laser Photocoagulator MC-500 (NIDEK CO., LTD, Japan), using the 532 nanometers (nm) green laser to create a pattern array of laser spots with the aid of ocular mainster PRP 165-lens. Laser parameters are described in Table **1**. Pupillary dilatation was achieved with one drop of 1% tropicamide and one drop of 10% phenylephrine. All procedures were performed under topical anesthesia using tetracaine 0.5% eye

drop.

Table 1. Laser Photocoagulation Parameters

Parameter	S-PRP Group	M-PRP Group
Number of Sessions	1: day 0	3: day 0,7, and 14
Type of Laser	NIDEK, Green 532nm	NIDEK, Green 532nm
Type of Laser Spot	Pattern Spot, Square 4x4 arrays	Pattern Spot, Square 4x4 arrays
Number of Burns, ± SD	2518.4±683	2699.4±587.4
Spot size, Micrometers	200-400	200-400
Pulse Duration, ms	50	50
Laser Burn Spacing	1-1.5 Burn Widths	1-1.5 Burn-Widths
Laser Burn Intensity	Grade 2, 3: Mild, Moderate	Grade 2, 3: Mild, Moderate

SD = Standard Deviation

2.2. Statistical Analysis

Statistical analysis was performed using statistical software (SPSS for Windows version 24.0, SPSS Inc, Chicago, IL, USA). Shapiro-wilk test was used to determine if the data were distributed normally. The change in CST comparing the pretreatment and posttreatment measurement was evaluated statistically with Independent t-test. Confidence interval 95% and p-value < 0.05 were considered statistically significant.

3. RESULTS

Twenty-eight eyes of 16 patients were enrolled in this study. Twelve patients had treatment on both eyes, and four patients had treatment in only one eye due to non-eligibility of the fellow eye. Twelve eyes underwent S-PRP, and 16 eyes had M-PRP. The subject characteristics are presented in Table **2**.

Table 2. Subject Characteristics.

Subject Characteristic	S-PRP Group	M-PRP Group
Number of Subjects, n	8	9
Number of Eyes, n	12	16*
Male: Female	4: 4	6: 3
Age, Mean ± SD, y	55.75±6.67	54.67±7.81
Age Range, y	45-63	45-65
DR Type, n (%) Severe NPDR PDR	10 (83%) 2 (17%)	4 (25%) 12 (75%)

*one eye was included in the S-PRP group and the fellow eye was included in the M-PRP group in one male participant.
SD = Standard Deviation

There were nine males and seven females included in this study. Four males and four females were recruited in the S-PRP group, and six males and three females in the M-PRP group. There was one male patient who had S-PRP in one eye and M-PRP in the fellow eye. Mean age was 55.75±6.67 years (range, 45-63 years) in the S-PRP group and 54.67±7.81 years (range, 43-65 years) in the M-PRP group.

Laser parameters used in this study were similar between the two groups except for the number of sessions and laser burns performed which were 2518.4±683 and 2699.4±587.4 in the in the S-PRP and M-PRP group, respectively. Mean baseline CST as measured by OCT was 342.91±109.51 micrometers in the S-PRP group and 354±171.7 micrometers in the M-PRP group (p >.05). Four weeks post laser, mean CST in the S-PRP group was 305.83±81.95 micrometers and 389.75 ±229.51 micrometers in the M-PRP group (p>.05). There was no statistically significant difference in baseline and four weeks post laser CST between the two groups. CST change was defined as the induced change of CST from the baseline CST and the post laser CST, counted by substracting the value of baseline CTS and four weeks post laser CST. Comparison of changes in CST between the two groups is presented in Table **3**.

Mean CST change in the S-PRP group was 37.08±94.21 micrometers and in the M-PRP group, it was -35.75±123.62 micrometers (p=0.101). There was no statistically significant difference in CST changes between the S-PRP and M-PRP procedure groups.

Table 3. Changes in CST value.

CST (Micrometers)	S-PRP Group	M-PRP Group	*p*-value
Baseline, Mean, ±SD	342.92± 109.51	354± 171.79	0.847
4 Weeks Post Laser, Mean, ±SD	305.83± 81.95	389.75± 229.51	0.239
OCT Change*, Mean, ±SD	37.08± 94.21	-35.75± 123.62	0.101

* subtraction from baseline CST and 4 weeks post laser CST
SD = Standard Deviation

DISCUSSION

Laser treatment is generally accepted as the gold standard and mainstay therapy for severe NPDR and PDR since the studies on DR were established. The primary aim of laser treatment is to convert ischemic retina to anoxic state, thus reducing the ischemic-induced vascular endothelial growth factor release, preventing neovascularization and in turn, increased retinal oxygenation [1 - 5, 12].

Although laser PRP has been shown to reduce the risk of severe visual loss in severe NPDR and PDR, there might be concern that the progression of diabetic macular edema can occur after PRP, leading to decrease in visual acuity [3, 6, 13]. Several theories indicate that the increased level of inflammatory reactions may be involved in the pathogenesis of macular edema [14].

Generally, PRP is performed in 2 or more sessions. Some clinicians prefer to complete the procedure in one session which might be more convenient, cost-effective, and time-saving for both patients and doctors. However, there is concern that completion of PRP in one session might increase the development of macular edema and vision loss [3, 9, 15]

Doft and Blankenship [15], in 1982, reported that there were no long-term increased complications in performing S-PRP compared to the M-PRP procedure. The incidence of macular edema was not different between pre-treatment and six-month post-treatment in either group in their study. However, there were transient complications such as choroidal and retinal detachment in the S-PRP group.

Our study demonstrated that the change of CST following S-PRP was not significantly different from the M-PRP group. In 2009, the DR clinical research network [3] also reported that clinically meaningful differences of OCT thickness are unlikely following application of conventional PRP in one sitting compared with four sittings in a nonrandomized, prospective, multicenter clinical trial, which is consistent with the result from our study.

In the Manchester Pascal Study, Muqit *et al.* [8, 9] evaluated the change of macular thickness between pattern multi-spot S-PRP vs conventional single spot M-PRP and concluded that the S-PRP procedure did not cause macular edema after adequate treatment. However, they excluded patients with macular edema at presentation. In contrast, our study included those patients with macular edema along with DR at the time of presentation.

The present study showed no statistically significant difference of OCT changes between S-PRP and M-PRP, with an average of 2518 and 2699 laser spots delivered in each group, respectively. Oh *et al* [16] and Nawat *et al.* [1], in their study performed S-PRP with an average 2150 and 3125 laser spots delivered respectively with 20ms spot duration and found a statistically significant increase of CST and macular edema during four weeks follow up. The higher number of laser spots in their study may explain the increased CST observed compared to the study by Muqit *et al.* [2], who performed the application of 1500 laser spots with 20 ms spot duration in the S-PRP group, which is comparable to the conventional PRP arm. However, we used 50 ms spot duration in our study, which is lower than the 100-200 ms spot duration needed in the conventional PRP [3]. This may explain the higher number of laser spots needed to perform PRP in our study because the expansion of scars is less than that required using conventional PRP. Moreover, the number of laser spots delivered in our study may not express the real number of spots producing burn expected since the procedure was not performed by a single clinician.

This study has several limitations. The sample study was relatively small, and the total follow up for this study was short. Another limitation is that we did not account for other factors such as the type and duration of diabetes, the type, and dosage of systemic treatment, blood glycosylated hemoglobin level, as well as the presence of diabetic nephropathy, all of which can affect the diabetic retinopathy. Further study is warranted to adequately evaluate the safety and efficacy of PRP performed in a single session.

CONCLUSION

Even with limitations, our study demonstrated that patients treated with PRP procedure performed in the single session did not show statistically significant change of CST value compared with the PRP performed in multiple sessions, suggesting that completion of S-PRP can be effective and more convenient for both patients and doctors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by Universitas Padjadjaran Ethical Committee.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT OF PUBLICATION

An informed consent was taken from all the participants when they were enrolled.

CONFLICT OF INTERESTS

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Watanachai N, Choovuthayakorn J, Patikulsila D, Ittipunkul N. Changes in central macular thickness following single session multispot panretinal photocoagulation. J Ophthalmol 2015; 2015: 529529.
[http://dx.doi.org/10.1155/2015/529529] [PMID: 25694825]

[2] Muqit MM, Marcellino GR, Henson DB, *et al.* Single-session *vs* multiple-session pattern scanning laser panretinal photocoagulation in proliferative diabetic retinopathy: The Manchester Pascal Study. Arch Ophthalmol 2010; 128(5): 525-33.
[http://dx.doi.org/10.1001/archophthalmol.2010.60] [PMID: 20457972]

[3] Brucker AJ, Qin H, Antoszyk AN, *et al.* Observational study of the development of diabetic macular edema following panretinal (scatter) photocoagulation given in 1 or 4 sittings. Arch Ophthalmol 2009; 127(2): 132-40.
[http://dx.doi.org/10.1001/archophthalmol.2008.565] [PMID: 19204228]

[4] Chehade L, Chidlow G, Wood J, Casson RJ. Short-pulse duration retinal lasers : A review. Clin Exp Ophthalmol 2016; pp. 1-8.

[5] Chhablani J, Sambhana S, Mathai A, Gupta V, Arevalo JF, Kozak I. Clinical efficacy of navigated panretinal photocoagulation in proliferative diabetic retinopathy. Am J Ophthalmol 2015; 159(5): 884-9.
[http://dx.doi.org/10.1016/j.ajo.2015.02.006] [PMID: 25703478]

[6] Soman M, Ganekal S, Nair U, Nair K. Effect of panretinal photocoagulation on macular morphology and thickness in eyes with proliferative diabetic retinopathy without clinically significant macular edema. Clin Ophthalmol 2012; 6: 2013-7.
[PMID: 23271879]

[7] Oh J-H, Kim S-W, Kwon S-S, Oh J, Huh K. The change of macular thickness following single-session pattern scan laser panretinal photocoagulation for diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol 2014; 1-7.
[PMID: 24862300]

[8] Muqit MMK, Marcellino GR, Gray JCB, *et al.* Pain responses of Pascal 20 ms multi-spot and 100 ms single-spot panretinal photocoagulation: Manchester Pascal Study, MAPASS report 2. Br J Ophthalmol 2010; 94(11): 1493-8.
[http://dx.doi.org/10.1136/bjo.2009.176677] [PMID: 20558423]

[9] Muraly P, Limbad P, Srinivasan K, Ramasamy K. Single session of Pascal *versus* multiple sessions of conventional laser for panretinal photocoagulation in proliferative diabetic retinopathy: A comparitive study. Retina 2011; 31(7): 1359-65.
[http://dx.doi.org/10.1097/IAE.0b013e318203c140] [PMID: 21423068]

[10] Nagpal M, Marlecha S, Nagpal K. Comparison of laser photocoagulation for diabetic retinopathy using 532-nm standard laser *versus* multispot pattern scan laser. Retina 2010; 30(3): 452-8.
[http://dx.doi.org/10.1097/IAE.0b013e3181c70127] [PMID: 20216293]

[11] Zhang S, Cao GF, Zhong Xu X, Wang CH. Pattern scan laser *versus* single spot laser in panretinal photocoagulation treatment for proliferative diabetic retinopathy. Int Eye Sci 2017; 17(2): 205-8.

[12] Mukhtar A, Khan MS, Junejo M, Ishaq M, Akbar B. Effect of pan retinal photocoagulation on central macular thickness and visual acuity in

proliferative diabetic retinopathy. Pak J Med Sci 2016; 32(1): 221-4.
[PMID: 27022379]

[13] McDonald HR, Schatz H. Macular edema following panretinal photocoagulation. Retina 1985; 5(1): 5-10.
[http://dx.doi.org/10.1097/00006982-198500510-00002] [PMID: 4001591]

[14] Nonaka A, Kiryu J, Tsujikawa A, *et al.* Inflammatory response after scatter laser photocoagulation in nonphotocoagulated retina. Invest Ophthalmol Vis Sci 2002; 43(4): 1204-9.
[PMID: 11923267]

[15] Doft BH, Blankenship GW. Single versus multiple treatment sessions of argon laser panretinal photocoagulation for proliferative diabetic retinopathy. Ophthalmology 1982; 89(7): 772-9.
[http://dx.doi.org/10.1016/S0161-6420(82)34734-X] [PMID: 6181452]

[16] Oh J-H, Kim S-W, Kwon S-S, Oh J, Huh K. The change of macular thickness following single-session pattern scan laser panretinal photocoagulation for diabetic retinopathy. Graefes Arch Clin Exp Ophthalmol 2014; 1-7.
[PMID: 24862300]