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Conventional and Pattern Scanning Pan-Retinal Photocoagulation Laser in Diabetic Patients' Visual Field

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Abstract

Introduction: In this study, we aimed to compare visual field defects in two different laser methods, namely conventional pan-retinal photocoagulation (PRP) and pattern scanning PRP, in patients with either proliferative diabetic or very severe non-proliferative diabetic retinopathy.

Methods: This study was a randomized, single-blind, prospective clinical trial. Twenty patients with either proliferative or very severe non-proliferative diabetic retinopathy were enrolled in this study. Notably, only those patients with the same severity scores in both eyes were included. One eye underwent the conventional PRP laser and another eye underwent the pattern scanning PRP laser simultaneously. Swedish interactive threshold algorithms (SITA) standard perimetry was performed at baseline and one month after the treatment, and visual field defects were evaluated.

Results: The pattern standard deviation (PSD) significantly increased in both the pattern and conventional PRP laser groups after one month. The change of the PSD at baseline and after the treatment was not significant between the groups. The mean deviation (MD) level significantly decreased in the conventional group after one month. The change in the MD level at baseline and after the treatment was not significant between the pattern and conventional groups. The change in the mean best corrected visual acuity (BCVA) between the groups was not significant.

Conclusion: Changes in visual acuity and visual fields of the patients between the pattern and conventional PRP laser methods showed no significant difference; however, the pattern PRP method caused a smaller reduction in overall sensitivity in the patient's visual field.

Keywords: Diabetic retinopathy; Laser thermo-coagulation; Visual field.

Introduction

Diabetic retinopathy is one of the most common causes of vision loss in developed countries worldwide. Long-term hyperglycemia causes physiological and biochemical changes that could eventually lead to vascular endothelial damage, capillary obstruction, and retinal ischemia. 0divided into two groups of non-proliferative and proliferative diabetic retinopathy. In this regard, the effective treatments include pharmacologic treatments (intravitreal injections of anti-vascular endothelial growth factors (VEGF)) and photocoagulation lasers.[1] The primary mechanism of pan-retinal photocoagulation (PRP) is the regression of neovascularization by destructing retinal ischemic regions. Consequently, this improves the oxygen uptake of the remained retina and also reduces angiogenic factors.[2-4] The complications related to the photocoagulation laser are the following: retinal injury caused by the laser, choroidal neovascularization, visual field impairment, contrast sensitivity reduction, and color vision reduction.[5-8] Novel methods are currently applied to improve the efficiency and reduce the side effects of the lasers, including pattern scanning PRP. In Conventional PRP, laser energy is continuously used for longer periods, so it can cause more discomfort. In the pattern scanning method, which is also known as short duration, shortening the pulse duration of the laser reduces total energy, which consequently causes less thermal damage to the retina and less patient discomfort compared to the conventional method.[9-12] One of the side effects of PRP is peripheral vision damage. This study aimed to compare the visual field defects in two different methods of conventional PRP and pattern scanning PRP in patients with proliferative and very severe non-proliferative diabetic retinopathy.

Materials and Methods

This study was a randomized, single-blind, prospective, controlled clinical trial. The study design was parallel with a 1:1 allocation ratio. The inclusion criteria were proliferative diabetic retinopathy or very severe non-

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proliferative diabetic retinopathy with the same ETDRS severity scores in both eyes. The exclusion criteria were any history of previous trauma, retina surgery or laser procedure or other ocular diseases that could affect visual field studies such as concurrent diabetic maculopathy, glaucoma, severe cataract and other causes of opaque media, uveitis, posterior synechiae formation, degenerative or inherited retinal disease with a visual field defect. The patients with poor cooperation for visual field studies were excluded. The patients referred to the retina clinic of Nikookari Eye Hospital at Tabriz University of Medical Sciences were enrolled in this study.

The patients' diagnosis was performed based on slit lamp examination and fluorescein angiography. Visual acuity was obtained according to the Snellen chart at baseline. One day prior to PRP, the patients underwent the Swedish interactive threshold algorithms (SITA) Standard 30-2 perimetry with Humphrey perimeter (Zeiss Meditech, model 750, USA) for both eyes. Notably, the patients were well-trained before starting the perimetry. Before PRP, topical anesthesia with the Tetracaine 0.5% eye drop (Tetracaine Hydrochloride and Benzalkonium Chloride, Sina Darou, Iran) was applied. Thereafter, one eye underwent the conventional PRP (Topcon slit, Japan) and the fellow eye underwent the Pattern Scanning PRP simultaneously (Ellex, Australia).

In the conventional PRP method, a power of 250-700 mW, laser spot size of 400 μm, and pulse duration of 100 ms were applied. Spot spacing was 200 μm. On the other hand, in the pattern scanning method, power of 250-700 mW, pulse duration of 10-30 ms, laser spot size of 400 μm, and laser spot spacing of 0.75 spot size were applied. Additionally, in the pattern scanning group, the frequency-doubled Nd: YAG laser (a wavelength of 561 nm) was used, and in the conventional PRP group, the argon green laser (a wavelength of 561 nm) was used. A retinal lens (Volk Super Quad 160, 2.0×) was used for PRP. The intensity of the laser used in both study groups was moderate, which was defined as moderate whitening of the retina. Laser spots were applied one disc diameter away from superior and inferior retinal vascular arcades. Nasal and temporal retinae were also spared. Two sessions of PRP were then applied within one week.

SITA Standard perimetry was repeated one month after the last PRP session and was evaluated for reliability and visual field defects in order to compare those variables that were measured at baseline and one month after the intervention. Visual acuity assessment was repeated one month after PRP.

The primary endpoints of this study were changes in patients' visual field after PRP, and secondary endpoints were changes in visual acuity, macular edema magnitude and any complication after the intervention.

In this study, one eye of every patient was in the pattern group and the other eye was in the conventional group. Only patients with the same retinopathy severity score in both eyes were included. Despite this similarity between the two groups, randomization was performed. The right eyes of the patients were simply randomized to get either conventional or pattern PRP, and then the left eye of every patient was allocated to receiving the other remaining treatment not used for the patient's right eye.

Statistical Analysis

The sample size required for this study was calculated based on sample size formula for the comparison of two means: $(z_{1-\alpha/2}+z_{1-\beta})^2\ (\delta_1^2+\delta_2^2)/(\mu_1^2-\mu_2^2)$. Considering the 95% confidence level and 80% test power, 24 patients was calculated for each group.

Descriptive statistics was used to evaluate the distribution of the obtained data. Continuous data with normal distribution were presented as mean ± standard deviation. In this paper, we studied both eyes of one subject and this may consequently cause some significant errors using the usual *t* test analyses due to the dependency of both eyes in one subject. Therefore, another statistical analysis based on the GLM (generalized linear model) was conducted using STATA software version 14.0 (StataCorp, College Station, Texas, USA). Finally, generalized estimation equations (GEE) were used to compare means and percentages between the two groups. A *P* value of 0.05 or less was considered statistically significant.

Results

Twenty-four patients were included in the present study. Of them, three patients did not return for re-examination after the initial PRP and one patient did not come for a one-month follow-up, so they were excluded from the study. Finally, 20 patients were fully followed during the period of this research. The mean age of the patients was 54.5 ± 6.1 years. 12 patients were men and 8 were women.

There were 14 eyes with very severe NPDR and 26 eyes with PDR diabetic retinopathy. The mean spherical equivalents before PRP in the Conventional group and in the pattern group were 0.15 ± 1.68 D and 0.13 ± 1.57 D respectively, with no statistically significant difference ($P=0.51$). The primary specifications of the patients are presented in Table 1.

The mean best corrected visual acuity (BCVA) of the eyes before PRP was 0.19 ± 0.15 logMAR and 0.20 ± 0.18 logMAR in the pattern PRP and in the conventional PRP group respectively, and then they reached 0.21 ± 0.17 Log MAR and 0.21 ± 0.20 logMAR one month after treatment respectively. There was no significant difference in mean BCVA in both groups before and after the treatment ($P=0.41$ and $P=0.62$ respectively). The change in BCVA before and after the treatment was not significant between the pattern and conventional groups ($P=0.85$).

Notably, no significant difference was found between

Table 1. Changes in Perimetry Parameters During a One-Month Follow-up

Parameter		Group		*P* Value[a]
		Pattern(n = 20)	Conventional (n = 20)	
Number		20	20	
Age		54.5 ± 6.1	54.5 ± 6.1	
Male/female		12/8	12/8	
Right/left		7/13	13/7	
Spherical equivalent	Mean ± SD	0.13 ± 1.57	0.15 ± 1.68	0.51
Pre BCVA (logMAR)	Mean ± SD	0.19 ± 0.15	0.20 ± 0.18	
BCVA 1 month	Mean ± SD	0.21 ± 0.17	0.21 ± 0.20	0.85
P[b]		0.41	0.62	
Pre MD	Mean ± SD	-1.68 ± 2.67	-0.80 ± 2.30	
MD 1 month	Mean ± SD	-2.07 ± 2.86	-2.46 ± 3.84	0.78
P[b]		0.28	0.008	
Pre PSD	Mean ± SD	2.88 ± 1.24	3.31 ± 1.74	
PSD 1 month	Mean ± SD	3.98 ± 2.00	4.61 ± 2.20	0.33
P[b]		0.001	< 0.001	
First session Power	Mean ± SD	537.37 ± 115.85	537 ± 155.67	
Second session power	Mean ± SD	528.42 ± 150.75	538.40 ± 159.13	0.91
P[b]		0.32	0.49	

logMAR: logarithm of minimal angle of resolution, BCVA: best-corrected visual acuity, PSD: pattern standard deviation, MD: mean deviation.
[a] Group effect analysis, based on GEE analysis.
[b] Between groups analysis, based on GLM analysis.

the mean BCVA values of the two groups at baseline and after PRP ($P = 0.94$ and $P = 0.98$, respectively).

The mean MD of the patients before PRP in the pattern group was -1.68 ± 2.67, which reached -2.07 ± 2. 86 within 1 month after PRP; however, it was not statistically significant ($P = 0.28$). The mean MD of the patients before PRP in the conventional group was -0.80 ± 2.30, which reached -2.46 ± 3.84 within one month after PRP; however, it was statistically significant ($P = 0.008$). There was no significant difference between the two study groups in terms of the mean of MD before PRP and one month later ($P = 0.27$ and $P = 0.72$ respectively). The change in the mean of MD at baseline and after the treatment was not significant between the pattern and conventional groups ($P = 0.78$).

The mean pattern standard deviations (PSDs) of the patients before PRP were 2.88 ± 1.24 and 3.31 ± 1.74 in the pattern PRP group and in the conventional PRP group respectively. PSDs reached 3.98 ± 2.00 and 4.61 ± 2.20 within a one-month follow-up respectively ($P = 0.001$ and $P < 0.001$).

There was no significant difference between the mean PSD values of the two study groups before PRP and after one month ($P = 0.37$ and $P = 0.34$ respectively). The change in PSD before and after the treatment was not significant between the groups ($P = 0.33$). Parameters of the perimetry before and after laser therapy are shown in Table 1.

The mean powers used in the first session of the conventional PRP and in the second session of the conventional PRP (which were applied depending on the evaluation of the laser effects) were 537.00 ± 155.67 mW and 538.40 ± 159.13 mW respectively. Moreover, in the pattern group, these mean powers were 537.37 ± 115.85 mW and 528.42 ± 150.75 mW respectively, which were not statistically significant between the two study groups in the first and second sessions ($P = 0.87$ and $P = 0.84$ respectively).

There was no significant difference in applied laser power in the pattern and conventional groups between the first and second sessions ($P = 0.32$ and $P = 0.49$ respectively).

The total spot laser used in the pattern group was 2260.90 ± 252.71, and in the conventional group, it was 1317.14 ± 223.12. Notably, a statistically significant difference was found between the two groups in the number of Spots ($P < 0.001$).

Two cases in the conventional group and one case in the pattern group developed macular edema and were subjected to intravitreal injection of 1.25 mg bevacizumab during the first three weeks of PRP. In these patients, no symptomatic complications were observed.

Discussion

The photocoagulation laser is used for the treatment of retinal diseases such as proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy, retinal ischemia, retinal vascular occlusion, and choroidal neovascularization.[1] The laser light is absorbed by the retinal pigment epithelium layer. Thereafter, the absorbed laser power turns to thermal energy, which results in the denaturation of the proteins in the retinal cells, the death of the cells, and coagulative necrosis. Subsequently, the level of VEGF decreases with the destruction of a large part of the ischemic retina, which consequently reduces the amount of neovascularization.

The complications related to PRP are the reduction of visual acuity and contrast sensitivity, macular edema, spread of laser scarring, and subretinal fibrosis.[13,14]

In a study, Yilmaz et al. compared the change in pupil size after the conventional laser and the pattern scan laser. The conventional laser and the pattern scan laser were applied to two groups with 20 eyes. Pupil size was assessed by automated infrared pupillometry at baseline and one month later. A significant increase was observed in pupil size within a one-month follow-up (under photopic, mesopic, and scotopic conditions) in both groups ($P < 0.001$), which reduced overall sensitivity in the visual field. Pupil size was less affected in the pattern

laser group, probably due to the lower intensity of the laser burn, shorter laser pulse duration, and less damage to short ciliary nerves.[15] In our study, more effects of the conventional laser on the visual field can be due to more dilation of the pupil afterward.

In a review study, Çeliker et al.[16] examined the benefits and side effects of multi-spot lasers in comparison with the conventional laser for the treatment of diabetic retinopathy in Turkey. They found that the multi-spot laser causes less damage to the retinal tissue, and patients feel more comfortable and less pain compared to the conventional laser. The efficacy of the multi-spot laser was similar to that of the conventional laser, but higher numbers of spots were needed.[16]

Muqit et al[17] conducted a prospective study to examine retinal photocoagulation using the pattern scan laser (Pascal) method in proliferative diabetic retinopathy. To do this, 28 eyes were enrolled in this study. Thereafter, capillary non-perfusion and ischemic areas in widefield angiography were treated with 1500 pascal laser burns with pulse duration of 20 ms and a spot size of 200 μm. Finally, patients underwent 24-2 SITA-Standard visual field assessments after 12 and 24 weeks. The study showed an average improvement of 1.25db MD.[17]

This may indicate that it is preferable to burn the retina on a targeted pattern. It was shown that applying the laser on ischemic and non-perfused retinae and sparing the normal retina may help the remained watershed retina to be better perfused with the improved function and visual field. In this study, it was observed that the lower intensity of the laser could increase the ischemic retina oxygen supply by better diffusion from the outer retina. In this setting, the inner retina is preserved from the destructive effect of high pulse intensity as in the ETDRS study, and better oxygenation also yields better nerve fiber function even in ischemic areas.[18-21]

Nagpal et al[18] compared the 532-nm solid-state green laser (GLX) to the multi-spot 532-nm pattern scan laser (PASCAL) in diabetic retinopathy. Sixty patients underwent PRP using GLX and PASCAL methods and they were evaluated for the visual field one month later. Patients treated with the PASCAL method had higher retinal sensitivity; however, this difference was not statistically significant between the two groups, which was consistent with the result of our study.[18]

In Peter Pan's study, there was no significant difference in the MD of the patients treated with either standard intensity PRP or minimally traumatic PRP after 12 weeks. The visual acuity of the patients in both groups was not significantly different at the same time. The regression of disease activity was almost the same for both groups. This indicates that lower laser intensity can make a comparable effect like the standard intensity laser.[22]

In a recent review article, there was no significant difference in the visual field of the patients treated with conventional or other laser approaches.[23]

Brucker et al showed that one-session conventional laser PRP had no significant difference in terms of the magnitude of post-laser macular edema compared to 4-session PRP with mild or no macular edema at baseline.[20] This can be extrapolated to the multi-spot laser, and one-session multi-spot PRP can be applied with fewer side effects compared to the conventional laser. In our study, just one patient in the pattern group and two patients in the conventional group needed anti-VEGF for macular edema after PRP. However, regarding macular edema rates, further studies with higher sample sizes are needed.

In the present study, the reduced BCVA in both groups was not statistically significant after one month. PSD significantly increased in each group one month after PRP. The MD level significantly decreased in the conventional group one month after PRP compared to the pre-laser; however, this decrease was not statistically significant in the pattern group. In general, changes in visual acuity and visual field after the two pattern and conventional methods had no significant difference. By considering the significant decrease in MD in the conventional group, it can be postulated that the pattern method causes less reduction in the overall sensitivity in the patient's visual field. This may be due to lower pulse duration in the multi-spot laser with less tissue destruction, albeit with similar efficacy to that of the conventional laser. It should be considered that a lower defect of the visual field in our study in the pattern group compared to the conventional group was in the setting of significantly higher laser spots in this group. Correspondingly, with the same number of spots visual field could be much better preserved in Pattern group.

Study Limitations

The small sample size and the short-term follow-up duration can be considered major limitations of this study.

Conclusion

Although changes in the visual acuity and visual field of the patients between the two pattern and conventional PRP methods showed no significant difference, the pattern PRP method was observed to cause less reduction in the overall sensitivity in the patient's visual field. Significantly more spots used in the pattern laser with better preservation of the visual field yielded a less destructive effect of this method.

Authors' Contribution

Surgical and medical practices: MRN, MHA. Concept and design: MRN. Data collection or processing: AL, NH. Analysis or interpretation: NH, MRN. Literature search: NH, MRN. Writing: NH, MRN.

Conflict of Interests

There is no conflict of interests/competing interests for all authors.

Ethics Considerations

This study was conducted in terms of the principles of the Declaration of Helsinki and was supervised and approved by the Ethical Committee of Tabriz University of Medical Sciences. (Ethical code: TBZMED. REC 1397.269) and registered in the Iranian Registry of Clinical Trials website (identifier: IRCT20181123041737N1; https://www.irct.ir/trial/35431). Written informed consent was received from all the participants or from their legal parents to participate in this study and publish the obtained data.

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