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# Efficacy of Pan Retinal Photocoagulation Sub- Threshold Micropulse Diode Laser in Diabetic Retinopathy

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## ABSTRACT

**Background:** Diabetic retinopathy is a complication of systemic diabetes that is a main reason of vision loss. It poses a real challenge in its management due to the high financial impact it has on health care systems worldwide. Laser therapy may be used to treat severe non proliferative diabetic retinopathy (SNPDR) and early PDR provides another dimension in the management owing to its long-term effects and relatively low costs. The proposed protection of subthreshold diode micropulse laser opens up the door to using it in situations of SNPDR and early PDR.
**Objective:** Evaluate the efficacy of sub threshold micro pulse diode laser in pan retinal photocoagulation for severe non proliferative and early proliferative diabetic retinopathy.
**Patient and Methods:** This prospective research involved 40 eyes from 22 diabetic retinopathy patients between November 2019 to December 2020. History taking and ophthalmological examination and Fundus Fluorescein Angiography (FFA) have been performed on all patients prior to intervention. After informed written approval to the therapy protocol was received, a diode laser (810 nm) treatment was performed. Follow up was conducted at 3 visits at two weeks , 1 and 3 months. During each of these visits the patient's BCVA were measured and FFA was done after 3 months.
**Results:** There was a statistically significant rise in the BCVA at 2 weeks after treatment as compared with the initial BCVA that decreased again at 1 month and 3 months postoperative with no statistically significant difference as compared with the initial BCVA. Regarding the changes in VA according to the stage of the disease; 28 eyes remain stable with final VA similar to their initial VA, 7 eyes' VA improved, while 5 eyes' VA deteriorated.
**Conclusion:** There was no proof of laser impact or damage to the retinal pigment epithelium (RPE) or neurosensory retina in terms of safety, and there were no negative therapy impacts or complications. Improvement in final visual acuity was insignificant . SDM may have a preventive role to delay progression of SNPDR and early PDR during the follow up period.

**Keywords:** *Subthreshold , micropulse , photocoagulation, diabetic retinopathy, angiography.*

## INTRODUCTION

Diabetes mellitus (DM) is a worldwide medical problem. It causes many systemic complications that have considerable impacts as the disease usually strikes people in their prime working years.[1] Diabetes is becoming more prevalent all over the globe.[2]

Ophthalmic complications like corneal anomalies, iris neovascularization, glaucoma, cataracts, and neuropathies are widespread in diabetic patients. Diabetic retinopathy (DR) has been the most prevalent and potentially blinding of this complications.[3]

The most critical step in the treatment of patients with systemic diabetes is to prevent loss of vision. This is achieved by improving treatment of systemic disorders, managing modifiable risk factors, and providing routine ophthalmic screenings.[4]

Retinopathy progresses gradually, beginning with mild anomalies accompanied by high vascular permeability and progressing to moderate to severe non-proliferative DR distinguished by the formation of new blood vessels on the retina and on the posterior surface of the vitreous.[5]

Laser photocoagulation was shown to save vision in people who have advanced diabetic retinopathy in two pivotal trials: (1) The Diabetic Retinopathy Study (DRS),[6,7] found that pan retinal photocoagulation (PRP) had a major vision-saving potential in high risk PDR, and (2) Early Treatment DRS (ETDRS), where in patients with CSME received major vision benefit from focal/grid laser photocoagulation.[8] In these trials and subsequent research, laser photocoagulation was found to be one of the most effective first-line therapies for PDR and CSME.[9]

Despite traditional photocoagulation's efficacy, there is no indication that the retinal destruction associated with visible end point photocoagulation is needed for a therapeutic advantage in the management of retinal vascular disease.[10-15]

## PATIENTS AND METHODS

This was a prospective interventional research that performed in the period between November 2019 to December 2020 in Al Azhar university hospitals, Cairo, Egypt.

Twenty-two persons with severe non proliferative diabetic retinopathy and early proliferative diabetic retinopathy were involved in this study, which included forty eyes. The cases with the following conditions were ruled out; previous conventional PRP and presence of dense media (as dense vitreous haemorrhage and dense cataract).

After approval from the local ethics committee of Al-Azhar Faculty of Medicine and obtaining an informed written consent from the participants, all cases were subjected to complete history taking and through full general examination.

In the preoperative stage, full detailed ophthalmic examination was done for all the cases including assessment of the visual acuity and intraocular pressure with evaluation of the anterior and posterior segments. Fundus investigations included Colour fundus photography , Fluorescein Angiography and Optical coherence tomography.

Operative technique:

Pupil dilatation using topical Cyclopentolate 1% eye drops. All procedures were done under topical anesthesia using benoxinate HCL 0.4%. Using methylcellulose fluid, an inverting wide-field contact lens (Volk 160 Panfundus lens, Volk Corporation, Mentor, OH, USA) has been applied to the cornea. In its MicroPulse operating mode, a subthreshold diode micropulse laser (810 nm, Iris Medical Oculight Slx Laser, Iridex Corp, Mountain View, CA, USA) was used as follows: The spot size was selected to be 500 microns. The power was initially adjusted upward to the minimum threshold value for a barely visible greying of the retina (initial 2.0W power) and duration of 0. 2 s (test shot). The test shot was applied in the nasal field. Then the power was reduced by 50 % with a duty cycle of 15% and 0.20s pulse envelope duration (300ms ‘on’ time separated by 1700ms). A tight grid pattern of SDM was applied to all regions of the fundus outside of the posterior main vascular arcades and all the way to the retinal periphery. Since the laser lesions were absent, the fundus is visually divided into sectors delineated by the retinal vascular tree, allowing for the formation of a short-term mental 'inventory' of the treated regions. After that, these sectors were handled sequentially until PRP was complete.

Postoperative phase :

Visual acuity, slit lamp, and fundus examinations were performed on patients two weeks, one month, and three months after surgery.

All eyes are followed after 3 months by FFA to evaluate the difference in disease progression.

## RESULTS

As shown in table (1), after meeting the inclusion criteria, a total of 40 eyes from 22 participants were chosen for the research. The research included four participants who contributed only one eye and eighteen participants who contributed both eyes. The patients' ages varied from 35 to 75 years, with an average age +/- SD of 54.55 years ± 10.04. Nine patients were males while thirteen were females; the male to female ratio being 9:13. Twenty-one right eyes and nineteen left eyes received treatment, with oculus dexter (OD): oculus sinister (OS) ratio of 21:19. The length of DM varied from 10 to 25 years, with an average +/- SD of 14.82 years ± 5.3. According to initial FFA; SNPDR was present in twenty-nine eyes while early PDR was present in eleven eyes.

| **Age (Years)** | |
|---|---|
| **Mean ± SD** | 54.55 ± 10.04 |
| **Median (Range)** | 56 (35-75) |
| **Gender** | |
| **Male** | 9 (22.5%) |
| **Female** | 13 (77.5%) |
| **Right** | |
| **Left** | 19 (47.5%) |
| **Right** | 21 (52.5%) |
| **Disease duration (Years)** | |
| **Mean ± SD** | 14.82 ± 5.3 |
| **Median (Range)** | 13 (10 - 25) |
| **Initial FFA** | |
| **Early PDR** | 11 (27.5%) |
| **SNPDR** | 29 (72.5 %) |

**Table 1:** Demographic, clinical and pretreatment assessment in the included cases.

Table (2) shows that the baseline BCVA ranged from 0.2 to 0.8 with a mean +/- SD of 0.52 ± 0.14. Two weeks after PRP, the BCVA ranged from 0.3 m to 0.8, with a mean +/- SD of 0.56 ± 0.14 with statistically significant change (P= 0.001). At one month, the BCVA ranged from 0.2 to 0.8 with a mean +/- SD of 0.53 ± 0.17 with no statistically significant difference (P= 0.555). At three months, the BCVA ranged from 0.05 to 0.8 with a mean +/- SD of 0.54 ± 0.17and with no statistically significant difference (P= 0.352).

As a consequence of the changes in VA according to the stage of the disease; 28 eyes remain stable with final VA similar to their initial VA, 7 eyes' VA improved, while 5 eyes' VA deteriorated.

The eyes that showed worsening included 2 eyes with initial SNPDR that progressed to early PDR and 3 eyes with initial early PDR that progressed to HRPDR.

| | Initial VA (N=40) | VA at 2 weeks (N=10) | VA at 1 months (N=10) | VA at 3 months (N=10) | P value |
|---|---|---|---|---|---|
| **Mean ± SD** | 0.52 ± 0.14 | 0.56 ± 0.14 | 0.53 ± 0.17 | 0.54 ± 0.17 | 0.005* |
| **Percent of change (%)** | | (-16.67: 50) | (- 50: 40) | (- 50: 40) | |
| **$P_1$** | | < 0.001** | 0.555 | 0.352 | |
| **$P_2$** | | | 0.039* | 0.031* | |
| **$P_3$** | | | | 0.785 | |
| **Outcomes** | | | | | |
| Stable | | 28 (70%) | | | |
| Progression | | 5 (12.5%) | | | |
| Stable with improved VA | | 7 (17.5 %) | | | |

**Table 2:** Analysis of VA according to the study period.

Table (3) shows that after 3 months of treatment, the results of FFA showed that 27 eyes showed SNPDR, 10 eyes showed early PDR and 3 eyes showed HRPDR.

| FFA at 3 months | Eyes (n=40) |
|---|---|
| Early PDR | 10 (25%) |
| HRPDR | 3 (7.5 %) |
| SNPDR | 27 (67.5%) |

**Table 3:** Analysis of FFA at 3 months in the cases of the study.

Table (4) shows that the average +/- SD number of laser shots utilized in cases with SNPDR was 2212.69 ± 72.76 while the average +/- SD number of laser shots utilized in cases with early PDR became 2248.09 ± 192.05 with no statistically significant difference(P=0.397).

| | SNPDR (N=29) | Early PDR (N=11) | P value |
|---|---|---|---|
| **Number of laser shots** | 2212.69 ± 72.76 | 2248.09 ± 192.05 | 0.397 |

**Table 4:** analysis of the number of laser shots according to grade of DR (Initial FFA).

Table (5) shows that the number of laser shots and other variables including age, duration of DM, initial visual acuity, and percent change in VA at 2 weeks, 1 month, and 3 months of treatment had no statistically significant association.

| Variables | Number of laser shots | |
|---|---|---|
| | r | P |
| Age (Years) | 0.282 | 0.203 |
| Duration of DM (Years) | -0.069 | 0.759 |
| Initial visual | -0.050 | 0.760 |
| percent of change in VA at 2weeks | -0.112 | 0.493 |
| percent of change in VA at 1 month | 0.024 | 0.881 |
| percent of change in VA at 3 months | -0.014 | 0.934 |

**Table 5:** Association among the number of laser shots and other variables in the study.

## DISCUSSION

We described a novel traumatic photocoagulation strategy for diabetic retinopathy therapy in this study. A micropulsed diode laser with a low duty cycle was used to achieve subthreshold photocoagulation.

We noticed none of the complications correlated with traditional visible end point photocoagulation as a result of this process. Our 'high-density/low-intensity' SDM PRP technique, which uses a large retinal laser spot size and low laser irradiance level to treat severe non-proliferative and low-risk proliferative diabetic retinopathy, seemed to be efficient.[14,16-20]

The wavelength of 810 nm is thought to be suitable for both safe and efficient SDM laser therapy within the fovea.[7,8,21]

Most patients do not require clinical adjustment of laser parameters to accommodate individual differences in lens or media status, fundus coloration, or DME severity because of these characteristics and the broad therapeutic range when delivered with a low micropulse duty cycle.[22-24]

Luttrull et al. identified the pulsed subthreshold microsecond laser low-intensity/high-density subthreshold microsecond (STM) laser for PRP for proliferative diabetic retinopathy for the first time in 2008. They pointed out that photocoagulation's visible endpoint of retinal damage isn't currently needed for therapeutic advantage in the therapy of retinal vascular disease.[25]

Subthreshold diode microsecond laser, on the other hand, is thought to work solely on the retinal pigment epithelium (RPE), normalizing rather than destroying its function.

We set out to evaluate changes in visual acuity and disease progression in eyes of early PDR or extreme non-proliferative diabetic retinopathy (NPDR) stages in the current research.

Our findings raise serious questions about the commonly held assumption that retinal destruction is needed to control the progression of disease. 35 eyes showed arrest of progression of the disease of them 7

eyes showed improvement in visual acuity and we noticed clinical progression in only 5 eyes.

SDM was well accepted by patients. In a single session under topical anesthesia, SDM PRP was well tolerated.

According to the study of Mahima Jhingan et al., microsecond PRP is not-inferior to CWL PRP, [26] Because of its superior safety (no laser-caused retinal damage), comfort, and repeatability, we think SDM should be favored.

The lack of widely accepted therapies for SNPDR and early PDR is due to the harmful treatment results correlated with traditional PRP that contradicts the advantages of early therapy and has been the only mode of therapy accessible thus far.

It's important to note that preventive treatment does little but decrease the chances of disease progression.

The present study was conducted on 40 eyes of 22 subjects having met the inclusion criteria. The period of diabetes ranged from 10 to 25 years, and 29 eyes had extreme non proliferative diabetic retinopathy and 11 eyes had early proliferative diabetic retinopathy. The research included 4 participants who contributed only one eye and 18 participants who contributed both eyes. 16 eyes belonged to male subjects while 24 belonged to female subjects. None of our subjects had any retinal intervention prior to the study neither had significant degrees of cataract. FFA of these eyes was either SNPDR or early PDR.

Preoperative visual acuities were 0.2 (1 eye), 0.3 (1 eye), 0.4 (13 eyes), 0.5 (8 eyes), 0.6 (8 eyes) and 0.7 (8 eyes) and 0.8 (1 eye)

The used laser parameters were in accordance to Luttrull et al. review in 2008 based upon the retrospective study of Subthreshold diode micropulse pan retinal photocoagulation for proliferative diabetic retinopathy.[25]

Similar parameters were used by Jhingan et al. in the study that was conducted in 2018 where subthreshold diode micropulse laser was regarded as being secure and efficient and non-inferior to CWL for the treatment SNPDR and early PDR.[26]

In the present study, outside of the posterior major vascular arcades, standard SDM was performed, which consisted of high-density placement of contiguous and confluent laser spots over all areas of the fundus. The total shots used ranged from 2112 to 2822 shots. All patients were examined the next day following treatment and none of them showed any subjective loss of visual acuity or field defects nor any trace of laser treatment.

Follow up was then performed in three sessions, two weeks, one and three months after laser treatment with assessment of VA and fundus examination in each visit and FFA after 3 months.

Medical examination and fundus fluorescein angiogram in any eye postoperatively revealed no evidence of laser impact or damage to the retinal pigment epithelium (RPE) or neurosensory retina. Treatment has no negative effects or complications. This was in accordance to evidence presented by Luttrull et al in 2008 **[25]** and Jhingan et al in 2018.[26]

Regarding FFA, after 3month follow up period, 35 eyes showed no progression and only five eyes showed clinical progressive DR with development of transient vitreous haemorrhage in one of them which was treated medically and conventional CWL PRP was added.

As to the visual acuity, in the current research, SDM laser did not have a statistically significant role in stabilizing or improving visual acuity postoperatively, there was improvement in the BCVA at 2 weeks after treatment as compared with the initial BCVA which was statistically significant. But it decreased again at 1 month and 3 months postoperative with no statistically significant difference as compared with the initial BCVA.

Overall, visual acuity stayed stable during the period of follow-up, with a slight enhancement observed after 3 months in 7 eyes postoperatively which was not statistically significant, which was in accordance to the previous study by Jhingan et al in 2018.[26]

But our study differs from that presented by Luttrull et al in 2008 **[25]**, as we treated eyes with SNPDR and early PDR, but not high-risk DR, since, despite the fact that it is late in the disease's course, there is no widely recognized necessity for or mode of therapy which can be called "preventative" at this stage.

In our study we tried to use SDM as a preventing tool rather than therapeutic treatment aiming to delay or prevent further progression.

This research has significant limitations including small size, a short follow-up period, lack of controls, and the novelty of the technique. However, the results are compatible with those of all prior SDM reports for SNPDR and early PDR regarding safety, even if it did not show a statistically proven effectiveness in increasing regression or improving visual acuity.

SDM, however, appears to be ideally suited to be continuously proposed in the treatment of SNPDR and early PDR due to its safety profile.

We agree that further research into the ability of new early interventions like SDM to improve SNPDR and early PDR management is warranted.

## CONCLUSION

Although improvement in visual acuity was insignificant , our study proposes microsecond PRP could be a safe and effective preventive method used in severe NPDR and early PDR to delay progression and related complications.

The SDM laser was not shown to be successful as a sole treatment in the regression of proliferative diabetic retinopathy in the present study.

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