Research Article

Functional and anatomical treatment effect after subthreshold micropulse diode laser photocoagulation for diabetic macular edema

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Abstract
Purpose: To evaluate treatment effect of subthreshold micropulse diode (SDM) laser photocoagulation for diabetic macular edema (DME) both functionally by changes of best corrected visual acuity (BCVA) and anatomically by changes of optical coherence tomography (OCT) central subfield thickness. **Methods:** Twenty eyes of fifteen patients with diffuse DMO were treated with SDM laser. BCVA measured by Snellen acuity chart and central subfield thickness measured by OCT before and ٣ months after SDM laser. The pretreatment values of BCVA and OCT central subfield thickness were compared with the corresponding values at ٣ months after SDM laser. **Results:** At ٣ months, the BCVA was significantly improved (P<٠.٠٠١) and the central subfield thickness was significantly reduced (P<٠.٠٠١). **Conclusions:** SDM laser treatment of DME significantly improve BCVA and reduce OCT central subfield thickness ٣ months after treatment
Keywords: diabetic macular edema; optical coherence tomography; subthreshold micropulse diode laser photocoagulation

Introduction
DME is a major cause of visual decrease and the decrease can reduce the quality of life markedly in patients with diabetic retinopathy. The results of the Early Treatment of Diabetic Retinopathy Study (ETDRS) indicated that visible end-point laser photocoagulation reduced the risk of vision loss in patients with clinically significant DME.[١] However, photocoagulation with conventional continuous wave laser systems can damage the microstructures of the neural retina by the spread of heat from the retinal pigment epithelium (RPE).[٢] The damage created by laser photocoagulation can be reduced by reducing the laser exposure time and the laser power to the subvisible level. It was recently reported that SDM laser photocoagulation could minimize the chorioretinal damage in eyes with clinically significant DME.[٣]

The purpose of this study To evaluate treatment effect of subthreshold micropulse diode (SDM) laser photocoagulation for DME both functionally by changes of BCVA and anatomically by changes of OCT central subfield thickness.

Patients and methods
This study was an interventional prospective comparative nonrandomized study performed in the Ophthalmology Department of Minia University Hospital between November ٢٠١٥ to January ٢٠١٧.

The study was approved by the Ethics Committee of Minia University. The aim of the study and the used methodology were thoroughly explained to the patients and informed consent was obtained.
Twenty eyes of fifteen patients (٣ males and ١٢ females) were included in the study.

Inclusion criteria:
- Type ٢ DM patients with centrally involving DME less than ٤٠٠um

Exclusion criteria:
- Patients with type ١ DM
- Patients with macular ischemia detected by fluorescein angiography
- Patients with vitreoretinal traction and interruption of external limiting membrane (ELM) or inner segment-

outer segment (IS-OS) junction detected by OCT

- Patients with proliferative retinopathy
- Previous focal or grid conventional or SMD laser photocoagulation
- Previous intravitreal injection of steroid or anti-VEGF
- Previous vitreo retinal surgery
- Previous cataract surgery within six months
- Patients with media opacities interfering with adequate fundus observation
- Patients with macular diseases other than DME such as age-related macular degeneration (AMD)
- Patients with optic disc pathology or other ocular disorders that may affect visual outcome
- Patient with lack of regular follow-up

At baseline, all patients were subjected to a detailed assessment including the following:

١) Complete history taking including:

- Duration of DM
- Past glycemic control (HbA١c)
- Medications
- General medical history (e.g., renal disease, systemic hypertension, serum lipid levels and pregnancy)
- Ocular history (e.g., trauma, other eye diseases, ocular injections, photocoagulation and ocular surgery)

٢) Full ophthalmological examination including:

- BCVA using Snellen VA chart then converted to decimal acuity for statistical analysis.
- Pupillary assessment
- Anterior segment examination using Slit-lamp biomicroscopy
- Detailed fundus examination with indirect ophthalmoscopy and stereoscopic examination using +٧٨D lens to assess the DME and other diabetic changes in the fundus
- Intraocular pressure (IOP) measurement using applanation tonometry

٣) Ophthalmological investigations:

A) Colored fundus photography and fluorescein angiography:

This was performed using (**Topcon)™** fundus camera to detect site of leakage and macular ischemia. ٥ ml of ١٠٪ sodium fluorescein solution dye is injected intravenously through an antecubital vein. Images are acquired immediately after injection and continue for ten minutes.

B**) OCT examination**:

Examinations were done using the Cirrus HD-OCT ٤٠٠٠ **(Zeiss, Germany)™**. After pupillary dilatation two scan types were done for each eye. The first is the macular cube ٥١٢ × ١٢٨. This generates a cube of data through a ٦ mm٢ grid by acquiring a series of ١٢٨ horizontal scan lines each composed of ٥١٢ A-scans, except for the central high-definition vertical and horizontal scans, which are composed of ١,٠٢٤ A-scans; this scan helps in giving an idea about the regions of maximum height so they are better assessed and scanned by the high-definition ٥-line raster. The second scan is the high-definition five-line raster. This scan gives the highest resolution of all the Cirrus scan types. It scans through five parallel lines of equal length, and each line is composed of ٤,٠٩٦ A-scans. It is used to evaluate the mean retinal thickness from the innermost ILM to the RPE at the fovea. Multiple scans were taken throughout the whole macular area. Scans with the strongest signal strength were selected (signal strength of more than ٦/١٠). In this study the central subfield retinal thickness in the macular cube map, which is the central ١-mm diameter circular zone representing the foveal area was used for statistical analysis before and after treatment of DME by intravitreal injection of ranibizumab or SDM. Any disruption of the ELM was searched for within the central ١ mm of the fovea. If the ELM line appeared to be complete at the fovea in all scans, this was considered as an intact ELM. Any discontinuity or interruption of the ELM line in one scan or more was considered a disrupted ELM layer. The integrity of the IS/OS line beneath the fovea was evaluated using the same criteria described for the ELM line. If the line appeared to be complete at the fovea in all scans, it was diagnosed as an intact IS/OS line. If there was an incomplete IS/OS line in one scan or more, it was considered a disrupted IS/OS layer. Other findings that were evaluated during scan analysis included neurosensory detachment and vitreoretinal traction.

SDM laser was performed with an ٨١٠ nm infrared diode laser using (Iris Medical Iridex Corporation, Mountain View, CA, USA) after pupillary dilation and topical anesthesia Mainster focal grid contact lens (×١.٠٥ laser magnification) was applied. Fixed treatment parameters were used in all cases: ٢٠٠-µm spot size, ٢٠٠-ms exposure duration, ٤٠٠-mW powers, and a ٥٪ duty cycle. Confluent applications with no spacing were administered over the entire edematous area including the fovea.
Follow-up examination was performed ٣ months after SDM laser treatment with recording of the BCVA and central subfield thickness on OCT. These recorded data then compared with base line data

Statistical analysis

Data were analyzed using the statistical package for the social sciences (SPSS, version ٢٠) software.one way ANOVA test was used for parametric quantitative data between the ٣ groups. Independent sample t test was used for parametric quantitative data between ٢ groups. Paired sample t test was used for parametric quantitative data within each group. The level of significance P value significant if < ٠.٠٥.

Results

٢٠ eyes of ١٥ Patients with a mean age of ٦١.٧ ± ١.٧ years and mean duration of DM ١٢.٥ ± ٣.٢ years in the SDM laser group were enrolled in this study. None of the eyes were excluded from the study during follow-up. Demographic and baseline characteristics of the patients are illustrated in table ١.

Table١: Demographic and general characteristics of the patients

	(n=١٥)
Age Range Mean ± SD	 (٥٩-٦٥) ٦١.٧±١.٧
DM duration Range Mean ± SD	 (٨-٢٠) ١٢.٥±٣.٢
Sex Male Female	 ٣(٢٠٪) ١٢(٨٠٪)
Side Unilateral Bilateral	 ١٠(٦٦.٧٪) ٥(٣٣.٣٪)

The mean and the standard deviation of BCVA (in decimal) before and ٣ months after treatment summarized in table ٢ There was significant improvement in BCVA before treatment and ٣ months with P value <٠.٠٠١.Also the mean changes of BCVA improvement was ٣١ ± ٢٦.١٪.

Table ٢: illustrate baseline BCVA and ٣ months after treatment in group ١ and ٢ mean % of decrease in both groups

	(n=٢٠)
(١)BCVA pre Range Mean ± SD	(٠.٢٥-٠.٥٠) ٠.٤٣±٠.١
(٢)BCVA post Range Mean ± SD	(٠.٣٢-١) ٠.٥٦±٠.١٦
(٣)% increase BCVA Mean ± SD	٣١±٢٦.١
(٤)P value ***(pre vs post)***	<٠.٠٠١*

*: Significant level at P value < ٠.٠٥

The mean and the standard deviation of central subfield thickness of OCT before and ٣ months after treatment summarized in table ٣. There was significant improvement in central subfield thickness before treatment and ٣ months after treatment with P value <٠.٠٠١.Also the mean changes of central subfield thickness improvement was ٥.٨ ± ٤.٧٪.

Table ٣: illustrate OCT central subfield thickness at baseline and ٣ months after treatment.

	(n=٢٠)
(١)OCT pre Range Mean ± SD	(٢٨٣-٣٢٠) ٣٠٠.٧±١١.٨
(١)OCT post Range Mean ± SD	(٢٤٨-٣٠٠) ٢٨٣±١٢.٩
(٢)% decrease OCT Mean ± SD	٥.٨±٤.٧
(٣)P value ***(pre vs post)***	<٠.٠٠١*

: Significant level at P value < ٠.٠٥

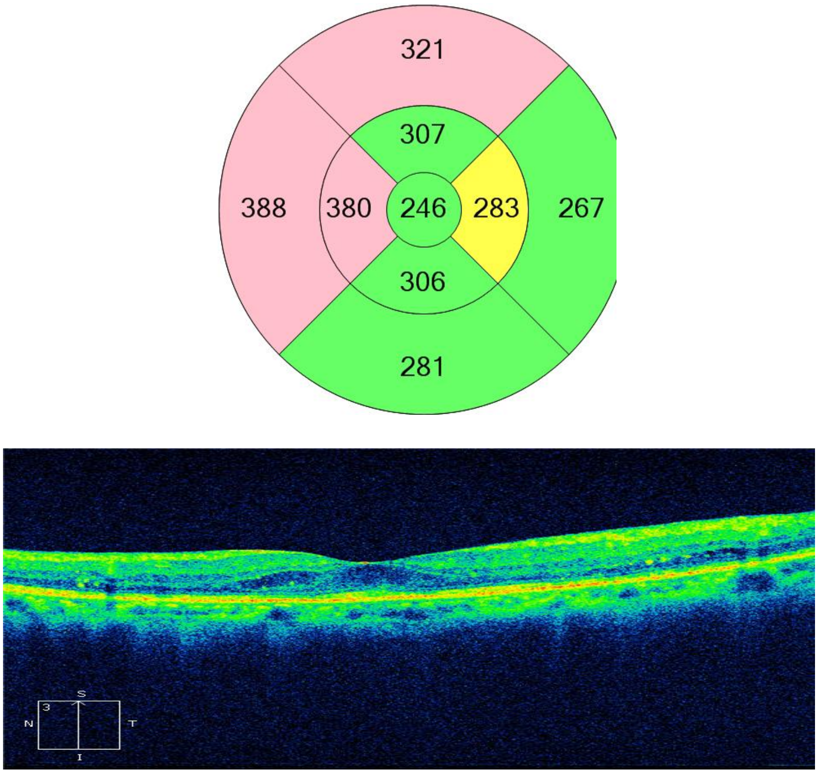

Figure ١: baseline OCT revealed diffuse retinal thickness and central subfield thickness ٢٤٦um

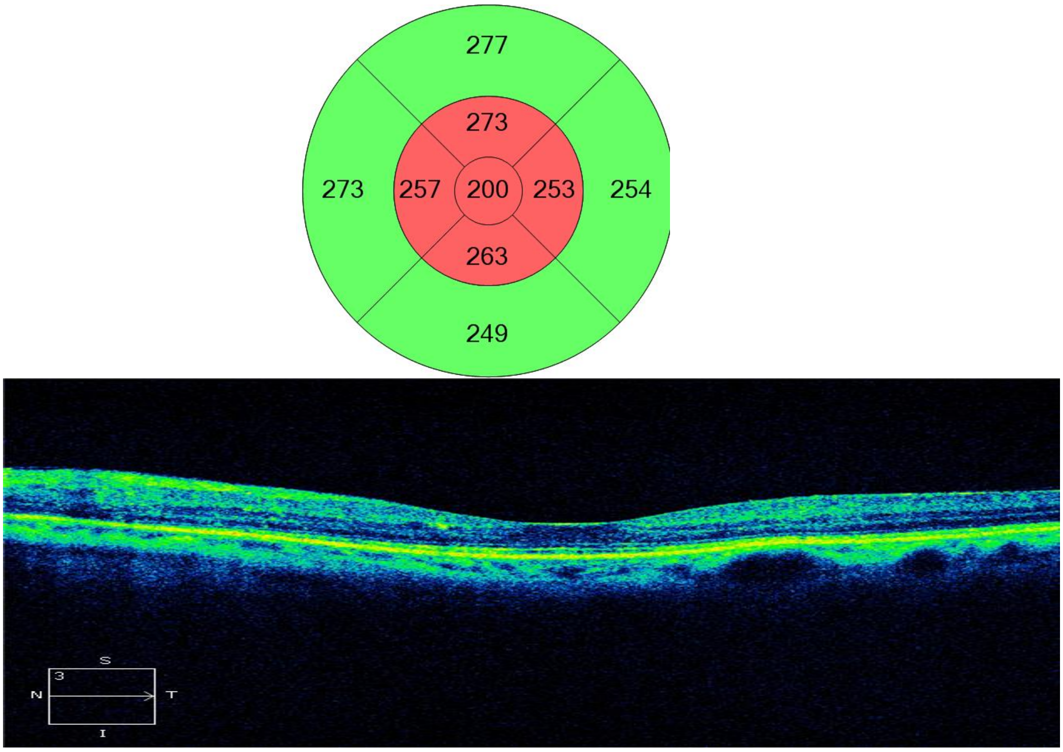

Figure ٢: three months after treatment by SDM laser, OCT revealed reduction of central subfield thickness to ٢٠٠ um.

Discussion

A quantity of randomized clinical trials proved the efficacy of intravitreal injection of ranibizumab for treatment of DME but due to its economic burden, complications of intravitreal injections (such as endophthalmitis, vitreous hemorrhage and IOP rise) and patients who refused the intravitreal injection, this study aimed to evaluate other treatment modality which is SDM laser that is believed that it produces the same clinical effects as the conventional laser photocoagulation in destruction of the RPEs and decreasing retinal hypoxia , in addition it has several advantages as cheap, no complications of intravitreal injection and has several advantages over conventional laser photocoagulation as it invisible retinal phototherapy with no retinal damage by laser and consequently there is no inflammatory response and loss of functional retina, well tolerated by the patients because of invisible infrared wavelengths and lesser pain sensation during laser procedure and much fewer complications than conventional laser . Laser photocoagulation of the enrolled patients was performed by a single surgeon. Laser parameters were a spot size of ٢٠٠ um, the power was ٤٠٠ mW and ٢٠٠ ms duration. All macular areas were treated including the fovea .Follow up did not encounter any treatment-related complications such as lens opacity, choroidal hemorrhage or retinal hemorrhage.

This study revealed that SDM laser significantly improved BCVA from ٠, ٤٣±٠, ٠١ at base line to ٠, ٥٦±٠, ١٦ after three months (P<٠,٠٠١) and the percent of increase was ٣١±٢٦.١٪. Also OCT central subfield thickness significantly reduced from ٣٠٠,٧±١١.٨ um at base line to ٢٨٣,١±١٢,٩um after three months (P<٠,٠٠١) and the percent of decrease was ٥,٨±٤,٧%. Significant improvement in BCVA due to significant reduction in macular edema. Results of this study are in accordance with the following studies.

The first report of treating patients with DME with SDM laser was by Friberg and Karatza. They reported a decrease of macular edema in ٨٧.٥٪ of treated eyes.[٤] Subsequently, Laursen et al., compared the efficacy of SDM laser and conventional argon laser in a randomized trial and reported that SDM laser was equally efficacious.[٥] A year later, Luttrull et al., reported that visual acuity was maintained in ٨٥٪ of eyes treated with SDM laser and that macular edema resolved in ٧٩٪ of patients.[٦] A subsequent report, again by Luttrull et al., provided OCT changes following SDM laser. They found that macular thickness did not change significantly in the first ٢ months after treatment. At ٣ months, however, reduction of macular thickness was observed.[٧] Figueira et al., included ٨٤ previously untreated eyes with CSME secondary to type ٢ DM that exhibited a best-corrected visual acuity of ٢٠/٨٠ or better. The patients were randomized to receive ٨١٠nm SMD photocoagulation or conventional argon laser treatment. Results showed no statistical difference in visual acuity at one-year follow-up however there was a trend for better vision in the SMD group. Additionally, there was no significant difference in contrast sensitivity or central retinal thickness between the two groups at any point during follow-up.[٨] Ohkoshi and Yamaguchi have reported early and rapid reduction of DME following treatment of Japanese patients with SDM laser.[٩] Luttrull and Sinclair evaluate the ability to treat the fovea directly with a micropulse laser in cases of centre involving DME. They included patients treated with a transfoveal SMD laser for fovea involving DME. They reported that no eye showed evidence of laser induced macular damage by any imaging means postoperatively. There were no adverse treatment effects. The logMAR VA and central foveal thickness improved during follow-up. They concluded that a transfoveal SMD laser was safe and effective for the treatment of fovea involving DME. This study has some limitations like a relatively small sample size, short follow-up duration and absence of macular visual function testing such as contrast sensitivity and microperimetry.[١٠]

Conclusions

SDM laser treatment of DME significantly improve BCVA and reduce OCT central subfield thickness ٣ months after treatment

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