Evaluation of mean retinal sensitivity using MP-1 microperimeter in patients with diabetic macular edema before and after laser photocoagulation treatment

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ABSTRACT

INTRODUCTION Diabetic macular edema (DME) is a common cause of visual acuity deterioration among patients with diabetes. Laser photocoagulation still remains the most common treatment of DME and diabetic retinopathy.

OBJECTIVES The aim of the study was to assess mean central retinal sensitivity among patients with DME before and after laser photocoagulation treatment. Additionally, we estimated the best-corrected visual acuity (BCVA) and retinal macular thickness before and after treatment.

PATIENTS AND METHODS The study included 30 patients (35 eyes with DME). The mean age was 61.9 ± 4.8 years. Insulin was administered in 22 patients and oral antidiabetics in 8. Laser photocoagulation in the macular area was performed in all patients using the Pascal laser. We measured the BCVA, mean central retinal sensitivity, and retinal thickness in the macula (divided into 9 segments). The measurements were performed before and at 1, 3, and 6 months after laser treatment. Central retinal sensitivity was assessed with the MP-1 microperimeter and macular thickness with optical coherence tomography (Stratus OCT).

RESULTS The statistical analysis did not reveal significant differences between BCVA and central retinal sensitivity in the study group before and after laser treatment. The analysis of the mean central retinal thickness showed a significant decrease in macular edema in the individual segments at 1, 3, and 6 months after photocoagulation.

CONCLUSIONS Photocoagulation of DME with the Pascal laser did not cause significant changes either in the BCVA or central retinal sensitivity. Laser treatment in patients with DME significantly reduced central retinal edema in most segments.

KEY WORDS diabetic macular edema, mean central retinal sensitivity, mean central retinal thickness, MP-1 microperimeter, optical coherence tomography
the retinal vessels are the ocular manifestation of systemic microvascular disease, while permanent hyperglycemia is the direct cause of retinal angiopathy.\textsuperscript{7,13,14}

Pathological changes in the macula within diabetic patients are called diabetic maculopathy. There are 3 types of diabetic maculopathy: edematous (diabetic macular edema [DME]), ischemic, or mixed.\textsuperscript{15}

DME may occur at any stage of the disease. It leads to a rapid deterioration of eyesight.\textsuperscript{16-18} It is characterized by the thickening of the macular area and is associated with impaired microvascular circulation. Endothelial damage, pericyte atrophy, and capillary dilatation result in the breakdown of the blood-retinal barrier, but also microaneurysms and hard exudate formation.\textsuperscript{19,20}

The type of macular edema depends on the degree of diabetic changes.\textsuperscript{9,21} Focal macular edema is characterized by the thickening of limited retinal area. Diffuse macular edema results from a diffuse leakage from the damaged capillaries and often occurs symmetrically in both eyes. Cystoid macular edema is a form of diabetic maculopathy that involves the middle of the macula, where fluid accumulates in the radially formed microcystes. It leads to severe visual acuity impairment. Ischemic maculopathy develops because of inadequate amount of oxygen in nonperfused areas. It leads to severe visual acuity impairment without visible changes in the eye fundus and only the fluorescein examination discloses ischemic areas within the macula.\textsuperscript{15,22} Mixed maculopathy involves both the ischemic and edematous lesions.\textsuperscript{15}

Recently, a distinction has been made between clinically significant and nonsignificant macular edema. The Early Treatment for Diabetic Retinopathy Study (ETDRS) defined the diagnostic criteria for clinically significant macular edema (CSME), which is an indication for laser photocoagulation treatment.\textsuperscript{9,15,16,20,21,23} The criteria for CSME are as follows: retinal thickening at or within 500 µm of the macular center; and/or hard exudates at or within 500 µm of the macular center if associated with the thickening of the adjacent retina; and/or a zone or zones of retinal thickening 1 disc area in size, at least part of which was within 1 disc diameter of the center.

The aim of laser treatment of the macula is to reduce retinal edema; however, it causes morphological changes in the spots of laser marks. The resulting scars may affect the retinal function.\textsuperscript{24} Other significant complications include scotomas, deterioration of central visual acuity, color vision impairment, and choroidal neovascularization. If laser energy is excessive, the Bruch’s membrane may rupture and cause subretinal fibrosis.\textsuperscript{10,14}

The main objective of the study was to determine the mean central retinal sensitivity before and after laser photocoagulation in patients with DME scheduled for laser treatment.

Additionally, we assessed the best-corrected visual acuity (BCVA) and retinal macular thickness.

**Patients and Methods** A total of 30 patients (35 eyes) were examined. All patients were recruited from the Department of Ophthalmology of the Silesian University of Medicine in Katowice, Poland, between 2009 to 2011.

The inclusion criteria were as follows: type 2 diabetes (duration >5 years) with CSME confirmed by fluorescein angiography, distance BCVA at least 5/50, age from 50 to 70 years.

The exclusion criteria were current inflammatory disease within the eye, distance BCVA less than 5/50, DME with vitreoretinal traction, high myopia (>–6.0 Dsph), proliferative diabetic retinopathy, current or previous vitreous hemorrhage, previous retinal laser photocoagulation, no clarity of optical media, intraocular surgery, diseases of retina other than diabetic retinopathy (retinal vein occlusion, glaucoma, etc.), duration of diabetes longer than 5 years, noncompliance.

The trial included 30 patients with CSME. Before inclusion, all patients underwent internal examination that assessed cardiac efficiency, blood pressure, mean hemoglobin A1c (HbA1c) level, and lipid metabolism. We also analyzed drug intake. A similar evaluation was conducted after 6 months.

Insulin was administered in 22 patients and oral antidiabetic drugs in 8 (glimepiride in 3; metformin and glitazones in 5 patients). Mean HbA1c levels at baseline were 7.5% ±0.8% (all patients). No significant differences were observed at 6 months either in diabetic treatment or HbA1c levels (mean HbA1c levels, 7.4% ±0.7%). Systolic blood pressure at baseline was 136 ±12 mmHg and diastolic blood pressure was 84 ±8 mmHg; at 6 months, the values were 138 ±15 mmHg and 86 ±10 mm Hg, respectively. The differences were not statistically significant. With regard to drug intake due to coexisting diseases (hypertension, cardiovascular disease, and blood lipid disorders), 21 patients were taking angiotensin-converting enzyme inhibitors, 26 acetylsalicylic acid (75 mg), 12 statins, 14 calcium channel blockers, and 15 indapamide. Drug intake was similar before and after treatment. Lipid metabolism did not change significantly.

The total of 35 eyes were examined (1 eye in 25 patients and both eyes in the remaining 5 patients). All patients underwent fluorescein angiography (obtained within the previous month), which confirmed CSME without ischemic components. All patients underwent Pascal laser treatment after complete ophthalmologic examination, including distance BCVA testing with a Snellen chart, intraocular pressure measurement, anterior segment and ocular fundus examination, microperimetry, and optical coherence tomography (OCT) (through dilated pupils). Ophthalmologic examination, microperimetry, and OCT were repeated at 1, 3, and 6 months of follow-up.

Retinal sensitivity was evaluated by the MP-1 microperimeter (Nidek Technologies, Italy). A microperimetric radial grid pattern was used for the trial group covering the central 12º of the macula, with starting standard attenuation (Goldmann III) and 45 points within.
The results, involving age, were reported numerically with colors and in decibels (dB). The results were reported as central retinal sensitivity in dB. This is the arithmetic mean of all measured thresholds in dB, complemented with the normative data (Figure 1).

The mean retinal thickness was measured using Stratus OCT (Carl Zeiss, Germany).

The scanning protocol used in the study was the Fast Macular Thickness program, which involves 6 radial cross-sectional B scans, each 6 mm long. Each B scan consists of 128 A scans of 1.9-second duration. A map is presented as a circle divided into 9 zones. According to the Early Treatment Diabetic Retinopathy Study (ETDRS), we can distinguish 1 central zone relating to the foveal thickness, 4 parafoveal zones as well superior, nasal, inferior, and temporal perifoveal zones (Figure 2).

Statistical analysis All data were analyzed with the Statistica software. We calculated the mean value, standard deviation, and median for measurable parameters (edema, BCVA, central retinal sensitivity). The Kolmogorov-Smirnov test was performed for normally distributed quantitative values. Because data showed abnormal frequency distribution, nonparametric tests were performed. The parameters between time profiles were compared with the Wilcoxon test.

RESULTS The statistical analysis did not reveal any significant differences in distance BCVA before laser treatment and at 1, 3, and 6 months of follow-up (Wilcoxon test Z, P; Figure 3). There were no significant differences in the mean central retinal sensitivity determined with microperimetry before laser treatment and at 1, 3, and 6 months of follow-up (Wilcoxon test Z, P; Figure 4).

To assess the effect of laser treatment on the retina in patients with CSME, we measured the degree of retinal edema in particular segments before and after treatment. The results are shown in Table 1. In the statistical analysis of the results of central retinal thickness measurement, we considered potential changes (increase or decrease of edema). The results are presented in Table 2.

Of note, the follow-up did not reveal a significant increase in macular edema in the analyzed segments, but the statistical analysis revealed a decrease of retinal thickness at 6 months. At 1 month, a significant decrease of retinal edema was observed (P = 0.01) in the parafoveal inferior segment (8) compared with the baseline.
values. At 3 months, a significant decrease of edema was observed in the central (1) \( (P = 0.03) \), parafoveal inferior (4) \( (P = 0.001) \) and parafoveal inferior (8) \( (P = 0.002) \) segments compared with the baseline values. At 6 months, in all segments except the perifoveal temporal segment, a significant decrease of retinal edema was detected compared with the baseline values \( (P = 0.75) \).

**DISCUSSION** DME is a common cause of visual acuity deterioration in diabetic patients and remains the leading medical problem. Laser photocoagulation is one of the oldest treatment techniques of diabetic retinopathy and DME. The ETDRS study\(^{31} \) showed that laser photocoagulation significantly decreases the risk of vision loss due to CSME.

We evaluated distance BCVA before and after laser treatment in patients with diabetes and confirmed CSME. No significant changes in the BCVA were observed during a 6-month follow-up.

Similar results were reported by Vujosevic et al.\(^{16} \) who assessed the BCVA in patients with macular edema before and after treatment either with argon laser or micropulse diode laser. During a 12-month follow-up of both groups, no significant differences in the BCVA were observed. Jain et al.\(^{24} \) also did not reveal any significant differences in the BCVA before and after treatment in patients with macular edema. They also used the Pascal laser and the follow-up was 4 months. Soliman et al.\(^{32} \) assessed the BCVA after photocoagulation with argon laser in patients with DME. No differences were observed in a 6-month follow-up. In conclusion, despite using different types of laser, all authors reported BCVA stabilization.

In our study, we also measured central retinal sensitivity using the MP-1 perimeter in patients with DME before laser treatment and at 1, 3, and 6 months and revealed no significant alterations.

Vujosevic et al.\(^{16} \) assessed central retinal sensitivity using MP-1 in patients with DME before and after treatment with argon laser photocoagulation and micropulse diode laser. They did not observe significant differences during a 9-month follow-up, but a significant increase in retinal sensitivity was reported at 12 months in the eyes treated with argon laser.

Hudson et al.\(^{33} \) evaluated central retinal sensitivity using the Humphrey’s perimeter in patients with CSME before and after argon laser treatment. Their study revealed a decrease in retinal sensitivity at 12 months of follow-up. A decrease after argon laser photocoagulation due to DME was also reported by Bandello et al.\(^{34} \) Central retinal sensitivity was determined with the Humphrey’s perimeter, and at 12 months a decrease at 10º of the macula was observed.

There have been only a few studies that assessed central retinal sensitivity with MP-1 in patients after laser treatment due to DME, which may explain the differences between the reported findings. The authors of the above studies\(^{11,20-23} \) determined retinal sensitivity using different methods. Therefore, we cannot unequivocally compare the results. There are a few methods to assess retinal sensitivity, but MP-1 seems to be the most accurate.\(^{36,37} \)

Another difference between the cited studies is the use of different types of lasers for photocoagulation. Most studies reported a decrease in central retinal sensitivity using standard argon laser,\(^{16,33-35} \) which causes greater damage compared with micropulse diode laser.\(^{16} \) We did not identify any studies that would use the Pascal laser for DME treatment.

The analysis of retinal thickness, involving segmental division, revealed a significant decrease of edema in 8 of 9 segments at 6 months of follow-up. Similar results were reported by Jain et al.\(^{24} \) They assessed central retinal thickness with Stratus OCT in patients with DME who underwent laser treatment with the Pascal laser and showed a significant decrease of macular edema at 4 months \( (P = 0.0049) \).

Kumar et al.\(^{38} \) showed a significant decrease of macular edema in patients with DME after photocoagulation treatment with the Pascal laser. Central retinal thickness was determined with Stratus OCT. They reported a decrease of macular edema after 6 weeks of treatment and a progressive decrease of edema at 12 and 18 weeks \( (P < 0.01) \).

**FIGURE 4** Mean central retinal sensitivity among patients with clinically significant macular edema before and after laser treatment (Wilcoxon test Z, \( P \))

Abbreviations: MCRS – mean central retinal sensitivity, others – see **FIGURE 3**
who underwent laser treatment. MP-1 measurements complement OCT and visual acuity examination. Macular morphology and diabetic-related changes assessed with OCT enable doctors to determine severity or treatment effects and should not be underestimated. Also, the use of MP-1 to assess central retinal function seems to be valuable. The evaluation of central retinal sensitivity within the macula provides information about macular function before and after treatment and also determines treatment effectiveness. Although we obtained satisfactory results, it is important to remember that laser photocoagulation is only a symptomatic treatment that slows the disease progression. This is why it is particularly important to control blood glucose levels (according to the Polish Diabetes Association) in order to prevent or limit complications.

The use of the Pascal laser for macular edema treatment helps stabilize visual acuity, does not affect central macular sensitivity, and has a positive effect on the decrease of macular edema. Diabetic patients should remain under ophthalmological care because immediate detection of diabetic changes in the eye fundus is needed to implement appropriate treatment strategies aimed at securing and retaining visual acuity as long as possible.

Soliman et al.\textsuperscript{33} reported changes in central retinal thickness in patients with DME after laser treatment. Macular edema was evaluated with Stratus OCT, involving a 9-sector division (as in our study): central (foveal), 4 parafoveal, and 4 perifoveal. The authors observed a significant decrease of foveal retinal thickness 1 month after treatment and later during a 4-month follow-up. Similar results were reported by Vujosevic et al.\textsuperscript{16} in patients with DME who were scheduled for laser treatment. Central retinal thickness was assessed with Stratus OCT and no significant decrease of retinal macular edema was reported at 1 year after treatment (\(P < 0.001\)).

Opposite results were reported by Fong et al.,\textsuperscript{39} who evaluated retinal thickness in the macula before and after argon laser treatment in patients with DME. Retinal thickness was determined with Stratus OCT, involving segmental division. During a 12-month follow-up, a significant decrease in retinal edema within the foveal and parafoveal segments was reported. The change was not statistically significant. In our study, we also noted a statistically significant decrease of retinal edema in the central and parafoveal segment at 6 months of follow-up.

Based on the available literature, we may assume that microperimetry provides valuable data on the macular function in patients with DME who underwent laser treatment. MP-1 measurements complement OCT and visual acuity examination. Macular morphology and diabetic-related changes assessed with OCT enable doctors to determine severity or treatment effects and should not be underestimated. Also, the use of MP-1 to assess central retinal function seems to be valuable. The evaluation of central retinal sensitivity within the macula provides information about macular function before and after treatment and also determines treatment effectiveness. Although we obtained satisfactory results, it is important to remember that laser photocoagulation is only a symptomatic treatment that slows the disease progression. This is why it is particularly important to control blood glucose levels (according to the Polish Diabetes Association)\textsuperscript{40} in order to prevent or limit complications.

The use of the Pascal laser for macular edema treatment helps stabilize visual acuity, does not affect central macular sensitivity, and has a positive effect on the decrease of macular edema. Diabetic patients should remain under ophthalmological care because immediate detection of diabetic changes in the eye fundus is needed to implement appropriate treatment strategies aimed at securing and retaining visual acuity as long as possible.

<table>
<thead>
<tr>
<th>Segment</th>
<th>n</th>
<th>Retinal thickness, µm</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>before</td>
</tr>
<tr>
<td>1. foveal</td>
<td>22</td>
<td>333 ± 71 (311)</td>
</tr>
<tr>
<td>2. parafoveal superior</td>
<td>22</td>
<td>357 ± 58 (334)</td>
</tr>
<tr>
<td>3. parafoveal nasal</td>
<td>17</td>
<td>371 ± 67 (340)</td>
</tr>
<tr>
<td>4. parafoveal inferior</td>
<td>16</td>
<td>378 ± 63 (369)</td>
</tr>
<tr>
<td>5. parafoveal temporal</td>
<td>20</td>
<td>360 ± 62 (336)</td>
</tr>
<tr>
<td>6. perifoveal superior</td>
<td>13</td>
<td>359 ± 67 (322)</td>
</tr>
<tr>
<td>7. perifoveal nasal</td>
<td>8</td>
<td>363 ± 41 (363)</td>
</tr>
<tr>
<td>8. perifoveal inferior</td>
<td>13</td>
<td>346 ± 55 (329)</td>
</tr>
<tr>
<td>9. perifoveal temporal</td>
<td>10</td>
<td>333 ± 35 (327)</td>
</tr>
</tbody>
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Data are presented as mean ± standard deviation (median).

<table>
<thead>
<tr>
<th>Segment</th>
<th>Retinal thickness, µm</th>
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<tr>
<td></td>
<td>before; 1 month</td>
</tr>
<tr>
<td>1. foveal</td>
<td>0.7; 0.49\textsuperscript{a}</td>
</tr>
<tr>
<td>2. parafoveal superior</td>
<td>0.38; 0.7</td>
</tr>
<tr>
<td>3. parafoveal nasal</td>
<td>1.48; 0.14</td>
</tr>
<tr>
<td>4. parafoveal inferior</td>
<td>1.29; 0.19</td>
</tr>
<tr>
<td>5. parafoveal temporal</td>
<td>0.09; 0.93</td>
</tr>
<tr>
<td>6. perifoveal superior</td>
<td>0.63; 0.53</td>
</tr>
<tr>
<td>7. perifoveal nasal</td>
<td>0.07; 0.94</td>
</tr>
<tr>
<td>8. perifoveal inferior</td>
<td>2.67; 0.01</td>
</tr>
<tr>
<td>9. perifoveal temporal</td>
<td>0.52; 0.6</td>
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\textsuperscript{a} Wilcoxon test (\(Z, P\))
Ocena czułości centralnej siatkówki za pomocą mikroperymetru MP-1 u pacjentów z cukrzycowym obrzękiem plamki przed laseroterapią i po niej

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SŁOWA KLUCZOWE

cukrzycowy obrzęk plamki, grubość centralna siatkówki, mikroperymetr MP-1, optyczna koherentna tomografia, średnia czułość centralna siatkówki

STRESZCZENIE

Cukrzycowy obrzęk plamki (diabetic macular edema – DME) jest częstą przyczyną obniżenia ostrości wzroku u pacjentów z cukrzycą. Fotokoagulacja laserowa jest nadal najczęstszą metodą leczenia DME i retinopatii cukrzycowej.

CELE

Celem badania była ocena średniej czułości centralnej siatkówki u pacjentów z DME przed zastosowaniem fotokoagulacji laserowej i po niej. Dodatkowo oceniano ostrość wzroku z najlepszą korekcją (best-corrected visual acuity – BCVA) oraz grubość siatkówki w plamce przed leczeniem i po nim.

PACJENCI I METODY

Badaniu poddano 30 pacjentów (35 oczu z cukrzycowym obrzękiem plamki). Średnia wieku wynosiła 61,9 ± 4,8 roku. U 22 pacjentów stosowano insulinoterapię, a 8 pacjentów leczono dostępnymi lekami przeciwcukrzycowymi. U wszystkich badanych wykonano fotokoagulację laserową okolicy plamki laserem Pascal. Oceniano BCVA, średnią czułość centralną siatkówki oraz grubość siatkówki w plamce z uwzględnieniem podziału na 9 segmentów. Badania wykonywano przed laseroterapią oraz miesiąc, 3 i 6 miesięcy po leczeniu. Czułość centralnej siatkówki badano za pomocą mikroperymetru MP-1, a grubość plamki za pomocą optycznej tomografii koherencyjnej (Stratus OCT).

WYNIKI

Analiza statystyczna nie wykazała znamienitych różnic pomiędzy wartościami BCVA i czułości centralnej siatkówki w badanej grupie pacjentów przed leczeniem i po nim. Analiza uzyskanych wyników grubości centralnej siatkówki wykazała istotne zmniejszenie obrzęku plamki w poszczególnych segmentach po upływie 1, 3 i 6 miesięcy od fotokoagulacji.

WNIOSKI

Fotokoagulacja cukrzycowego obrzęku plamki laserem Pascal nie powodowała istotnych zmian zarówno BCVA, jak i czułości centralnej siatkówki. Laseroterapia u pacjentów z DME istotnie zmniejszyła obrzęk centralnej siatkówki w większości segmentów.