PERIMETRIC LONG-TERM FOLLOW-UP OF DIABETIC CYSTOID MACULAR EDEMA AFTER LASER TREATMENT EXTENDED TO THE FOVEAL AVASCULAR ZONE

FRANCESCO MORESCALCHI, ENRICO GANDOLFO, STEFANO FORMENTI, SIMONA SANCASSANI and EMANUELE SCURI

Clinica Oculistica Università degli Studi di Brescia, Spedali Civili, Brescia, Italy

Introduction

Cystoid macular edema (CME) is due to polycystic expansion of the external granular and plexiform layer of the macula filled by serous exudate. The typical polycystic aspect of diabetic CME may be caused either by extra macular exudation or by leakage from the perifoveal capillaries. Grid or focal laser photocoagulation can improve the fluorangiographic aspect of CME even though this is not often effective in significantly improving visual acuity1-7. It is reported that CME may resolve spontaneously or fluctuate for months before causing severe loss of vision8. However, when visual acuity decreases to less than 0.6-0.5, an attempt at laser grid photocoagulation is indicated9,10.

A perifoveal laser grid extending up to the edge of the foveal avascular zone has been proposed to dry the cystoid spaces inside the macular area6-8. The aim of this study was to detect whether a perifoveal grid would improve visual function or prevent the visual loss caused by diabetic CME; to evaluate whether this laser treatment could lead to a significant decrease in retinal sensitivity in the macular area; and to assess the usefulness of automated perimetry in monitoring change in retinal function after a laser grid treatment.

Patients and methods

In 1996, 54 patients affected by CME were randomized to either a laser standard grid or to modified laser therapy extending close to the foveal area (perifoveal grid). Follow-up was conducted for a minimum of 12 months to a maximum of 36 months (28.5 ± 3.5 months).

Address for correspondence: Francesco Morescalchi, MD, Clinica Oculistica Università degli Studi di Brescia, c/o Spedali Civili, Piazzale Spedali Civili 1, 25125 Brescia, Italy
At the start of the study, all patients had good glycemic compensation (glycemia <170 mg/dl at the last two controls) and glycosylated hemoglobin of less than 10 mg/ml. Diastolic blood pressure was well controlled (<100 mmHg). Patients with renal failure requiring dialysis were excluded from the study. Sixty-six eyes of 54 patients (32 females and 22 males) aged from 34 to 75 years (mean 67.5) were still included in the study at the end of the follow-up. Thirty-eight patients had non-insulin-dependent diabetes mellitus (NIDDM) (18 were on insulin, 20 were controlled with oral hypoglycemic agents) and 16 had IDDM. The duration of diabetes averaged eight years (±20, range 5-32 years). All treated eyes had an initial visual acuity of ≥0.3 (0.47 ± 0.3). Thirty-two eyes were treated by a standard grid (Group A) and 34 by a perifoveal grid (Group B). The baseline examination included the following parameters: best corrected distance and near visual acuity; a fluorangiographic examination using 5 ml of 10% sodium fluorescein intravenously with late phase (>500 seconds) frames. Static threshold testing of the visual field was performed with the Octopus 101 perimeter using the M2 program in which central and paracentral sensitivity is tested using a pattern of 45 locations in the central 4° and 36 locations distributed between 4° and 9.5°. This grid is capable of detecting defects of 0.7° within the central 4°. Each threshold in every location was tested twice, and Goldmann stimulus size III (= 0.43°) was utilized.

An additional examination was performed with a custom program using Goldmann stimulus size I (= 0.18°), the retinal diameter of which is 54 μm. This new program tested 45 locations in the central 5° and 36 locations between 5° and 18° of the visual field. The photometric correspondence between stimulus size III and stimulus size I requires increasing the luminance by a factor of 10, so the average threshold values should be at least 10dB lower.

On the fluorangiographic photograms, 10° of visual field corresponded to a retinal area of two disc diameters centered on the macula. To correlate the scotomas to the laser scars, the visual fields were inverted and superimposed on the retinal area.

Statistical analysis was performed using the two-sample Student t test to show differences between the visual acuity before and after the treatment, and using the Wilcoxon matched-pair signed ranks test to evaluate the statistical differences between the perimetric data.

All eyes were treated using a coherent argon dye laser (514 nm), using a Mainster or a Volk ‘area centralis’ lens, converging the entry beam to obtain the smallest diameter of the spots. All treatments were performed by the same ophthalmologist (ES) who used 50-150 μm spots, with an exposure time of 0.2 seconds and 200-250 mW of power. In Group A, argon laser therapy consisted of (1) focal photocoagulation of the microaneurysms and dilated capillaries that displayed focal fluorescein leakage near the macula on angiography, and (2) a grid of two or three rows of spots regularly applied around the area of CME. In Group B, treatment was extended into the perifoveal region (inside the edge of the avascular zone). Light burns were performed in order to create a mild fading of the retina; an average of 41.3 (± 14.5) spots per eye were used. In the perifoveal zone, four to eight spots of 50 μm were converged in order to obtain the minimum diameter inside the FAZ, 150-200 μm away from the fovea.

Results

A comparison of visual improvement, visual loss, and reduction-elimination of macular edema showed statistically significant differences between the groups. At 28 months’ follow-up, fluorescein angiograms showed that 14 (43%) of 32 eyes treated with a standard laser grid (Group A) and 22 (61.7%) of 34 eyes treated with a perifoveal grid (Group B) had
Perimetric long-term follow-up of diabetic cystoid macular edema

(reduction or elimination of CME. In Group B, CME resolved in 17 (50%) and decreased in five (11.7%) eyes. In Group A, only a decrease in CME was observed. CME remained unchanged in 18 (56%) of 32 eyes treated with a standard grid and in 12 (35.2%) of 34 eyes treated with a perifoveal grid.

The results are summarized in Table 1. The changes in visual acuity after 28 months were significant in Group B, improving from 0.48 ± 0.27 (pretreatment) to 0.65 ± 0.3 (post-treatment, t test: p=0.019), while it was not statistically significant in Group A, ranging from 0.47 ± 0.25 (pretreatment) to 0.49 ± 0.5 (post-treatment, p=0.81). Visual acuity improved in six (18.7%) of 32 eyes in Group A and in 12 (35.2%) of 34 eyes in Group B. Visual acuity remained stable in ten (31.2%) of 32 eyes in Group A and in 15 (44.1%) of 34 eyes in Group B. There was a significant improvement in the subjective (assessed by the patient) and objective capacity to read fluently, despite distance acuity remaining unchanged. Visual acuity worsened in 16 (50%) of 32 eyes in Group A and in seven (20.5%) of 34 eyes in Group B.

Perimetric findings

The typical visual field of patients with CME was characterized by a relative central scotoma with clusters, varying in depth and size, scattered all over the paracentral area, corresponding to thickened retina, exudates or hemorrhages. Perimetric data generally showed a depression of the foveal threshold, as well as abnormal values of the mean sensitivity, the mean defect and the loss variance. Twenty-eight months after the grid treatment, the effect on the sensitivity of the central 10° of the visual field was statistically significant in Group B (Table 2). In Group B there was both a significant improvement of the foveal threshold (average +1.72dB; p<0.06) and the mean sensitivity (average +3.74dB; p<0.06) and a decrease of both the mean defect (average -2.15; p<0.06) and the loss variance (average -5.11dB; p<0.06).

The positive effect of the laser treatment was more evident after 24 months than after 12 months. Average sensitivity variation was higher than long-term fluctuation. It was noteworthy that the pattern of the scotomas did not change after the laser treatment. In a significant group of patients, no scotomas could be detected in the paramacular area, even though many laser scars were evident close to the fovea. In almost all patients, only mild
relative scotomas and no absolute defects could be detected in the central 5° of the visual field after treatment. This was surprising in patients where the laser scars occupied 15-30% of the retinal area around the macula. The width of the laser scars on the photograms ranged between 300 and 75 \( \mu m \) (average 120 \( \mu m \)) and remained unchanged during follow-up. The retinal dimension of Goldmann stimulus III is 129 \( \mu m \), so we decided to test the macular area with the custom program using Goldmann stimulus I, the diameter of which is 54 \( \mu m \). This procedure detected a larger amount of relative defects than the M2, proving to be more specific. However, the number of absolute defects remained low. A questionnaire given to the patients did not reveal the subjective awareness of the small paracentral scotomas created by the laser.

**Discussion**

The hypothetical laser effect could be due to closure of leaking intraretinal microvascular anomalies, stimulation of RPE metabolism and mechanical elimination of the edema caused by the scars. Regeneration of the RPE or the release by these cells of a diffusible factor inducing endothelial reparation can promote intraretinal fluid absorption\(^{17,18}\). Also, a mechanical effect could be supposed, since multiple regular scars may thin the retina, reducing the space available for fluid accumulation. A laser grid not extending over 500 \( \mu m \) from the fovea did not cover the CME area, and gave uncertain results. Conclusions to be drawn from these data include:

- patients treated with the perifoveal grid seemed to maintain or improve their visual acuity better than patients treated with a standard grid after long-term follow-up;
- small and isolated laser scars apparently did not produce a subjective effect on visual perception. Treated subjects usually did not perceive their visual defects, possibly because of a filling-in phenomenon which consists of visual input from areas surrounding the scotoma invading the defect area;
- it was difficult to detect the grid scotomas after accurate visual field examination. Using either Goldmann stimulus sizes III or I, it was rarely possible to demonstrate the absolute defects caused by the laser in the central 5°. Two explanations are possible: small absolute scotomas may not be detected because of the larger diameter of the perimetric stimulus or

<table>
<thead>
<tr>
<th>Table 2. Static perimetry findings (dB)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before treatment</strong></td>
</tr>
<tr>
<td><strong>Visual field modification in Group A</strong></td>
</tr>
<tr>
<td>MS 17.2 ± 8</td>
</tr>
<tr>
<td>MD 10.9 ± 6</td>
</tr>
<tr>
<td>LV 31.9 ± 22.3</td>
</tr>
<tr>
<td>SF 2.38 ± 0.3</td>
</tr>
<tr>
<td>Fovea 20.9 ± 6.2</td>
</tr>
<tr>
<td><strong>Visual field modification in Group B</strong></td>
</tr>
<tr>
<td>MS 19.24 ± 5.64</td>
</tr>
<tr>
<td>MD 9.44 ± 4.86</td>
</tr>
<tr>
<td>LV 22.05 ± 13.65</td>
</tr>
<tr>
<td>SF 2.3 ± 0.6</td>
</tr>
<tr>
<td>Foveal threshold 22.52 ± 7.5</td>
</tr>
</tbody>
</table>
inadequate eye fixation; retinal or cortical receptive fields may be enlarged. A significant increase of relative defects was evident using Goldmann stimulus size I. In our opinion Goldmann stimulus size I was more effective and specific in detecting the central 5° of the visual field;

– after two to three years of follow-up, no enlargement of the laser scars was evident in the perifoveal area;
– perimetry showed a gradual increase of mean sensitivity and of foveal threshold and a decrease in loss variance and of mean defect after the laser grid treatment that apparently did not change the pattern of the scotomas and had a stabilizing effect on the visual field. Other authors reported that laser grid treatment with very crowded laser spots (200-500 per treatment) could be followed by significant drop in central sensitivity.

The improvement of the foveal threshold in Group B was well correlated with the increased visual acuity and reading ability noted by many subjects after the treatment. The same phenomenon has already been observed by other authors.

In conclusion, the perifoveal laser grid had a positive effect on increasing visual performance without worsening the quality of vision. It should not be delayed in patients whose visual acuity is not yet severely impaired. This treatment should only be performed by expert, well-trained ophthalmologists, in order to lower the risks involved in foveal treatment and excessive laser power, which may cause paracentral laser scotomas, subretinal neovascularization and progressive enlargement of laser scars to occur.

References