Original Article/นิพนธ์ต้นฉบับ

การศึกษาเชิงปริมาณในการวัดขนาดความหนาของจุดรับภาพโดยใช้เครื่อง Optical Coherence Tomography (OCT) ในผู้ป่วยโรคเบาหวานที่มีภาวะจุดรับภาพบวมน้ำ หลังจากได้รับการรักษาโดยเลเซอร์ที่บริเวณจุดรับภาพ

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาถึงผลการยิงเลเซอร์ ต่อการรักษาภาวะจุดรับภาพบวมน้ำในผู้ป่วยโรคเบาหวานเข้าจอประสาทตาในด้าน anatomical success และ functional success

วิธีการ: ทำการศึกษาแบบ Prospective interventional clinical study ในผู้ป่วย 30 คน (33 ตา) ที่ได้รับการวินิจฉัยว่าเป็นโรคเบาหวานเข้าจอประสาทตาที่มีภาวะ diffuse macula edema (ตาม criteria ของ Early Treatment Diabetic Retinopathy Study, ETDRS) และได้รับการรักษาโดยการเลเซอร์บริเวณจุดรับภาพซึ่งจะได้รับการตรวจตาเพื่อประเมินระดับสายตาและวัดความหนาของจุดรับภาพด้วย optical coherence tomography (OCT) ก่อนเข้ารับการรักษาและหลังได้รับการยิงเลเซอร์ที่ 1, 3, และ 6 เดือน ตามลำดับ

ผลการศึกษา: ผู้ป่วยที่เข้ารับการรักษามีอายุเฉลี่ย 58.9±8.4 ปี ค่าเฉลี่ยของระดับสายตาที่ระยะมองไกลโดยใช้ ETDRS charts เพิ่มขึ้นจาก 31.5±14.7 (ช่วง 3-55) ก่อนการรักษา เป็น 35.2±14.8 (ช่วง 5-55) (P=0.137), 37.2±16.5 (ช่วง 5-65) (P=0.035), 38.6±15.6 ตัวอักษร (ช่วง 5-60) (P = 0.005) หลังจากรับการรักษาแล้ว 1 เดือน, 3 เดือน, 6 เดือน ตามลำดับ หลังการรักษา 6 เดือนไปแล้ว พบว่า 18 ตา (ร้อยละ 54.5) มีระดับสายตาที่ดีขึ้นมากกว่าหรือเท่ากับ 2 แถว 13 ตา (ร้อยละ 39.4) ไม่มีการเปลี่ยนแปลง หรือเปลี่ยนแปลงเพียง 1 แถว 2 ตา (ร้อยละ 6.1) มีระดับสายตาลดลงมากกว่าหรือเท่ากับ 2 แถว ค่าเฉลี่ยความหนาของจุดรับภาพหลังการรักษาลดลงอย่างมีนัยสำคัญทางสถิติจาก 356.7±165.3 ไมครอน เป็น 329.6±145.6 (P=0.026), 317.8±141.6 (P=0.013), 292.1±126.7 (P<0.001) ที่ 1 เดือน 3 เดือน และ 6 เดือนตามลำดับ ทั้งนี้ 9 ตาจาก 33 ตา มีจุดรับภาพบวมน้ำมากขึ้นอีกครั้งหลังการเลเซอร์ที่จุดรับภาพ ในจำนวนนี้มี 3 ตาที่ต้องรักษาโดยการเลเซอร์บริเวณจุดรับภาพซ้ำใหม่ โดยรวมหลังการรักษาไปแล้ว 6 เดือน ความหนาเฉลี่ยของจุดรับภาพจะลดลงจากก่อนรักษาร้อยละ 18.1 (-64.6 ไมครอน) ผู้ป่วย 27 ตา มีความหนาของจุดรับภาพลดลง ในจำนวนนี้ 14 ตา (ร้อยละ 51.9) มีระดับสายตาที่ดีขึ้น 11 ตา (ร้อยละ 40.7) ไม่มีการเปลี่ยนแปลงของระดับสายตา หรือมีระดับสายตาที่เปลี่ยนแปลงเพียง 1 แถว 2 ตา (ร้อยละ7.4) มีระดับสายตาแย่ลง

สรุป: การรักษาภาวะจุดรับภาพบวมน้ำจากเบาหวานขึ้นตาโดยวิธีการเลเซอร์ที่จุดรับภาพ พบว่าสามารถทำให้จุดรับภาพยุบบวมลง และระดับสายดีขึ้นอย่างมีนัยสำคัญทางสถิติ แต่ไม่พบความสัมพันธ์ระหว่างขนาดความหนาของจุดรับภาพ กับระดับสายตาที่เปลี่ยนแปลงไป และพบว่า OCT เป็นเครื่องมือที่มีประโยชน์อย่างมากในการตรวจและติดตามผลการเปลี่ยนแปลงของจุดรับภาพหลังการรักษาด้วยเลเซอร์ นอกเหนือไปจากการประเมินระดับสายตา **จักษุเวชสาร 2551; กรกฎาคม-ธันวาคม 22(2): 97-103.**

ภาควิชาจักษุวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

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Original Article/นิพนธ์ต้นฉบับ

The Quantitative Assessment of Macular Thickness Using OCT After Grid Laser Treatment in Diabetic Macular Edema

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Abstract

Purpose: To evaluate the clinical outcome of macular grid laser photocoagulation in the treatment of diffuse diabetic macular edema and improving visual acuity compare to anatomical improvement by OCT.

Methods: In this prospective study included 30 consecutive patients (33 eyes) who were treated by macular grid laser photocoagulation for diffuse diabetic macular edema. Examinations that included slit-lamp examination, assessment of visual acuity and central macular thickness (CMTs) using optical coherence tomography (OCT) were performed pre-treatment and at 1 month, 3 and 6 months after treatment

Results: Mean age of the patients was 58.9±8.4 years. Mean best-corrected visual acuity (BCVA) for distance (using ETDRS charts) improved from 31.5±14.7 (range, 3-55) pretreatment to 35.2±14.8 (range, 5-55) (P=0.137), 37.2±16.5 (range, 5-65) (P=0.035), 38.6±15.6 (range, 5-60) (P = 0.005) letters at 1 month, 3 months, 6 months after treatment. Six months after treatment, eighteen (54.5%) eyes improved in visual acuity by two or more lines. Thirteen (39.4%) experienced no change, or changed by only one line; two eyes (6.1%) experienced a decrease in visual acuity by two or more lines. Mean central macular thickness decreased significantly from 356.7±165.3 pre-treatment to 329.6±145.6 (P=0.026), 317.8±141.6 (P=0.013), 292.1±126.7, (P<0.001) microns at 1 month, 3 months and 6 months after treatment respectively. Nine of 33 eyes had recurrence macular edema and 3 eyes were repeated grid laser treatment at 1 month after the first treatment. After 6 months of grid treatment, the mean foveal thickness showed 18.1% (-64.6 μm) reduction from the initial value. Twenty-seven eyes that has decreased central macular thickness, fourteen (51.9%) eyes improved in visual acuity, eleven (40.7%) experienced no change, or changed by only one line. two eyes (7.4%) experienced a decrease in visual acuity.

Conclusion: Grid laser treatment in diabetic macular edema led to a significant improvement in mean macular thickness confirmed by OCT and visual acuity in some patients with diabetic macular edema. These findings suggest that quantitative retinal thickness measurement provides an objective assessment of the degree of macular edema and can be useful for monitoring the efficacy of grid laser treatment in reducing the thickening and relating the latter to visual outcome. **Thai J Ophthalmol 2008; July-December 22(2): 97-103.**

Keywords: central macular thickness, optical coherence tomography (OCT), grid laser, diabetic macular edema

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Introduction

Macular edema is recognized as the most common cause of vision loss in diabetic eyes.[1-2] Macular edema is clinically significant, as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol, if retinal thickening or hard exudates associated with adjacent retinal thickening is observed within 500 μm of the center of the foveal avascular zone.[3] Reports from the ETDRS indicated that focal laser grid pattern photocoagulation for clinically significant macular edema was effective in reducing the risk of progressive visual loss in 50% of patients with diabetes.[3-5]

The mechanism causing the resolution of the edema after laser treatment is still debated. Laser treatment could open new pathways for metabolic exchange between the subretinal space and choriocapillaries by altering the barrier function of the retinal pigment epithelium, or grid pattern photocoagulation might improve the malfunctioning retinal pigment epithelium cells that are unable to maintain an effective outer blood-retinal barrier.[6] Another possible explanation is that grid pattern photocoagulation simply destroys the population of photoreceptors, which are high oxygen consumers and need adequate retinal blood flow, and the elimination of them leads to an increase in the level of inner retinal oxygen, a reduction of retinal blood flow, and vascular leakage.[7,13,19]

Objectives

The purpose of this study was to evaluate the clinical outcome of macular grid laser photocoagulation in the treatment of diffuse diabetic macular edema which included anatomical and functional success rate. Before and after the treatment, visual acuity by ETDRS chart, and retinal thickness by optical coherence tomography (OCT) were measured to estimate the efficacy of this treatment with a follow-up time of 6 months.

Patients and Methods

In this prospective interventional clinical study, 33 eyes of 30 consecutive patients with diabetes who had clinically significant macular edema were studied between March 2006 and December 2006. Fourteen patients were women and 16 were men. Three patients had bilateral and 27 had unilateral diffuse diabetic macular edema (19 right eyes and 8 left eyes). Patients' ages ranged from 43 to 82 years with a mean of 58.9±8.4 (mean±standard deviation [SD]) years. (Table 1) The possible merits and risks of treatment were explained to the patients, and an informed consent was obtained before inclusion in the study. Institutional Review Board approval and Research Ethics Committees, Faculty of Medicine Research Fund, Chiangmai University was required for this study.

The onset of diffuse diabetic macular edema ranged from 1 week to 12 months with a mean of 6.7±5.8 months. (Table 1)

Table 1. Baseline Demographic Data of 30 Patients in the study

	Laser Treatment
Total no.of eyes	33
No. of male patients	16 (53.3%)
No.of phakic eyes	29 (87.9%)
Duration of DME (mo) (SD)	6.7±5.8
Mean age (yrs) (SD)	58.9±8.4

DME = diabetic macula edema; SD = standard deviation

All of the patients had no history of panretinal photocoagulation and grid laser for macular edema before this study. Patients who had subfoveal exudates, initial examination macular edema less than 200 μm, severe diffuse macular edema, tractional component and who had undergone intraocular sur-

gery within 3 months prior to the beginning of this study were excluded.

After informing the patients of the purpose of this study and the possible outcomes, informed consents were obtained from all patients prior to the intervention.

All patients received a comprehensive ocular examination before and 1, 3, 6 months after treatment. Diffuse diabetic macular edema was defined as ETDRS criteria. Indirect ophthalmoscopy and slit-lamp biomicroscopy of the posterior segment with a +78 D non-contact lens (Volk, Mentor, OH) were performed to establish the presence of diffuse diabetic macular edema. Fundus photographs and optical coherence tomography (OCT) were taken prior treatment and 1, 3, 6 months after the treatment.

The best-corrected visual acuity (ETDRS letters) on a standard ETDRS chart, the foveal thickness by OCT scanner (Zeiss-Humphrey Systems, Dublin,CA,USA), were determined at prior treatment and 1, 3, 6 months after the treatment. Eyes were classified as improved (final visual acuity improved by more than 2 lines), unchanged (final visual acuity change within 2 lines), or worsened (final visual acuity decreased by more than 2 lines).

OCT images for determining the thickness of the central macular region were obtained by making vertical and horizontal scans through the fovea, and the average foveal thickness of the two images was taken as the foveal thickness. The thickness was determined by measuring the distance between the vitreoretinal interface and the anterior boundary of the red reflective layer corresponding to the retinal pigment epithelium. The thickness of vertical and horizontal axis were within 10 μm in all eyes. According to previous reports, retinal thickness by OCT measurement had the reproducibility of ±5% to ±6%.[8,14,18] Thus, retinal thickness was altered more than 10% from its original thickness (at the initial measurement), defined as an increase or decrease of the thickness or otherwise unchanged.

Patient Characteristics

Grid pattern laser treatment was performed by two experienced ophthalmologists. The spots were 100 μm in size, non-confluent, and placed around the fovea. The mean power used was 112.0±24.1 (range, 80-150) mW, and the mean spot numbers was 98.5±25.9 (range, 49-145) spots. No laser spots were placed within 500 μm of the center of the fovea. Double frequency neodymium: yttrium-aluminium-garnet laser (Laserex Technologies, SA, Australia) was used and a gray-white appearance of the retina was produced. Each spot was produced by 100-150 mW, duration 0.1 seconds. Topical anesthesia was used in all cases.

Statistical Analyses

The statistical significance of the differences between the pre and post-treatment data were assessed by Friedman test and Wilcoxon Signed Rank test (non-parametric) and repeated ANOVA (para-metric).

Results

One month after treatment, only 8 eyes had improved visual acuity, 24 had unchanged visual acuity, and 1 had worse visual acuity. Three months after treatment, 12 eyes had improved, 18 remained the same, and 3 had worsened. Six months after treatment, 18 eyes had improved, 13 remained the same, and 2 had worsened. The initial mean best-corrected visual acuity (BCVA) for distance (using ETDRS charts) was 31.5±14.7 letters (range, 3-55). Six months after treatment, the mean BCVA had improved to 38.6±15.6 letters (range 5-60), an improvement of 7.1±0.9 letters. Statistically, there was a significant difference of BCVA between the initial

Table 2. Visual acuity and foveal thickness values before treatment and during the 1st, 3rd, and 6th months of treatment

	Mean BCVA (letters) Using ETDRS charts	P value	Mean central macular thickness (micron)	P value
Initial	31.5 +/- 14.7		356.7 +/- 165.3	
1 month.	35.2 +/- 14.8	NS	329.6 +/- 145.6	0.026**
3 months.	37.2 +/- 16.5	0.035*	317.8 +/- 141.6	0.013**
6 months.	38.6 +/- 15.6	0.005*	292.1 +/- 126.7	<0.001**

* Repeated ANOVA.

** Wilcoxon Signed Rank Test

and the final measurements. (P=0.005). (Table 2)

At the initial examination, the mean foveal thickness in all 33 eyes was 356.7±165.3 μm., 329.6 +/- 145.6 (P=0.026), 317.8 +/- 141.6 (P=0.013), 292.1 +/- 126.7 at 1 month, 3 months and 6 months after treatment. The foveal thickness decreased in 23 eyes by 1 month after treatment and 22 eyes by 3 months after treatment. The difference between the visual acuity was no longer significant at 1 month because of the recurrence of macular edema in 9 of 33 and 3 of 9 eyes had repeated grid laser treatment at 1 month after the first treatment. At 6 months, twenty-seven eyes that had decreased central macular thickness, fourteen (51.9%) eyes improved in visual acuity, eleven (40.7%) experienced no change, or changed by only one line, two eyes (7.4%) experienced a decrease in visual acuity. Six months after treatment, the mean foveal thickness in all eyes was 292.1±126.7 μm, which corresponded to a 18.1% (-64.6 μm) decrease. Statistically, there was a significant difference in foveal thickness between the initial and the final measurements (P <0.001). (Table 2)

Discussion

The beneficial effects of grid pattern photocoagulation in reducing visual loss in patients with diffuse diabetic macular edema have been reports.[3,9] Our results showed that the visual acuity in 31 of 33 eyes (93.9%) with diffuse diabetic macular edema was maintained or improved for at least 6 months after grid pattern photocoagulation. These results confirmed the usefulness of grid pattern treatment for diffuse diabetic macular edema.

The macular thickness was decreased in 26 of 33 eyes (78.8%). With the use of OCT, the mean foveal thickness of eyes with diffuse diabetic macular edema has been reported to be 415 μm[8] and 368 μm[10] which is significantly thicker than the mean foveal thickness of 147 μm in normal subjects.[8] In our subjects with diffuse diabetic macular edema, the mean foveal thickness was 356.7±165.3 μm before treatment, which was comparable to the thickness reported earlier.[8] The mean thickness was reduced to 292.1±126.7 μm at 6 months after treatment, indicating a significant improvement but still an incomplete recovery of the macular edema. However, "clinically significant macular edema" represents a relatively late, severely advanced pathological state, and the retinal swelling must exceed 30% to 50% of the normal thickness before it can be detected.[11] At that point, there is already significant cellular injury.

Thus in our study, 82% decreases from the initial foveal thickness indicated that this treatment is effective. Twenty-seven of 33 eyes that has decreased central macular thickness, 51.9% eyes improved in visual acuity. The visual outcome after grid pattern photocoagulation was not correlated with

either the initial visual acuity or the initial retinal thickness. The mechanism of this positive correlation between the initial mean deviation and visual improvement has not been clarified. As previously discussed by some investigators,[6,7,20-24] the mechanism of grid pattern photocoagulation might be an opening of new pathways of the retinal pigment epithelium barrier to allow fluid transportation between the retina and choriocapillaries, a decrease in the population of photoreceptors to reduce the demand of oxygen, leading to the reduction of blood flow, or both and having severe damage to the retina; thus it is possible that there is no improvement of visual function even if the macular edema is improved.

Significant abnormalities of macular function have been found in eyes with clinically significant macular edema even when the visual acuity was normal, and none of the functions were normalized by the laser treatment.[12] This unusual situation can also sometimes be found in patients who have undergone photocoagulation and claim an improvement in their vision despite the absence of a recordable change in visual acuity. Thus, it is difficult to judge both the subjective and objective reports of the improvement of visual function before and after treatment.

We recognize that our study did not have adequate controls for statistical comparison, but more than 54.5% (18 of 33) of the patients stated their satisfaction with their visual function. We conclude that grid laser treatment in diabetic macular edema led to a significant improvement in mean macular thickness confirmed to OCT and visual acuity in patients with diabetic macular edema. These findings suggest that quantitative retinal thickness measurement provides an objective assessment of the degree of macular edema and can be useful for monitoring the efficacy of grid laser treatment in reducing the thickening and relating the latter to visual outcome.

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