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Role of 532 nm transfoveal subthreshold micropulse laser in non-resolving central serous chorioretinopathy with subfoveal leaks

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Abstract

Purpose: The purpose of this study was to evaluate the role of 532 nm transfoveal subthreshold micropulse laser in non-resolving central serous chorioretinopathy with subfoveal leak.

Methods: A retrospective chart analysis of 23 eyes of 21 patients with central serous chorioretinopathy was performed. Inclusion criteria include vision loss ⩾3 months and focal subfoveal leak on fluorescein angiography. Exclusion criteria include prior treatment for central serous chorioretinopathy and chronic central serous chorioretinopathy. All eyes were treated with 532 nm subthreshold micropulse laser (5% duty cycle). Visual acuity score, contrast sensitivity, autofluorescence, spectral domain optical coherence tomography, and fundus fluorescein angiography were assessed at baseline, 1, 3, 6 months.

Results: Average visual acuity score (letters) improved from 66.0 ± 8.51 (baseline) to 71.35 ± 8.48 (1 month, $p < 0.01$), 77.30 ± 11.34 (3 months, $p < 0.01$), 80.17 ± 9.30 (6 months, $p < 0.01$). Contrast sensitivity improved from 0.75 ± 0.30 to 1.30 ± 0.37 ($p < 0.01$) at 6 months. Two eyes needed rescue laser at 3 months followed by photodynamic therapy at 6 months; two eyes needed rescue laser at 6 months.

Conclusion: The 532 nm subthreshold micropulse laser is safe in non-resolving central serous chorioretinopathy with subfoveal leaks.

Keywords: central serous chorioretinopathy, micropulse laser, subfoveal leak, transfoveal

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Introduction

Central serous chorioretinopathy (CSC), an idiopathic disease that is more prevalent in middle-aged men, is characterized by serous macular detachment often found in association with retinal pigment epithelium (RPE) detachment. Stress and corticosteroid intake are well-known precipitating factors. Most of the cases resolve spontaneously within 3 or 4 months with good visual prognosis. Considerable visual impairment occurs if the subretinal fluid (SRF) persists for more than 3 months.

Focal laser photocoagulation of a focal leak on fundus fluorescein angiography (FFA), that is away from the foveal avascular zone, has been the conventional treatment of a non-resolving CSC. However, conventional laser photocoagulation cannot be applied in subfoveal and juxtafoveal leaks, as it carries the risk of central or paracentral scotomas, accidental foveal burn, and choroidal neovascularization. Subthreshold laser therapy and photodynamic therapy (PDT) are presently well-accepted and widely used therapy modalities in the treatment of CSC, and focal conventional laser is almost obsolete. PDT has its inherent risk of RPE atrophy, choroidal neovascularization, and choriocapillaris ischaemia, and is an expensive procedure.[1]

Unlike conventional laser, micropulse laser delivers short bursts of laser (on time) separated by pauses (off time). According to the selected duty cycle, the laser stays on only 5% to 15% of the

time, thus generating less heat and preventing build-up of thermal heat with subsequent less damage to the retina than continuous-wave photocoagulation. Subthreshold micropulse (STMP) laser emission without a visible burn endpoint appears to reduce the risk of structural and functional retinal laser damage, allowing treatment of foveal lesions without post-laser scotomas.[2]

STMP laser has been successfully used for diabetic macular edema.[3–5] In 2003, Bandello and colleagues[6] were the first to propose subthreshold diode micropulse (SDM) photocoagulation for the treatment of CSC, showing positive results in a series of five cases. Ricci and colleagues[7] showed that SDM can provide therapeutic benefits similar to those obtainable with standard-threshold continuous-wave laser photocoagulation, but without causing discernible chorioretinal lesions, allowing almost confluent therapy and retreatment of persistent or new leaking points. Micropulse laser causes stimulation of a biological response that restores the proper pump function of RPE cells, resulting in enhanced and rapid absorption of SRF.

All studies on role of micropulse laser in CSC have been conducted using 810 nm or 577 nm wavelength.[6–24] We found no studies reporting the role of transfoveal 532 nm STMP laser in treating CSC, even though it is the commonest wavelength of laser available with retinal physicians. This study was conducted to prove the safety and role of the 532 nm transfoveal STMP laser in treating non-resolving CSC specifically with subfoveal leaks.

Materials and methods

This retrospective study was carried out at a tertiary eye institute to evaluate the role of 532 nm STMP laser in treating cases of persistent CSC with focal subfoveal leaks on FFA. A retrospective analysis of records of all patients of persistent CSC, with subfoveal leak on FFA, treated with STMP laser in this institute from 2016 to 2018, was done. The approval was obtained from the institutional ethical committee (Base Hospital, Delhi; 1156/IEC/BHDC/10/2018). The study adhered to the tenets of the Declaration of Helsinki.

The inclusion criteria were (1) age $\geq$ 18 years; (2) diminution of vision for a duration of minimum 3 months due to persistent CSC; (3) subfoveal fluid seen on spectral domain optical coherence tomography (SD-OCT) imaging; (4) focal subfoveal leak on FFA; (5) follow-up of a minimum of 6 months post STMP laser.

The exclusion criteria were (1) chronic CSC characterized by RPE atrophy, diffuse leak on FFA; (2) history of treatment for CSC in the past; (3) multiple leaks on FFA; (4) any other vitreoretinal disorder currently or in the past; (5) any intraocular procedure in the past 6 months; (6) systemic or topical steroid therapy currently/ in the past 6 months; (7) presence of opaque media likely to affect quality of imaging; (8) spherical equivalent $\geq \pm$ 6D.

A detailed systemic and ocular history (onset of symptoms, present and previous treatment), the demography (age, gender), laterality, and systemic comorbidities were recorded.

A comprehensive ocular examination was done, which included an assessment of the best-corrected distance visual acuity (BCVA) by Early Treatment Diabetic Retinopathy Study (ETDRS) chart; contrast sensitivity (CS) measured uniocularly at 1 m using the Pelli-Robson chart and expressed as logarithmic CS; spherical equivalent of refractive status of the eye; slit lamp biomicroscopy with a noncontact lens; and indirect ophthalmoscopy. Colour fundus photograph was captured with a mydriatic camera (Zeiss FF450, Carl Zeiss Meditec, Jena, Germany).

FFA

FFA was performed using fluorescein sodium 20% and imaging on a mydriatic camera (Zeiss FF450, Carl Zeiss Meditec, Jena, Germany) at baseline, and at 3 and 6 months from baseline. A subfoveal leak on FFA was defined as a focal leak within 500 µm from the centre of fovea.

SD-OCT

All eyes underwent SD-OCT imaging using spectral domain OCT (Carl Zeiss Meditec, Inc, 5160 Hacienda Drive, Dublin, CA 94568 USA). The scanning protocols included HD 21-line raster and macular cube 512 $\times$ 128 scan. The central subfield retinal thickness (CRT) was determined automatically and analysed by the OCT software. The subfoveal height of neurosensory detachment was measured with callipers on the line scan passing through the fovea. The OCT imaging was

done at baseline and subsequently at each visit of follow-up.

Autofluorescence

Fundus autofluorescence (FAF) imaging (50°) was done using mydriatic camera (Zeiss FF450, Carl Zeiss Meditec, Jena, Germany) to assess any signs of subclinical laser burns at the site of application of the micropulse laser.

Subthreshold microsecond laser

The point of focal leakage in the subfoveal area was noted on FFA. All eyes were treated with the 532 nm STMP laser (Quantel Medical, Cedex, France) using slit lamp delivery. Initially, the power of 532 nm laser required to just produce a mild retinal whitening outside the vascular arcade was titrated, using a 'test' spot size of 100 µm, 5% duty cycle, and 200 ms exposure time. Following this, a 5×5 grid of confluent spots was applied over the area of focal leak, using the same settings with just 20% of the threshold power. Area centralis contact lens was used to deliver the laser.

Rescue laser

Rescue STMP laser, with the same settings as in primary laser treatment, was applied at the site of leakage if there was no change or if there was an increase in the height of neurosensory retinal detachment (NSD) at 3 months from the baseline.

Outcome measures

Primary outcome measures included change in BCVA and CS at 6 months follow-up compared with baseline. Secondary outcome measures included resolution of NSD and the incidence of adverse effects of the laser including subjective reports of scotoma, evidence of retinal tissue damage on FFA, AF, OCT, or clinical examination.

Statistical analysis

The BCVA was calculated as ETDRS visual acuity score in the form of number of letters and the CS as log CS. The changes from baseline in BCVA, height of NSD, and CRT at 1, 3, and 6 months were analysed with Wilcoxon signed-rank test. Value of $p < 0.05$ was regarded as statistically significant.

Results

We studied 23 eyes of 21 patients with a mean age of 37.09 ± 3.27 years. All patients were male. All study eyes were treatment-naïve eyes with persistent CSC of a duration of more than 3 months, with a single focal subfoveal leak on FFA. The average duration of visual symptoms was 4.48 ± 1.86 months. The baseline features of the study eyes are mentioned in Table 1. The clinical and imaging characteristics of the individual cases at baseline and at the end of follow-up of 6 months are summarized in Table 2. A representative case is illustrated in Figure 1.

All 23 eyes were treated with a sitting of STMP laser at baseline. The laser power used in our study ranged from 140 to 240 mW. There was an improvement in the BCVA from a visual acuity score (VAS) of 66.09 ± 8.51 ETDRS letters at baseline to 71.35 ± 8.48 ($p < 0.01$) letters at 1 month, 77.30 ± 11.34 ($p < 0.01$) letters at 3 months, and 80.17 ± 9.30 ($p < 0.01$) letters at 6 months, and the change was statistically significant at each visit when compared with baseline (Table 1). Similarly, the contrast sensitivity significantly improved from 0.75 ± 0.30 at baseline to 1.30 ± 0.37 ($p < 0.01$) at 6 months.

At 1 month, there was total resolution of SRF in nine (39.13% of 23) eyes and reduction in the NSD height in nine (64.29% of 14) of the remaining 14 study eyes.

At 3 months, 12 eyes (52.17% of 23) had no SRF. Of the remaining 11 eyes, two eyes did not show a progressive decrease in the height of NSD and were therefore given rescue laser. Both of these eyes did not show complete resolution of SRF even at 6 months and were subsequently treated with PDT and are presently under follow-up.

At 6 months, 16 (69.57% of 23) eyes showed complete resolution of SRF. Two of the remaining seven eyes showed an increase in the height of NSD in spite of rescue laser at 3 months from baseline and were therefore advised PDT at 6 months. Another two eyes showed a very gradual decrease in the height of NSD and were treated with repeat STMP laser.

Overall, the NSD height was significantly decreased from 260.96 ± 174.14 µm at baseline to 140.70 ± 134.90 µm ($p < 0.01$) at 1 month, 68.78 ± 89.79 µm ($p < 0.01$) at 3 months, and 47.96 ± 87.26 µm ($p < 0.01$) at 6 months.

Table 1. Baseline parameters and changes in follow-up after microsecond laser therapy.

Parameter	Baseline	1 month	3 months	6 months
Average BCVA (ETDRS letter score ± SD)	66.09 ± 8.51	71.35 ± 8.48 ($p < 0.01$)*	77.30 ± 11.34 ($p < 0.01$)*	80.17 ± 9.30 ($p < 0.01$)*
Contrast sensitivity (log CS)	0.75 ± 0.30	–	–	1.30 ± 0.37 ($p < 0.01$) *
Average CRT (μm) ± SD	416.43 ± 171.91	296.65 ± 117.48 ($p < 0.01$)*	240.74 ± 84.61 ($p < 0.01$)*	227.57 ± 69.10 ($p < 0.01$)*
Average NSD height (μm) ± SD	260.96 ± 174.14	140.70 ± 134.90 ($p < 0.01$)*	68.78 ± 89.79 ($p < 0.01$)*	47.96 ± 87.26 ($p < 0.01$)*

BCVA, best-corrected visual acuity; CRT, central subfield retinal thickness; CS, contrast sensitivity; ETDRS, Early Treatment Diabetic Retinopathy Study; NSD, neurosensory detachment; SD, standard deviation.
*Statistically significant when compared with baseline. All *p* values (in italics) are with respect to baseline.

Similarly, the CRT was significantly reduced from 416.43 ± 171.91 μm at baseline to 296.65 ± 117.48 μm ($p < 0.01$) at 1 month, 240.74 ± 84.61 μm ($p < 0.01$) at 3 months, and 227.57 ± 69.10 μm ($p < 0.03$) at 6 months (Table 1).

Safety

No laser spots were visualized during follow-up by biomicroscopy, SD-OCT, or on fundus autofluorescence. None of the patients had any procedure-related complications.

Discussion

Although there is ample literature on the use of 577 nm yellow laser or 810 nm diode STMP laser photocoagulation in the management of CSC,[6–24] we found only one study which specifically targeted subfoveal leaks in CSC with transfoveal STMP laser, using 577 nm microsecond laser.[20] Another study used 810 nm high-density SDM laser in CSC, which involved transfoveal laser in some eyes.[25] The current study is the first study to establish the role of 532 nm transfoveal STMP laser in eyes having subfoveal leaks on FFA. It is important to establish its role as it is the commonest wavelength of laser available with retinal physicians.

The characteristic feature of 810 nm laser is its deeper penetration, thus sparing inner retinal layers. Although this may or may not be relevant in STMP laser, however, this feature is definitely beneficial for treatment near the foveal avascular zone with minimal risk to the inner neurosensory retina.[26,27] The advantage of 577 nm yellow laser is that it is minimally absorbed by the xanthophyll pigment in the macula, thereby making it relatively safe in the foveal avascular zone.[28] The 532 nm is close to 577 nm but comparatively a higher energy wavelength which should need further reduction in parameters if it is to be used near the foveal avascular zone. So we titrated the power to even lesser (20% of threshold) than that reported in most of the studies using 577 nm laser.

All eyes in our study had SRF for a duration of 3 months or more. We found total resolution of SRF in 39.13% eyes at the end of 1 month after treatment and partial resolution of SRF in another 39.13% eyes. It implies that 532 nm STMP laser did expedite the resolution of SRF in these eyes. Two of the 23 eyes, in which SRF did not resolve at all or increased with time, were treated with PDT and are under follow-up.

The 532 nm STMP laser has an advantage over PDT in terms of cost-effectiveness and is a good option especially for patients who cannot afford PDT. Another advantage is the safety profile of the STMP mode of laser, which can be repeated in case of failure after the first intervention. Repeat STMP laser may be required in eyes that do not respond within 3 months after initial laser. But these eyes generally are less responsive to laser and might need an alternative therapy later.

The study has the inherent limitations of a retrospective study. The major limitations of our study are the small sample size and the lack of control arm, which make it difficult to prove the efficacy of this modality. Moreover, we cannot rule out

Table 2. Features of individual study eyes at baseline and at 6 months.

Case no.	Age/ gender	Eye	Disease duration (months)	Baseline			Rescue laser at 3 months	6 months			Rescue laser/ PDT advised at last visit
				BCVA (ETDRS letter score)	Log contrast sensitivity	NSD height (μm)		BCVA (ETDRS letter score)	Log contrast sensitivity	NSD height (μm)	
1	33/M	OD	8	64	0.80	384	–	58	0.65	166	Laser
2	34/M	OS	5	58	0.65	365	–	73	1.10	0	–
3	44/M	OD	3	73	0.65	139	–	88	1.40	0	–
4	35/M	OS	3	49	0.35	121	–	88	1.70	0	–
5	38/M	OD	4	64	0.5	459	–	82	1.55	93	–
6	37/M	OS	3	73	0.80	73	–	88	1.70	0	–
7	33/M	OS	3	58	0.35	744	–	73	0.95	259	Laser
8	33/M	OD	8	64	0.50	286	–	73	1.10	0	–
9	35/M	OD	6	58	0.35	239	–	73	1.10	0	–
10	42/M	OS	6	64	0.65	265	–	79	1.25	54	–
11	34/M	OS	3	58	0.65	624	–	88	1.55	0	–
12	40/M	OD	4	64	0.50	239	–	88	1.70	0	–
13	40/M	OS	3	73	1.10	157	–	88	1.55	0	–
14	41/M	OD	3	73	0.80	419	–	88	1.55	0	–
15	40/M	OS	3	49	0.35	134	–	88	1.70	0	–
16	40/M	OS	6	73	0.95	86	Yes	64	0.50	172	PDT
17	41/M	OS	5	64	0.95	134	–	79	0.80	79	–
18	35/M	OS	4	73	1.10	259	–	88	1.70	0	–
19	35/M	OS	3	79	1.10	112	–	88	1.70	0	–
20	36/M	OD	3	73	1.25	192	–	79	0.95	0	–
21	36/M	OS	4	79	1.10	93	–	88	1.55	0	–
22	34/M	OS	9	73	1.25	166	Yes	64	0.95	280	PDT
23	37/M	OD	4	64	0.65	312		79	1.25	0	–

BCVA, best-corrected visual acuity; ETDRS, early treatment diabetic retinopathy study; NSD, neurosensory detachment; PDT, photodynamic therapy.

spontaneous resolution in some of these eyes as these were not cases with chronic CSC. The small sample size is due to the rarity of occurrence of subfoveal leak as a cause of persistent CSC. The results would have been more reliable in a prospective study with a comparable treatment arm using an alternative wavelength or mode of laser.

Conclusion

The 532 nm transfoveal STMP laser appears to be a safe modality of treatment for persistent CSC with subfoveal leak on FFA. There may be a need for repeat micropulse laser in cases that do not respond or show recurrence. However, we recommend prospective studies on a larger sample size,

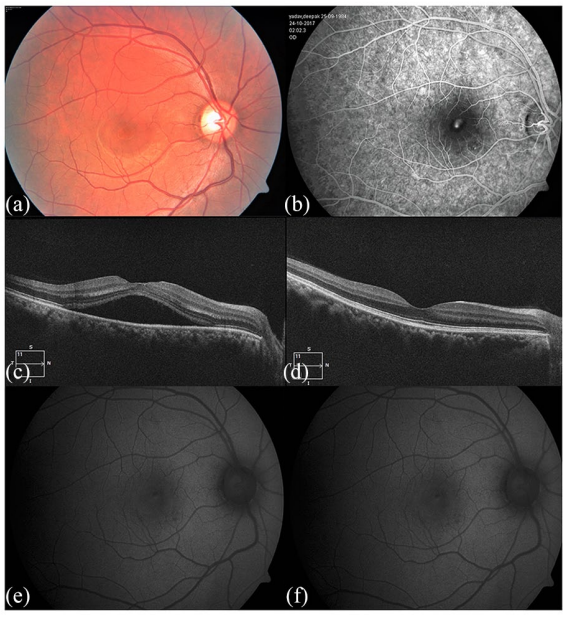

Figure 1. (a) Colour fundus photo of right eye of a 37-year-old male with persistent central serous chorioretinopathy (CSC), best-corrected visual acuity (BCVA) of 20/40. (b) Fundus fluorescein angiography (FFA) showing focal subfoveal leak with smoke-stack pattern. (c) Spectral domain optical coherence tomogram (SD-OCT) showing subfoveal fluid. (d) SD-OCT showing complete resolution of subretinal fluid 1 month after subthreshold micropulse laser with improvement of BCVA to 20/20. (e) Fundus autofluorescence of the right eye before laser showing no retinal pigment epithelial changes 6 months after laser (f).

with a comparative arm, and a longer follow-up to ascertain the safety and effectivity of this modality.

Authors' Notes

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Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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