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# Effect of subliminal diode-laser application in management of central serous chorioretinopathy

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## Abstract

### Background

Due to the possibility of spontaneous remission, invasive treatment in central serous chorioretinopathy (CSCR) is not to be commenced sooner than 3 months after onset of the disease. The aim of this work is to evaluate the effectiveness of subliminal diode-laser (SLDL) therapy for CSCR conducted 3–6 months after diagnosis.

### Aim

The aim of the work is to study the effectiveness of using transfoveal subliminal diode-laser application in treatment of CSCR.

### Patients and methods

The study included CSCR cases that last up to 1–3 months after acute onset of disease. All patients had transfoveal SLDL application and these patients were observed for 1 month and 3 months after SLDL treatment. Best-corrected visual acuity (BCVA) and retinal morphological alterations were the factors measured during the study.

### Results

In 81.25% of cases, the subretinal fluid complete resolution was observed after therapy, BCVA improved dramatically. Early SLDL was associated with an improved end BCVA ( $P = 0.0005$ ). The assessment in cases of nonresponding to SLDL demonstrated a decreased visual acuity than the baseline.

### Conclusions

SLDL application is considered a good and safe treatment modality in management of CSCR, early treatment results in better visual outcomes such as improving VA, decreasing central macular thickness, and absorption of subretinal fluid.

**Keywords:** Central serous chorioretinopathy, subliminal diode laser, subretinal fluid

## INTRODUCTION

Although central serous chorioretinopathy (CSCR) is a rather common clinical condition, the pathophysiology is uncertain [1]. Many of acute conditions resolve on their own without causing significant vision loss. Nonetheless, some retinal alterations (e.g. abnormal retinal pigmentation) can be noted during acute CSCR, and patients may have deterioration in their vision, particularly in the presence of chronic metamorphopsia [2]. Historically, waiting for symptoms to resolve spontaneously before initiating any invasive therapy was recommended [3] because most acute cases can spontaneously regress. Macular photocoagulation is applied

in certain circumstances where the leaky point is placed safely away from the fovea's center. Photodynamic therapy (PDT), on the other hand, can be employed closer to the fovea's center. PDT is typically deferred until 4–6 months after the onset of the condition in the hope that it may spontaneously resolve, as it entails the invasive technique of injection of

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drugs such as Verteporfin and the potentially bothersome requirement to avoid exposure to sun following the laser application [4–6]. Oral mineralocorticoid-receptor inhibitors may also be used, but the clinical evidence on these drugs is currently scarce [7,8].

Subliminal diode-laser application (SLDL) has revolutionized the treatment of CSCR. SLDL has been utilized successfully in the treatment of chronic CSCR, with the majority of cases achieving morphological success [9–12]. SLDL-stimulated retinal pigment epithelium (RPE) produces ‘heat shock proteins,’ which are chaperones that exhibit anti-inflammatory and anti-angiogenic activity [13–15]. SLDL enhances the trans-retinal pump by normalizing RPE function [subretinal fluid (SRF)]. Laser is supplied in a series of extremely brief shocks separated by cooling intervals that avoid heat accumulating to fatal levels for the RPE. Thus, SLDL has been established as a safe therapy with no known side effects [16,17]. Regrettably, this retinal morphology improvement after treatment may not be associated with a meaningful improvement in visual impairment [18–21]. Such worse visual outcomes are due to the disease’s longer duration, which results in higher photoreceptor degradation and thinning of the retina.

Due to the established safety of SLDL, it is possible to explore treating patients with CSCR early. Thus, the purpose of this study was to examine the relationship between the functional and morphological outcomes of transfoveal subliminal diode-laser application (STDL) and the timing of treatment beginning. Due to the fact that permanent retinal damage from CSCR occurs usually if disease duration is more than 6 months, the current study focused on CSCR earlier than 6 months to determine the effect of earlier intervention outcomes.

## PATIENTS AND METHODS

All methods were in agreement with our hospital research committee’s ethical requirements. In each case, written consent for the procedure was obtained.

In total, 47 eyes with CSCR were conducted from 47 patients treated with SLDL transfoveal application for ttt of CSCR between January 2018 and January 2022, at Sohag Teaching Hospital – Retina and Laser Unit. Patients with active CSCR lasting more than 1 and 3 months from the beginning of sure diagnosis by fundus fluorescein angiography (FFA) and optical coherence tomography (OCT), to detect the leaky points, calculation of SRF and central macular thickness (CMT). The CMT and average central retinal thickness were determined using OCT. Both methods of measurement are integrated into the OCT programs. CRT is when an average retinal thickness of 1 mm in diameter inside the center circle, whereas average central retinal thickness is an average retinal thickness of 6 mm within the central circle. At its highest point, the SRF height was manually measured using software by the OCT machine calibration maker.

All participants were scheduled for follow-up assessments 1 month after their SLDL session and 3 months after SLDL, by best-corrected visual acuity (BCVA), OCT scans, and FFA imaging after 1 and 3 months if needed. If there is persistent leaky point and the same SRF remaining after 1 month, a second SLDL session was conducted and the same investigation was done after 2 months of the second laser session, thus, two SLDL sessions can be conducted prior to the final measurements after 3 months of the beginning of SLDL.

A 577-nm laser machine (Easy ret 577, Quantel Medical, Cournon d’Auvergne, France) was used for SLDL. The method was carried out in accordance with FFA leakage locations (early fluorescein leaking point), in which the entire leakage area was covered with 160–200  $\mu\text{m}$  or totally included inside a suitable diameter-confluent laser-pattern shape.

Laser parameters are spot size (50–100  $\mu\text{m}$ ), exposure (0.200–0.300 ms), power (500–1200 mw) according to peripheral retinal laser-threshold testing, duty cycle (5%), pattern (square–circle), number of laser burns (100–300) in each session, and fluence (20–40  $\text{J}/\text{cm}^2$ ) were used in conjunction with Volk Area Centralis (0.94 $\times$ ) laser lens.

Volk Area centralis (0.94 $\times$ ) contact laser lens that is developed with a magnification of 1.06 $\times$  to provide magnified views of the posterior pole in great detail. This lens is appropriate for grid/focal laser operations on the central retina, such as those used to treat microaneurysms and edema associated with diabetic retinopathy.

Each follow-up examination included the acquisition of OCT (for CMT and SRF) and FFA if needed to assess the remaining leaky points.

### Statistical analysis

Statistical analysis was used to determine the efficacy of subliminal diode-laser therapy (SLDLT) and the association between treatment outcomes and the timepoint at which therapy was initiated. Also, retinal morphological changes and BCVA parameters were evaluated before and after treatment.

Statistica 10.0 software was used to conduct the statistical analysis (Stat Soft, Tulsa, Oklahoma, USA). The Shapiro–Wilk test was used to determine the normality of the distribution. The Wilcoxon test was used to determine the significance of the treatment findings. Correlations between the duration of symptoms and treatment outcomes were determined using Spearman rank coefficients.

The nonparametric Mann–Whitney *U* test was used to analyze group comparisons. When *P* value less than 0.05, the results were considered statistically significant.

## RESULTS

The disease duration was with an average of  $3.4 \pm 2.3$  months. The study group consisted of 20 females and 27 males. The mean age was  $47.25 \pm 12$  years, as shown in Table 1.

In 26 cases, complete resorption of SRF was seen. In eight cases, another session of SLDL was needed after 1 month of the first session – two cases responded well, with complete remission of SRF, but SRF persisted in the remaining six cases. Table 2 summarizes the study group’s baseline characteristics and treatment outcomes.

The Wilcoxon test indicated that the differences pretreatment and posttreatment were statistically significant ( $P = 0.001$  for each pair).

Correlation between illness duration and other characteristics defining retinal, morphological, and functional features indicated a high statistical correlation with BCVA only after treatment (Table 3). The change in BCVA following laser application is borderline statistically significant ( $P = 0.07$ ).

The entire study group is divided into two subgroups: those treated within 1 month and those after 3 months after the beginning of symptoms. The difference in BCVA logMAR values between these groupings is statistically significant ( $P = 0.00003$ ), as shown in Table 4.

The outcome parameters’ statistics of responders who had SRF resolved after SLDLT were similar to those of the entire cohort of patients. Table 5 shows the baseline features of the responders’ subgroup.

After therapy, all metrics showed statistically significant changes ( $P = 0.001$  for all pairs). The assessment of correlations is shown in Table 6.

The association between earlier treatment beginning and improved functional outcomes is also readily apparent in this cohort, as after dividing patients into two subgroups (Table 7).

When baseline features of responders and nonresponders to SLDL were compared, no statistically significant differences

were seen, however, the nonresponders’ group was small in size. Nonetheless, nonresponders’ baseline BCVA levels were lower ( $0.54 \pm 0.21$  logMAR vs.  $0.32 \pm 0.21$  logMAR), a result that approaches statistical significance ( $P = 0.06$ ). This result may become statistically significant with a bigger population sample.

\*Subliminal Easyret laser machine and its end-report images:

fx1

fx2

\*FFA and OCT of CSCR before SLDL (case I)

fx3

fx4

\*FFA and OCT of CSCR 3 months after SLDL (case I)

fx5

fx6

\*FFA and OCT of CSCR before SLDL (case II)

fx7

fx8

\*FFA and OCT of CSCR 1 month after SLDL first session (case II)

fx9

fx10

\*OCT of CSCR 2 months after SLDL second session (case II)

fx11

fx12

**Table 1: Age and the duration of the disease of the studied population**

	Number	Mean	Median	Minimum	Maximum	SD
Age	47	47.25	47.70	30.00	71.00	12.12
Duration (months)	3.36	4.00	0.60	6.00	2.26	

**Table 2: Results of subliminal diode-laser therapy**

Parameter	Number	Mean	Median	Minimum	Maximum	SD
Pre ttt CRT (µm)	47	373.6	367.40	248.00	658.00	89.59
Post ttt CRT (µm)	47	263.4	248.30	167.00	471.00	57.74
Pre ttt SRF (µm)	47	178.2	146.20	70.00	417.00	85.28
Post ttt SRF (µm)	47	23.18	0.00	0.00	304.34	61.51
Pre ttt CRTA (µm)	47	311.37	304.60	254.20	413.40	33.89
Post ttt CRTA (µm)	47	291.3	295.70	246.00	332.30	16.22
Pre ttt BCVA logMAR	47	0.47	0.20	0.11	1.10	0.23
Post ttt BCVA logMAR	47	0.25	0.30	0.00	0.90	0.24
EXP	47	317.81	274.80	119.80	647.80	153.94

BCVA, best-corrected visual acuity; CRT, central retinal thickness; CRTA; average central retinal thickness; EXP, number of laser shots per session; post, after laser treatment; pre, before laser treatment; SRF, subretinal fluid.

**DISCUSSION**

The best time of application of therapy CSCR is uncertain and has resurfaced as a topic of fresh attention as a result of

the advent of new treatment alternatives [22]. Historically, it has been recommended to avoid any invasive method to treat acute CSCR due to the dangers associated with treatment and the largely favorable outcomes obtained with spontaneous recovery. Additionally, PDT was considered the only option for persistent CSCR treatment [23,24]. Placing LPC patches near the fovea frequently resulted in metamorphopsia and raised the danger of unintentional foveal damage, as a result, LPC application is normally delayed and saved for chronic nonresolving cases. The link between the duration of CSCR and the associated visual-impairment degree has been demonstrated to be nonlinear [25].

Three major criteria, we feel, encourage reconsideration of the traditional guidelines for CSCR treatment, both in terms of timing and modality of treatment. To begin, micropulse laser technology is significantly safer than conventional laser photocoagulation for treating the retina, with no documented

**Table 3: Correlation analysis between illness duration and other characteristics**

Parameters	Number	r Spearman	T (N-2)	P
Post ttt CRT (m)	47	0.0987	0.5430	0.5911
Post ttt SRF (m)	47	0.2626	1.4909	0.1464
Post ttt CRTA (m)	47	0.0100	0.0550	0.9565
Post ttt BCVA logMAR	47	0.5802	3.9014	0.0005
BCVA logMAR (I-II)	47	0.3243	1.8775	0.0702
CRT (I-II)	47	0.0392	0.2149	0.8313
CRTA (I-II)	47	0.0818	0.4496	0.6562

BCVA, best-corrected visual acuity; CRTA, average central retinal thickness; I-II, the difference pre-laser and post-laser therapy; SRF, subretinal fluid.

**Table 4: LogMAR values of the final best-corrected visual acuity according to beginning of treatment**

Beginning of treatment	Number	Mean	Median	Minimum	Maximum	SD
Within 1 month	20	0.08	0.11	0.00	0.30	0.08
3 months	27	0.32	0.21	0.19	0.80	0.20

**Table 5: Outcome of subliminal diode-laser therapy in the responders**

Outcome measure	Number	Mean	Median	Minimum	Maximum	SD
Pre ttt CRT (m)	26	375.73	371.50	248.00	658.00	98.06
Post ttt CRT (m)	26	239.69	240.00	167.00	276.00	24.38
Pre ttt SRF (m)	26	180.73	148.50	70.00	417.00	88.47
Pre ttt CRTA (m)	26	313.00	305.50	254.00	413.00	36.63
Post ttt CRTA (m)	26	288.42	291.00	246.00	317.00	15.67
Pre ttt BCVA logMAR	26	0.33	0.30	0.10	1.00	0.21
Post ttt BCVA logMAR	26	0.17	0.20	0.00	0.60	0.14
No EXP	26	320.46	310.00	120.00	575.00	145.17

BCVA, best-corrected visual acuity; CRTA, average central retinal thickness; SRF, subretinal fluid.

**Table 6: Correlations between the duration of the disease and retinal morphology and function-evaluation parameter in responders**

Parameters	Responders' number	r	T (N-2)	P
Post ttt CRT (m)	26	0.1382	0.6834	0.5009
Post ttt CRTA (m)	26	0.1316	0.6506	0.5215
Post ttt BCVA logMAR	26	0.5444	3.1793	0.0040
BCVA logMAR (pre-post)	26	0.3629	1.9080	0.0684
CRT (pre-post)	26	0.1414	0.7000	0.4907
CRTA (pre-post)	26	0.0404	0.1981	0.8447

BCVA, best-corrected visual acuity; CRTA, average central retinal thickness.

**Table 7: LogMAR values of the final best-corrected visual acuity in responders of subretinal fluid according to the time of the beginning of therapy**

Time of application number of laser	Responders' number	Mean	Median	Minimum	Maximum	SD
1 month	15	0.08	0.10	0.00	0.33	0.09
3 months	11	0.27	0.21	0.20	0.62	0.13

The differences: statistically significant (P=0.0004).



adverse effects. In addition, outcomes of CSCR treatment are substantially related to the disease duration. Patients treated previously regain normal visual acuity and have morphology of the retina restored. In comparison, no treatment for chronic CSCR has resulted in adequate functional outcomes. Scholz *et al.* [26] showed an average improvement in BCVA of 6.34 ETDRS letters following SLDLT treatment for chronic CSCR in 12 investigations. Additionally, inadequate functional improvement is a result of traditional PDT therapy for persistent CSCR. Previous work showed an average ETDRS letter improvement of six in severe CSCR of long duration [27]. The same is true for the big PLACE study, which demonstrated an average BCVA improvement of 4.6 ETDRS letters following half-dose PDT in chronic CSCR [6]. When oral eplerenone medication was effective in chronic CSCR, it resulted in a similar minor rate of improvement in the majority of current trials [28,29].

Third, we know that, in the majority of patients, retinal architecture can be adjusted with SLDLT, with a considerable decrease in retinal thickness [20,21]. Functional enhancement may occur as a result of retinal architectural improvement. Permanent retinal damage occurs in chronic situations that limit laser-therapy responsiveness. Thus, while the majority of cases with acute CSCR recover spontaneously, prompt and effective treatment is critical to reduce vision-impairment chronicity.

SLDLT was both effective and safe in our study. It is considered the simplest, safest, and least-invasive option, as demonstrated by the safety of previous research on direct foveal therapy. PDT, on the other hand, needs to avoid sun exposure for several days following the therapy due to the possibility of photosensitivity. Males may experience systemic adverse effects, including gynecomastia, and such treatment needs periodic monitoring of potassium plasma levels [30–32].

Notably, it was previously reported in a study on the effects of SLDLT in a small group of 11 patients with disease durations ranging from 1 to 7 months and concluded that all patients experienced complete clearance of SRF independent of disease length [33]. Similar findings were observed in two trials on chronic CSCR, in a larger sample of populations [19,20].

Patients who underwent SLDLT within 1 month of the beginning of symptoms had significantly improved ultimate visual acuity compared with those who underwent SLDLT later. The conventional definition of chronic CSCR focuses exclusively on disease duration than on the form of RPE decompensation [34–37]. In our trial, nonresponders to SLDLT were not of chronic duration compared with good responders, but a substantial association was seen between final BCVA and disease duration prior to therapy beginning, even in eyes with complete remission of SRF. Our findings suggest that even patients who achieve complete remission of SRF may develop lingering BCVA deficits.

Additionally, previous work studied the acute cases with CSCR if treated for less than 2 months and compared their functional

outcomes to those of observation-only individuals [22]. Throughout follow-up, treated cases exhibited higher BCVA levels than nontreated cases. BCVA in the laser group and the nontreated group was highly significantly different ( $P = 0.008$ ). Additionally, significant improvements associated with timely SLDLT in CSRS occurred without any side effects, comparable with previous research [38–40].

### Limitations

Our work is of a small sample size according to CSCR percentage at our locality. It reported that early SLDLT treatment of CSCR is efficacious and may improve long-term outcomes, but additional research involving larger patient populations at multilocalities and multicenters is required for confirmation, particularly those incorporating the assessment of retinal functional changes and changes in BCVA. It will be required to compare these findings to those from prospective research. Additionally, a longer period of follow-up may be needed to evaluate the recurrence following SLDLT.

### CONCLUSIONS

SLDL using ttt of CSCR is a safe, effective modality of ttt. Using early (<3 months) SLDL resulted in better results such as improvement in visual acuity, decreased CMT, absorption of SRF, and ablation of leaky areas with a relatively safe treatment modality.

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### Conflicts of interest

There are no conflicts of interest.

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