Subthreshold diode micropulse laser versus observation in acute central serous chorioretinopathy

Central serous chorioretinopathy (CSC) is characterised by serous detachment of the neurosensory retina caused by focal leakage of fluid from the choroid to the subretinal space, due to impairment in the barrier function of the retinal pigment epithelium.\(^1\)\(^2\) CSC is mostly self-limiting, as 80 per cent of cases resolve spontaneously within six months, reaching a visual acuity of > 6/9.\(^3\) Therefore, the current standard of care for acute CSC is observation.

Treatment is indicated for chronic or recurrent CSC. Various treatment options such as photodynamic therapy,\(^4\)\(^5\) laser photocoagulation,\(^6\)\(^7\) and subthreshold diode micropulse (SDM) laser\(^8\)\(^9\) are available. However, fluid accumulation under the retina at the acute stage of the disease seems to cause a certain amount of damage to the photoreceptors, which seems to persist even after the fluid is reabsorbed. The disease results in diminished contrast sensitivity, which can be permanent and leave the patient visually impaired.\(^10\)

Hata et al.\(^11\) showed that in CSC, outer nuclear layer thinning at the central fovea should indicate cone photoreceptor loss, considering the distribution of rod and cone photoreceptors. Gawekgi et al.\(^12\) used SDM laser for treatment of chronic CSC and demonstrated that although the laser provided good morphological results, there was no significant improvement in visual acuity. They concluded that in order to achieve good visual results, SDM laser should be considered in acute cases.

Therefore, treatment options for acute CSC must be explored so as to avoid permanent damage to photoreceptors. However, the most important consideration for treating acute CSC is safety, or lack of side effects by the treating modality.

The present study evaluated the role of SDM laser in treating acute CSC compared with the current standard of care (observation).

**Methods**

This was a randomised controlled trial on 68 eyes of 68 consecutive patients with acute CSC, carried out at Guru Nanak Eye Centre, Maulana Azad Medical College, New Delhi, from September 2013 to August 2016. The study was performed in accordance with the tenets of the Declaration of Helsinki and approved by the institutional review board.

Inclusion criteria were: duration of symptoms less than two months; single active angiographic leak (foveal/juxtafoveal/extrafoveal); subretinal fluid involving the fovea on spectral domain optical coherence tomography; first episode of CSC; and absence of any other ocular disease. Patients who had a history of taking steroids and those who had undergone intraocular surgery, including retinal laser treatment, were excluded. Patients in whom fluorescein angiography was contraindicated were also excluded. Written informed consent was obtained from all patients before inclusion in the study.

Detailed history and examination, including best-corrected visual acuity, contrast sensitivity (Functional Acuity Contrast Testing chart), Amsler grid charting, fundus examination using slitlamp 90 D
bimicroscopy, and indirect ophthalmoscopy were performed. Visual acuity was assessed on a Snellen chart and converted to logMAR units for statistical analysis.

Investigations included fundus fluorescein angiography (VISUCAM 500; Carl Zeiss, New Delhi, India), spectral domain optical coherence tomography (Nidek RS 3000 Advance; Nidek Co. Ltd., Gamagori, Japan) and visual fields (10-2) (Humphrey Automated Visual Field Test). All tests were performed at baseline and at two, four, eight and 16 weeks, and six months. Parameters that were evaluated on spectral domain optical coherence tomography included height and width of neurosensory detachment and choroidal thickness. Maximum height and width of neurosensory detachment and choroidal thickness was measured four times in each eye: along the horizontal scan, vertical scan, and two oblique scans. An average of these four values was taken as Csubfoveal for each eye.

Eligible eyes were randomised into two groups using a centralised computer-generated randomisation list. All patients in the SDM laser group (Group A) were treated using an 810-nm infrared diode laser (Oculight SLX; Iridex Corp, Mountain View, California, USA), as per the technique described by Koss et al.13 In Group A, the minimum threshold power (P) for a light visible burn was determined by applying a test burn in the nasal mid-periphery (continuous wave emission mode, 125 μm spot size, 200 ms exposure duration). After determination of P, the laser mode was changed from continuous wave to micropulse emission mode at 15 per cent duty cycle and the power was doubled (2P) in micropulse emission mode.

Each laser envelope consisted of one hundred 300 μs micropulses, delivered over two milliseconds (300 μs on and 1,700 μs off). About 100 pulse envelopes were applied at the leaking point. Steps were taken to ensure that the SDM laser treatment was ‘invisible by biomicroscopy’, meaning laser treatment was not clinically discernable, on fundus fluorescein angiography, fundus autofluorescence or on spectral domain optical coherence tomography. Great care was taken if the colour of the retinal pigment epithelium changed during the laser treatment, prompting immediate cessation of laser application.

Eyes in the observation group (Group B) received no intervention and were followed up as per our follow-up protocol.

Persistence of neurosensory detachment and recurrence of neurosensory detachment in both groups were recorded.

### Results

Mean age of patients in the SDM laser group was 35.05 ± 2.53 years and in the observation group was 36.35 ± 6.38 years (p = 0.132). Males constituted 82.35 ± 17.65 per cent versus 91.18 ± 8.82 per cent in the laser and observation groups, respectively (p = 0.142). Duration of symptoms was 35.47 ± 10.64 days in the laser group and 39.26 ± 9.78 days in the observation group (p = 0.065).

Best-corrected visual acuity in the laser group as well as in the observation group increased significantly (p < 0.001) at two, four, eight and 16 weeks, and six months, compared to the baseline.

The two groups were matched in terms of best-corrected visual acuity at baseline (p = 0.427), but the laser group had significantly higher best-corrected visual acuity at two (p = 0.002), four (p < 0.001), eight (p < 0.001) and 16 weeks (p = 0.042), and six months (p = 0.008) (Table 1).

Contrast sensitivity (logMAR) at baseline was 1.14 ± 0.27 in the laser group and 1.04 ± 0.37 in the observation group (p = 0.123). Contrast sensitivity increased significantly at each visit (p < 0.001) compared to baseline in the laser group as well as in the observation group. The laser group had significantly higher contrast sensitivity.

### Visual acuity in logMAR

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>16 weeks</th>
<th>6 months</th>
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<tr>
<td><strong>Laser</strong></td>
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<tr>
<td>Mean</td>
<td>0.59</td>
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<td>0.06</td>
<td>0.04</td>
<td>0.03</td>
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<tr>
<td>SD</td>
<td>±0.27</td>
<td>±0.2</td>
<td>±0.1</td>
<td>±0.09</td>
<td>±0.09</td>
<td>±0.08</td>
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<tr>
<td>p-value (versus baseline)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
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<tr>
<td><strong>Observation</strong></td>
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<td></td>
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<tr>
<td>Mean</td>
<td>0.60</td>
<td>0.40</td>
<td>0.25</td>
<td>0.17</td>
<td>0.09</td>
<td>0.14</td>
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<tr>
<td>SD</td>
<td>±0.21</td>
<td>±0.16</td>
<td>±0.12</td>
<td>±0.15</td>
<td>±0.14</td>
<td>±0.24</td>
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<td>p-value (versus baseline)</td>
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<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
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<tr>
<td>p-value (laser versus observation)</td>
<td>0.427</td>
<td>0.002</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.042</td>
<td>0.008</td>
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</tbody>
</table>

Table 1. Comparison of laser group versus observation group in terms of best-corrected visual acuity over time

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Csubfoveal was 416.83 and six months. In the observation group, (p < 0.001) at two, four, eight and 16 weeks, the baseline. It decreased signifi-
cantly (p < 0.001) at two, four, eight and 16 weeks, and six months, com-
pared to the laser group (Table 3). The width of the neurosensory detachment was matched between the two groups at baseline (p = 0.439). The observation group had significantly greater width at eight weeks (p < 0.001) and six months (p = 0.032) compared to the laser group.

In the laser group, subfoveal choroidal thickness (Csubfoveal) was 410 ± 80.49 μm at the baseline. It decreased significantly (p < 0.001) at two, four, eight and 16 weeks, and six months. In the observation group, Csubfoveal was 416.83 ± 67.87 μm at baseline, and decreased significantly (p < 0.001) at two, four, eight and 16 weeks, and six months. Csubfoveal was matched between the two groups at baseline (p = 0.369) and significantly lower in the laser group at eight (p = 0.030) and 16 weeks (p = 0.049), and six months (p < 0.001).

Parafoveal choroidal thickness (Cparafoveal) was matched between the two groups at baseline (p = 0.270). It decreased significantly (p < 0.001) in the laser group at two, four, eight and 16 weeks, and six months, and it also decreased significantly in the observation group (p < 0.001) at two, four, eight and 16 weeks, and six months, compared to baseline. The laser group had a significantly lower Cparafoveal at four (p = 0.014), eight (p < 0.001) and 16 weeks (p = 0.0001), and six months (p < 0.001) (Table 4).

At six months, on Amsler grid testing, 17.65 per cent of patients in the laser group versus 29.41 per cent of patients in the observation group (p = 0.036) had persistent metamorphopsia. A recurrent/persistent neurosensory detachment was observed at the end of six months in 11.76 per cent of the laser treated eyes versus 38.24 per cent of eyes in the observation group (p = 0.036). No visual field abnormalities were noted in either of the groups. No laser-induced iatrogenic damage (clinically, on fundus fluorescence angiography, on fundus autofluorescence, or on spectral domain optical coherence tomography) was noted in any eye that underwent SDM laser.

**Discussion**

Many studies have demonstrated the efficacy of conventional laser photocoagulation6,7 and photodynamic therapy4,5,7 in CSC. Side effects of conventional laser photocoagulation include stimulation of choroidal neovascularisation, localised scotoma, and enlargement of the pigment epithelial atrophic scar over time.14,15 Side effects of photodynamic therapy include retinal pigment epithelium atrophy, persistent choriocapillaris hypoperfusion, and secondary choroidal neovascularisation at the treated area.16–18

Collateral damage invariably occurs in conventional laser photocoagulation because of the energy that is required to produce a visible burn. For this reason, conventional laser

<table>
<thead>
<tr>
<th>Height of neurosensory detachment in microns</th>
<th>Baseline</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>16 weeks</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laser</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td>254.53</td>
<td>111.59</td>
<td>38.32</td>
<td>6.12</td>
<td>14.18</td>
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<td>SD</td>
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<td>37.51</td>
<td>17.39</td>
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<td>p-value (versus baseline)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
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<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Observation</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>288.26</td>
<td>158.53</td>
<td>69.97</td>
<td>42.00</td>
<td>17.12</td>
<td>71.65</td>
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<tr>
<td>SD</td>
<td>96.65</td>
<td>73.92</td>
<td>48.99</td>
<td>45.26</td>
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<td>p-value (versus baseline)</td>
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<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
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</tr>
<tr>
<td>p-value (laser versus observation)</td>
<td>0.078</td>
<td>0.021</td>
<td>0.002</td>
<td>0.001</td>
<td>0.409</td>
<td>0.022</td>
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</tbody>
</table>

Table 3. Comparison of laser group versus observation group in terms of height of neurosensory detachment over time.

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**Contrast sensitivity**

<table>
<thead>
<tr>
<th>Laser</th>
<th>Baseline</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>16 weeks</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.14</td>
<td>1.29</td>
<td>1.39</td>
<td>1.56</td>
<td>1.65</td>
<td>1.65</td>
</tr>
<tr>
<td>SD</td>
<td>±0.27</td>
<td>±0.25</td>
<td>±0.32</td>
<td>±0.17</td>
<td>±0.22</td>
<td>±0.23</td>
</tr>
<tr>
<td>p-value (versus baseline)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 2. Comparison of laser group versus observation group in terms of contrast sensitivity (Functional Acuity Contrast Testing chart) over time.
Table 4. Comparison of laser group versus observation group in terms of average parafoveal thickness

<table>
<thead>
<tr>
<th>Average parafoveal thickness in microns</th>
<th>Laser</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td>406.20</td>
<td>416.73</td>
</tr>
<tr>
<td></td>
<td>±76.41</td>
<td>±64.11</td>
</tr>
<tr>
<td>p-value (versus baseline)</td>
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<td>&lt; 0.001</td>
</tr>
<tr>
<td>p-value (laser versus observation)</td>
<td>0.270</td>
<td>0.226</td>
</tr>
</tbody>
</table>

Table: Comparison of laser group versus observation group in terms of average parafoveal thickness

cannot be used in acute cases and when the angiographic leak is at a subfoveal location. SDM laser produces the same therapeutic effect as that of a conventional laser without producing a biomicroscopically visible end point. This saves the retinal tissue from structural and functional damage.

Recent hypotheses suggest that the benefits of laser photocoagulation may be derived from the up-and-down regulation of factors mediated by the biological reaction of retinal pigment epithelium cells. This is more likely to occur in retinal pigment epithelium cells that have been only sublethally injured by a lower thermal elevation than at ophthalmoscopically visible endpoints.19

Successful outcomes using SDM laser have been previously reported in chronic CSC26,20–26 however, there have been very few studies (retrospective and very limited sample size) on acute CSC20,27 Various studies on SDM differ in laser parameters and technique.20–30 Duty cycles varying from five per cent21,28–30 to 15 per cent22,23,27 have been used. Although some studies31 have shown that a duty cycle > 10 per cent has been associated with laser-induced damage and that a duty cycle of five per cent is safer, the protocol of this study was designed and approved before 2012. No iatrogenic laser-induced damage was noted in this study and therefore the laser parameters were not altered during the study.

Since SDM laser is believed to be free of side effects,20,31–33 the application of this technique was evaluated in this study in acute cases and in cases where the leak was subfoveal. Superior visual rehabilitation in the SDM-treated group was noted as compared to the observation group (best-corrected visual acuity was significantly better in the SDM laser group from two weeks onward; contrast sensitivity was better in the SDM laser-treated group from eight weeks onward; and there were fewer SDM laser-treated eyes with metamorphopsia at six months).

The above findings could be attributed to faster resolution of subretinal fluid in the laser group compared to the observation group (as evidenced by the significantly lower height of neurosensory detachment in the laser group at two, four and eight weeks, and six months, and a lesser width of neurosensory detachment at eight weeks and six months). At 16 weeks, the difference between the laser group and observation group in terms of height and width of neurosensory detachment was not significant due to the mean being deviated due to a case of recurrent CSC in the SDM laser group.

Another interesting observation was that choroidal thickness in eyes treated with SDM laser was significantly lower compared to the observation group (Csubfoveal was significantly lower in the laser group at eight and 16 weeks, and six months, and Cparafoveal was lower at four, eight and 16 weeks, and six months). Whether lesser choroidal thickness in SDM treated eyes was the cause or the effect of faster resolution of neurosensory detachment still remains to be elucidated.

The pathophysiology of CSC has been attributed to hyperpermeable choroidal vessels24,34 impaired choroidal vascular autoregulation and dysfunction of the retinal pigment epithelium barrier and pumping35. Choroidal thickness is an indirect measure of choroidal hyperpermeability.36

SDM laser causes resolution of CSC by normalisation of retinal pigment epithelium function and retinal autoregulation by means of sublethal retinal pigment epithelium heat-shock protein activation (reset to default theory)19,31–33,37–39 or possibly by causing cytokine expression which decreases choroidal hyperpermeability.

In cases of recurrent CSC, increase of choroidal thickness preceded the symptomatic deterioration of vision and optical coherence tomography evidence of neurosensory detachment (Figure 1). The incidence of recurrence or persistent CSC was much higher in the observation group compared to the laser group at the end of six months (six recurrent cases and four persistent cases in the observation group versus one recurrent and four persistent cases in the laser group). This could again be indicative of the effect of laser in decreasing choroidal hyperpermeability through a mechanism not completely understood. Other studies have also shown that SDM laser decreases recurrences of CSC.12

Longer follow up of SDM-treated eyes will reveal the true recurrence rate and whether the effect of laser is long-lasting or not. Limitations of this study are a small sample size, short follow-up period and lack of perimetric correlation.

**Conclusion**

SDM laser hastens visual rehabilitation quantitatively as well as qualitatively. It also reduces the chances of CSC going into chronicity and recurrence, compared to the current standard of care (observation). Since it has a high safety profile, SDM laser is recommended in acute CSC and in those cases of CSC where the angiographic leak is at a subfoveal location.
Figure 1. A: Right eye of a patient showing neurosensory detachment (NSD) at baseline.

Figure 1. B: NSD resolution after four weeks of observation. Subfoveal choroidal thickness is 309 μm.
Figure 1. C: At 16 weeks, there is no NSD but subfoveal choroidal thickness increases (compared to subfoveal choroidal thickness at four weeks) to 343 μ.

Figure 1. D: At six months, there is a recurrence of NSD. Subfoveal choroidal thickness is 351 μ.
REFERENCES