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Evaluation of Chronic Central Serous Chorioretinopathy after Subthreshold Yellow Micropulse Diode Laser Photostimulation at a Wavelength of 577 nm

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Abstract

Objective: This study evaluated the efficacy and safety of subthreshold yellow diode-laser micropulse 577 nm (SDM) in the treatment of chronic central serous chorioretinopathy (CSCR).

Methods: 40 eyes of 40 patients with non-resolving CSCR of >12 months duration were treated with SDM yellow laser (577 nm). Best corrected visual acuity (BCVA) and intraocular pressure (IOP) were measured. Amsler grid screening, ophthalmoscopy, fundus autofluorescence (FAF) and SD-OCT were performed. Follow up measurements were recorded from 3 to 12 months.

Results: Restoration of normal macular anatomy was obtained in 85.7% of cases with a significant reduction in mean central foveal thickness (CFT). Mean visual acuity gain was 14.95 ETDRS letters, subjective or objective deterioration after treatment was not recorded in any case.

Conclusion: The possibility of favouring reabsorption of subretinal liquid by stimulating the retinal pigment epithelium, even at the fovea, without damaging retinal tissue, opens up new frontiers for the therapy of chronic CSCR.

Keywords: Central serous chorioretinopathy; Micropulse diode laser 577 nm; Fundus autofluorescence; Optical coherence tomography

Introduction

Central Serous retinopathy or Chorioretinopathy (CSCR) is an idiopathic disease of the external blood-retina barrier [1] affecting the macular region of the retina. It involves limited detachment of the neuroepithelium (NE), sometimes associated with serous detachment of the Retinal Pigment Epithelium (RPE) [2]. The disorder is sporadic and generally unilateral, though it may affect both eyes more or less symmetrically [3]. It is more frequent in young adult males of anxious disposition [4]. Women with CSCR have a mean age higher than men. The most common symptoms are blurred or distorted vision. Aetiology is unknown, however onset and worsening have been associated with predisposing factors, such as emotional stress, arterial hypertension, organ transplant, gastroesophageal reflux, alcohol abuse, oral or inhaled steroid therapy, pregnancy and systemic diseases, such as lupus erythematosus and Cushing syndrome [5]. Acute CSCR tends to be self-limiting with absorption of the subretinal liquid within 3-5 months and complete or almost complete recovery of visual acuity. Persistence of diminished colour and contrast perception and relapses has been reported in the literature. CSCR may also become persistent, with detachment of the neuroepithelium for more than 5-6 months, healing spontaneously in about 8-12 months (subchronic CSCR). In a minority of cases, especially patients over 50 years of age, the disease may become chronic, permanently impairing visual acuity. In these cases the RPE may show chronic alterations (subneuroepithelial granulation tissue) and new blood vessels may form in the choroid [3]. Cases with a single, well-defined extrafoveal leakage point or RPE detachment can be treated by photocoagulation with a continuous wave green 532 nm laser [6-8]. This therapy is not indicated in cases with foveal leakage or multiple leakage points [9]. Retinal photocoagulation involves destruction of retinal tissue and may stimulate neovascularization, induce localized scotoma, or reduce contrast sensitivity and colour perception [10-15]. Photodynamic therapy (PDT) [16-20], indicated in cases with leakage points next to or under the fovea and in chronic forms, is another option not without possible side-effects, such as RPE atrophy and localised scotoma. Recent studies proposed the use of half-dose PDT alone [21,22] or followed by subthreshold micropulse laser, a new form of diode laser therapy that utilizes multiple shots of very short duration, usually at wavelength either of 810 nm or 577 nm, minimizing thermal damage to the surrounding structures, particularly the neurosensory retina [23-26]. The possibility of favouring reabsorption of subretinal liquid by stimulating the RPE, even at the fovea, without damaging retinal tissue, has opened new frontiers in CSCR therapy [24-26]. Our therapeutic option for CSCR was subthreshold yellow diode laser micropulse photostimulation (SDM) at a wavelength of 577 nm (IQ-577, Iridex Corporation,

Mountain View, CA), selective for RPE [27-29]. Aim of this prospective nonrandomized study is to evaluate the efficacy and safety of SDM 577 nm in 40 patients affected by chronic CSCR [27-31].

Materials and Methods

40 patients, 27 males and 13 females, with an average age of 50.38 years, diagnosed with CSCR, came to our attention at different times. Symptom history was from a minimum of 2 and a maximum of 9 years (mean 3.92); 5 eyes underwent previous intravitreal therapy with bevacizumab and 3 of these were also treated with photodynamic therapy and verterporfirin, 2 patients were treated with argon laser photocoagulation in addition to the therapies described previously. One patient had argon laser photocoagulation only and all the rest of the cohort had received oral therapies (diuretics, NSAIDS or both). None of the patients experienced improvement as a result of these previous therapies, even for a brief period, and all were free from any treatment for a minimum of 3 months. All patients complained of distorted vision, difficulty in reading and loss of visual acuity. The best corrected visual acuity (BCVA) was measured; applanation tonometry was performed with a Goldmann tonometer and also Amsler test. They underwent fundus examination under pharmacological mydriasis (Volk aspheric lens 90D), spectral domain optical coherence tomography (SD-OCT-Heidelberg Spectralis) and fundus autofluorescence (FAF) with ultrawide field imaging (Optos, Daytona). After obtaining their informed consent, all patients were treated with a single session of SDM 577 nm [27-32]. Our protocol included midriasis with 1% tropicamide drops, topical anaesthesia with 4% benoxinate drops, application of area centralis contact lens (field of view 70/84°, image magnification 1.06X, laser spot 0.94%, Volk Opticals, Mentor on the Lake, OH, USA) and photostimulation. The adopted laser parameters were: confluent spot laser at 70% of the minimum power necessary to obtain retinal whitening in micropulse mode, diameter 100 μm (100 μm × 0.94 laser factor=94 μm), pulse duration 200 ms, 5% DUTY cycle. Laser spots were applied to the whole area of the macula where the neuroepithelium was detached, according to the SD-OCT map and FAF area of hyperautofluorescence. The laser power used in our study ranged from 220 to 510 mW and the average number of burns placed was 578 (126-1348). Patients were medicated with tobramycin and no steroid anti-inflammatory drops (NSAID) twice a day for 15 days. Follow-up, involving evaluation of BCVA, Amsler test, IOP, SD-OCT and FAF, was conducted from 3, 6 to 12 months.

Results

Collected data before treatment and at the follow-up are described in Table 1. Statistical analysis was carried out by Student's t-test for paired data. p-values of ≤ 0.01 were considered statistically significant as showed in Statistical Analysis and in Figures 1a and 1b. Subjective or objective measurable deterioration after treatment was not recorded in any case. None of the patients complained of pain during treatment or follow-up. Five patients (12.5%), three men and two women, had to be retreated after six months and, among them, two men (7.5%) did not obtain resolution of CSCR at 12 months.

No	Age/sex at the time of treatment	Observation period, years	Initial BCVA (ETDRS letters)	Final BCVA (ETDRS letters)	Change in BCVA (ETDRS letters)	Initial CFT μm	Final CFT μm	Change CFT μm
1	45/M	5	93	100	7	438	195	-243
2 (1)	44/M	4	89	95	6	486	233	-253
3 (1)	56/F	9	65	85	20	348	233	-115
4 (1)	58/M	5	73	89	16	419	394	-25
5	58/F	3	73	85	12	485	398	-87
6	53/F	2	50	100	50	383	217	-166
7	38/M	2	80	89	9	216	187	-29
8	52/F	2	97	100	3	343	300	-43
9	45/M	4	85	95	10	436	292	-144
10	74/F	7	85	95	10	315	171	-144
11 (2)	53/M	2	73	89	16	352	162	-190
12 (2)	66/M	2	73	100	27	599	220	-379
13	38/M	2	89	100	11	476	185	-291
14	42/F	2	93	100	7	380	250	-130
15 (2)	54/M	4	85	100	15	504	477	-27
16	45/M	3	80	100	20	369	250	-119
17	45/M	2	89	100	11	437	237	-200

18	47/M	4	50	100	50	265	233	-32
19	49/F	7	85	100	15	503	223	-280
20 (1)	41/M	2	89	100	11	439	274	-165
21	44/M	3	100	100	0	515	289	-226
22	59/M	5	50	73	23	243	163	-80
23	47/M	4	89	95	6	267	202	-65
24	40/M	3	100	100	0	410	285	-125
25	47/M	6	80	100	20	383	229	-154
26 (1)	49/F	8	73	100	27	385	441	56
27	59/M	2	50	50	0	226	379	153
28	50/F	2	65	85	20	200	188	-12
29	67/M	10	50	80	30	241	225	-16
30	50/F	2	65	93	28	451	350	-101
31	51/F	11	85	97	12	444	200	-244
32	65/M	3	65	85	20	286	162	-124
33	48/M	2	97	100	3	269	210	-59
34	45/M	5	100	100	0	623	274	-349
35	57/F	5	85	89	4	300	291	-9
36	49/M	2	89	95	6	308	250	-58
37	46/M	3	73	93	20	312	247	-65
38	41/M	4	73	100	27	637	203	-434
39	60/F	2	89	93	4	425	186	-239
40	38/M	2	73	95	22	516	227	-28

Table 1: Data summary; (1) Retreatment after 6 months, then resolution; (2) Relapse at 12 months follow up

Statistical Analysis

Baseline (mean values)

- BCVA: 78.68 ± 14.81 ETDRS letters (range 100-50, median 82.5);
- IOP: 17.8 mmHg;
- SD-OCT: mean central foveal thickness (CFT) 390.85 ± 102.23 μm (range 200-599, median 444.50); neuroepithelial detachment (NED) in 40 eyes (100%), retinal pigment epithelium detachment (RPED) in 12 eyes (30%), foveal detachment (FD) in 37 eyes (92.5%), subneuroepithelial granulation tissue (SNGT) in 35 eyes (87.5%), irregular macular profile in 40 eyes (100%);
- Amsler test: positive, distorted vision;
- FAF: hyperautofluorescence of fundus in area affected by CSCR in 100% of sample

12 months follow up after SDM photostimulation (mean values)

- BCVA: 93.62 ± 9.73 ETDRS letters (Δm +14.95, +37.73%; range 100-50, median 96) ($p<0.001$);
- SD-OCT: mean CFT: 253.3 ± 22.62 μm (Δm -137.55 μm, -35.19%; range 162-477 μm, median 233.0 μm) ($p<0.001$); residual NED in 5/40 eyes (12.5%), residual RPED in 3/12 eyes (25%), FD in 3/37 eyes (8.1%), SNGT in 3/35 eyes (8.5%), altered neuroepithelial morphology and/or reflectance in 5/40 (12.5%), normal macular profile in 37/40 (91.5%);
- IOP: 17.6 mmHg (Δm -0.09 mmHg);
- Amsler test: negative in 35/40 eyes (87.5%);
- FAF: reduced hyperautofluorescence of fundus in area affected by CSCR in 38/40 eyes (95%), hypoautoflorescence of fundus in photostimulated areas in 5/40 eyes (12.5%);
- SD-OCT: residual NED in 5/40 eyes (12.5%), residual RPED in 3/12 eyes (25%), FD in 3/37 eyes (8.1%), SNGT in 3/35 eyes

(8.5%), altered neuroepithelial morphology and/or reflectance in 5/40 (12.5%), normal macular profile in 37/40 (91.5%).

Discussion

SDM 577 nm has proven to be painless, effective, safe and reliable for the treatment of chronic CSCR29, even in patients with a history of disease exceeding 24 months [32]. Reduction of CFT with consequent alleviation of symptoms (distorted vision) and BCVA improvement were recorded within 90 days of treatment in 85.7% of patients. Most of chronic forms recovered visual and anatomical function as early as the third month of follow-up.

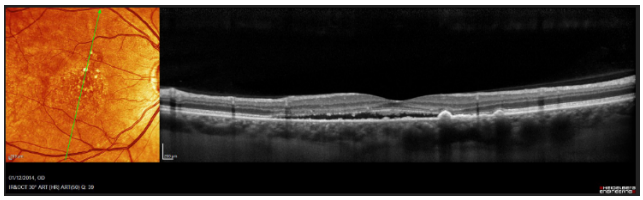

Figure 1a: SD-OCT in a 58-years-old woman with CSC in his right eye lasting from 2 years.

The absence of laser damage to retinal tissue was demonstrated by maintenance of normal anatomy and reflectance of the neurosensory retinal layers observed by SD-OCT. Changes in FAF, consisting in reduction of fundus fluorescence suggesting reduced RPE distress due to lower accumulation and faster clearance of cell metabolites (lipofuscin). At the 12 months follow-up, 35 patients (85.7%) showed complete adhesion of the neuroepithelium to the RPE. In 3/12 eyes (25%) RPED persisted, while in 3/40 eyes (7.5%) minimal hyper-reflecting sub neuroepithelial granulations (SNGT) were detected by SD-OCT but they weren't correlated with functional anomalies perceptible by patients. In 37/40 eyes (91.5%) foveal depression was restored. No significant changes in IOP were recorded in any case during the follow-up period. The success of treatment can be attributed to the stimulation of the RPE30. A major function of this cell layer is maintenance of a natural state of decongestion of retinal tissue by constant turnover and elimination of water from the subretinal space towards the choroid, ensured by the active Na^+/K^+ pump transport mechanism, which together with aquaporin-1 channels, apical interdigitations and the interphotoreceptor matrix, makes the role of the RPE fundamental for adhesion of the neuroepithelium [1,4]. Photostimulation of the RPE cell layer reactivates its fundamental activity with the reabsorption of residual subretinal liquid, typical of CSCR. The Iridex IQ-577 in micropulse mode emits a fractionated flow of energy in a train of brief impulses, the duration and interval of which limit the spread of heat into adjacent tissues, allowing extra time for cooling. The laser does not leave any SD-OCT or ophthalmoscopically detectable trace of its action on the retina, either during or after treatment [33-35]. The laser wavelength of 577 nm has its highest coefficient of absorption in melanin and oxyhemoglobin, present in the RPE and choroid capillaries, and is only minimally absorbed by xanthophylls of the innermost layers of the macular region. This may explain its selectivity for the RPE, and beneficial biological intracellular effects [36-40]. Photostimulation of the RPE reactivates cell metabolism by unclear mechanisms, probably involving production of growth factors (VEGF, PEDF). The possibility to treat CSCR with subfoveal leakage points without causing functional damage opens a new era of non-invasive retinal treatment [41]. At 12-months follow-up all patients had no SD-OCT evidence of neuroretinal alterations. Treatment improved vision and no side effects were recorded in any patient. In conclusion, latest generation IQ-577 aims to elicit cell and molecular changes in the RPE29 for the purpose of restoring homeostasis and physiological stability in the tissues, without resorting to their destruction or damage as demonstrated by SD-OCT evaluation [37,41]. If long-term randomised studies will confirm treatment efficacy, it will be possible to replace current therapeutic procedures, potentially deleterious for retinal tissue, with SDM 577 nm photostimulation.

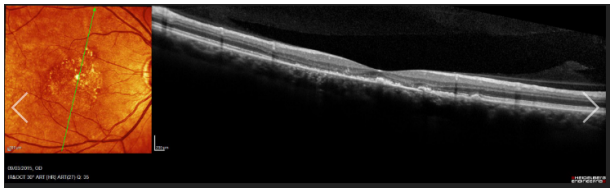

Figure 1b: Same case, 3 months after photostimulation.

Conflict of Interest

The authors have no financial or conflicts of interest to disclose.

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