



ISSN: 0975-833X

Available online at <http://www.journalcra.com>

INTERNATIONAL JOURNAL  
OF CURRENT RESEARCH

International Journal of Current Research  
Vol. 11, Issue, 06, pp.4439-4440, June, 2019

DOI: <https://doi.org/10.24941/ijcr.35378.06.2019>

## REVIEW ARTICLE

### FOCAL AND DIFFUSE CHRONIC CENTRAL SEROUS CHORIORETINOPATHY TREATED WITH HALF-DOSE PHOTODYNAMIC THERAPY OR SUBTHRESHOLD MICROPULSE LASER

Dan Călugăru and \*Mihai Călugăru

Department of Ophthalmology, University of Medicine Cluj-Napoca, Romania

#### ARTICLE INFO

##### Article History:

Received 18<sup>th</sup> March, 2019  
Received in revised form  
26<sup>th</sup> April, 2019  
Accepted 21<sup>st</sup> May, 2019  
Published online 30<sup>th</sup> June, 2019

##### Key Words:

Chronic Central Serous Chorioretinopathy;  
Half-Dose Photodynamic Therapy, High-  
Density Subthreshold micropuls Laser  
Treatment, Pachychoroid Disease  
Phenotype.

\*Corresponding author: Mihai Călugăru

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Citation: Dan Călugăru and Mihai Călugăru. 2019. "Focal and diffuse chronic central serous chorioretinopathy treated with half-dose photodynamic therapy or subthreshold micropulse laser", *International Journal of Current Research*, 11, (06), 4439-4440.

#### INTRODUCTION

We enjoy reading the study by van Rijssen *et al.* (2019) which compared the outcome between high-density subthreshold micropulse laser (HSML) treatment and half-dose photodynamic therapy (PDT) in chronic central serous chorioretinopathy (cCSC) patients, subdivided based on either focal and diffuse leakage on fluorescein angiography (FA). The authors concluded that PDT is superior to HSML treatment in cCSC patients, regardless of the presence of focal or diffuse leakage on FA. However, the study relied on a retrospective analysis of multicenter randomized controlled trial data and had a relatively short-term follow-up (7 – 8 months). Moreover, not all patients could be investigated due to either direct cross-over to the other treatment arm before final visit, loss to follow-up, use of intranasal corticosteroids, or insufficient quality of the data obtained, which might cause an inadvertent bias. Taken together these issues make interpretation of the results challenging, owing to the following reasons:

- The cCSC resides within the pachychoroid disease spectrum. However, the characteristic abnormalities of the pachychoroid disease phenotype and retinal pigment

#### ABSTRACT

The authors are commenting on the article entitled "Focal and diffuse chronic central serous chorioretinopathy treated with half-dose photodynamic therapy or subthreshold micropulse laser" published by van Rijssen *et al.* in *Am J Ophthalmology*. 2019; 205 (September):1-10. The authors concluded that half-dose photodynamic therapy is the preferred treatment over high-density subthreshold micropulse laser treatment for chronic central serous chorioretinopathy patients, both with focal and diffuse leakage on fluorescein angiography. However, the validation, extrapolation, and generalizability of these outcomes can be made only after inclusion in the stepwise multivariate logistic regression analysis of all the missing data mentioned by us in addition to the baseline characteristics already assessed in this study.

epithelium (RPE), which are primarily involved in the cCSC and have a contribution in its pathogenesis, have not been fully documented with the multimodal imaging in both the focal and diffuse leakage groups at presentation and at the completion of the study.

- With reference to the pachychoroid phenotype, there were no data on the assessment of the following alterations: the distribution of the pachyvessels in the Haller's layer (in a diffuse or patchy manner) localized within the areas of increased choroidal vascular hyperpermeability; the focal or diffuse attenuation of the inner choroid (thinning/absence of the choriocapillaris and intermediate caliber vessels within Sattler's layer in areas overlying abnormally dilated Haller's layer vessels); and the focal choroidal excavations. Of note, the perfusion indices (density of blood vessels and flow index) were not calculated for the choriocapillaris zone on the optical coherence (OCT) angiography. In addition, the OCT angiography, which allows detection of choroidal neovascularization (CNV) secondary to cCSC not visible with other imaging techniques (neovascular cCSC) and which seems to be helpful to show an abnormal blood flow corresponding to CNV complicating the cCSC, has not been used.

- Regarding the qualitative status of the RPE, there are no data relating to the OCT patterns of some alterations of the retinal pigment epithelial band – Bruch membrane complex including: pigment migration within the neurosensory retina, RPE porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE hypertrophy, pigment epithelial detachment with internal hyper and hyporeflexivity, and diffuse ooze within or adjacent to the decompensated RPE (Călugăru *et al.*, 2018).
- There were no data referring to the following changes of the overlying photoreceptor cell layer: thinning of the outer nuclear layer, disruption of the ellipsoid zone, elongation of the photoreceptor outer segments, interdigitation zone loss, and external limiting membrane band defects allowing fluid to enter the retina, sometimes referred to as “cystoid macular degeneration” (Călugăru *et al.*, 2018a). Likewise, the OCT location of these intraretinal cystoid spaces without intraretinal leakage on fluorescein angiography (FA) (ganglion cell layer or inner/outer retinal layers) was not highlighted. Moreover, the perfusion indices for the outer retina zone (photoreceptor) were not calculated on OCT angiography. Of note, although the outer retina does not have vessels, the perfusion indices can be still determined.
- The authors substantiated that half-dose PDT was superior to HSML treatment in inducing a complete resolution of subretinal fluid (SRF) irrespective of a focal or diffuse leakage pattern on FA. As regards the assessment of the rest of the parameters investigated, namely, the increases in best-corrected visual acuity, NEI-VFQ25, retinal sensitivity, and central foveal thickness as well as the decrease in subfoveal choroidal thickness (SFCT), the superiority of PDT over HSML treatment was significant only in patients with diffuse leakage who had more extensive choroidal and RPE dysfunctions in comparison with patients with focal leakage. Specifically, no significant differences from baseline to final visit were detected concerning these parameters in the focal leakage group whereas there were significant differences in terms of both the SFCT decrease and retinal sensitivity increase in the diffuse leakage group.
- There were no data on the recurrences of the disease occurred over the follow-up period. The current study

was a subgroup analysis of the Place trial (van Dijk *et al.*, 2018) and included 158 patients out of 179 patients that had been enrolled in the Place trial. Importantly, the Place trial reported 5 patients in whom SRF recurred during the course of the trial, namely, 4 patients in the half-dose PDT group and 1 patient in the HSML group.

Altogether, the validation, extrapolation, and generalizability of the outcomes of this study can be made only by statistical analyses including all the missing data mentioned by us in addition to the baseline characteristics already assessed.

Dan Călugăru  
Mihai Călugăru  
Cluj-Napoca, Romania

**Conflict of interest:** All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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