



ISSN: 0975-833X

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

International Journal of Current Research  
Vol. 10, Issue, 10, pp.74701-74702, October, 2018

DOI: <https://doi.org/10.24941/ijcr.32771.10.2018>

INTERNATIONAL JOURNAL  
OF CURRENT RESEARCH

## REVIEW ARTICLE

# HALF-TIME PHOTODYNAMIC THERAPY IN TREATMENT OF CHRONIC CENTRAL SEROUS CHORIORETINOPATHY

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### ARTICLE INFO

#### Article History:

Received 24<sup>th</sup> July, 2018  
Received in revised form  
18<sup>th</sup> August, 2018  
Accepted 09<sup>th</sup> September, 2018  
Published online 31<sup>st</sup> October, 2018

#### Key words:

Chronic Central Serous Chorioretinopathy;  
Photodynamic Therapy; Best-corrected  
Visual Acuity; Subretinal Fluid.

### ABSTRACT

The authors are commenting on the article entitled "Half-time photodynamic therapy in treatment of chronic central serous chorioretinopathy" published by Sheptulin *et al.* in Graefes Archive for Clinical and Experimental Ophthalmology; <http://dx.doi.org/10.1007/s00417-018-4086-6>. Published online August 10, 2018. The authors concluded that the duration of the symptoms from the chronic central serous chorioretinopathy diagnosis to photodynamic therapy, pigment epithelial detachment, and best-corrected visual acuity before treatment significantly correlated with an achievement of the photodynamic therapy effect. However, the validation, extrapolation, and generalizability of these outcomes can be made only after inclusion in the multivariate stepwise regression analysis of all the missing baseline potential predictive factors mentioned by us in addition to the baseline characteristics already assessed in this study, which serve as potential prognosticators influencing functional and anatomic improvements.

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Citation: Dan Călugăru and Mihai Călugăru. 2018. "Half-time photodynamic therapy in treatment of chronic central serous chorioretinopathy", *International Journal of Current Research*, 10, (10), 74701-74702.

## INTRODUCTION

We would like to address several issues with the study of Sheptulin *et al.* (2018).

- The study was retrospectively conducted with large percentages of patients lost until the months 12 and 24 (64% and 79%, respectively) of the follow-up period.
- The characteristic abnormalities of the choroid (choroidopathy) and the retinal pigment epithelium (RPE) (localized and diffuse retinal pigment epitheliopathy), which are primarily involved in the chronic central serous chorioretinopathy (CSC) and have a contribution in the CSC pathogenesis, have not been substantiated with the multimodal imaging in subjects with chronic CSC of this study (Călugăru *et al.* 2018).
- Importantly, there were no data on the sub foveal choroidal thickness at enrollment and at the end of the study. Noting was stated with regard to the following alterations of the choroid: the choroidal thickening and vascular hyper permeability which can result from focal or diffuse dilatation of large choroidal

vessels, commonly localized within areas of increased choroidal vascular permeability on indocyanine green angiography (ICGA); the thinning of the inner choroidal layer, localized above the dilated choroidal vessels, which includes the loss of medium and small vessels with baring of larger vessels as well as the loss of pigmented cells, with clumping of preserved pigmented cells in various regions in the choroid; 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 tomography (OCT) angiography. In addition, the OCT angiography, should have been used for detection of the choroidal neovascularization (CNV) not visible with other imaging techniques (neovascular chronic CSC) and which appears to be helpful to show an abnormal blood flow corresponding to CNV complicating the chronic CSC.

- The qualitative status of the retinal pigment epithelial band – Bruch membrane complex and grading of the retinal pigment epithelium (RPE) changes (pigment migration within the neurosensory retina, RPE porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE hypertrophy, diffuse or scattered leakage points of fluid through the RPE into the subretinal space on fluorescein angiography, and hyperfluorescent areas of

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leakage seen on ICGA) were not documented in this study.

- There were no data referring to the multimodal imaging of the overlying photoreceptor cell layer, which may suffer progressive and irreversible damages in cases of the chronic CSC because of the persistence of the subretinal fluid caused by pronounced dysfunctional RPE outer blood-retinal barrier. These alterations include outer nuclear layer thinning, external limiting membrane band disruption, discontinuity of the junction between the inner and outer segments, elongation of the photoreceptor outer segments, interdigitation zone loss, intraretinal cystic changes, hyper-reflective deposits frequently accumulated in the subretinal space below the detached neurosensory retina, and decrease in foveal thickness. Moreover, the perfusion indices (density of blood vessels and flow index) 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 comparison between the effective and ineffective photodynamic therapy (PDT) cases revealed the main features of the patients in the unsuccessful PDT-treated group, namely, more advanced age, a greater CSC duration before PDT (2 times higher), and a significantly less best-corrected visual acuity (BCVA). The highlighting of the peculiarities of patients with an absence of the PDT effect would have had also to take into account the following variables: the baseline serum potassium levels, the renal function, the level of endogenous and exogenous corticosteroids, the personality type of the patients, and the testing of patients with regard to the *Helicobacter pylori* infection.

Altogether, the results of this series were beneficial for patients with chronic CSC, namely the half-time PDT was found to be effective in overall 79.8% of the eyes during the sixth months with a subsequent further improvement till 86.84% by the 12<sup>th</sup> month after treatment. The authors concluded that the duration of the symptoms from the chronic CSC diagnosis to PDT,

pigment epithelial detachment, and BCVA before the treatment significantly correlated with an achievement of the PDT effect. However, the validation, extrapolation, and generalizability of these outcomes can be made only after inclusion in the multivariate stepwise regression analysis of all the missing baseline potential predictive factors mentioned by us in addition to the baseline characteristics already assessed in this study, which serve as potential prognosticators influencing functional and anatomic improvements.

**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.

**Acknowledgments/disclosure:** All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No financial disclosures. Both authors (D.C and M.C) were involved in the design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript. The authors have full control over the primary data and they agree to allow the International Journal of Current Research to review their data if requested.

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