Original Article

Half-dose Photodynamic Therapy for Chronic Central Serous Chorioretinopathy

Masood Naseripour[1], MD; Khalil Ghasemi Falavarjani[1], MD; Ahad Sedaghat[1], MD
Arezoo Karimi Moghaddam[1], MD; Sadaf Nasserisina[1,2], Sayyed Amirpooya Alemzadeh[1], MD

[1]Eye Research Center, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
[2]Medical Student Research Committee, Iran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: To report the outcomes of half-dose photodynamic therapy (PDT) in patients with chronic central serous chorioretinopathy (CSC).
Methods: A chart review of patients with chronic CSC who had received half-dose verteporfin PDT (3 mg/m^2) was performed. The main outcome measures were resolution of subretinal fluid and best corrected visual acuity (BCVA).
Results: Fifty-three eyes of 51 patients with mean age of 45.01 ± 8.9 years were studied. Three, 6 and 12 months after half-dose PDT, subretinal fluid was completely resolved in 51 eyes (96.2%). In 2 eyes (one patient), subretinal fluid decreased at 3 months but one year later, an increase in subretinal fluid was detected on optical coherence tomography (OCT) which completely resolved following additional PDT. Another patient with recurrence of subretinal fluid rejected further treatment. Mean baseline central subfield thickness was 385 ± 113.0 μm which was decreased to 235 ± 39.7, 247 ± 49.7, and 244 ± 49.52 μm after 3, 6 and 12 months, respectively (all *P*-values < 0.001). Mean BCVA was 0.33 ± 0.27 LogMAR before PDT and 0.11 ± 0.18, 0.11 ± 0.17, 0.17 ± 0.26 and 0.10 ± 0.23 LogMAR, 3, 6 and 12 months and at final visit (up to 60 months) after PDT, respectively (all *P*-values < 0.001). Improvement ≥2 lines in BCVA occurred in 20 eyes (37.7%). Statistically significant correlations were found between improvement in BCVA and baseline BCVA, baseline central subfield thickness and central subfield thickness after resorption of subretinal fluid (*P* < 0.001, *P* = 0.04 and *P* = 0.01, respectively). No complications attributed to PDT were observed.
Conclusion: Half-dose PDT is effective for treatment of patients with chronic CSC.

Keywords: Optical Coherence Tomography; Central Serous Chorioretinopathy; Photodynamic Therapy

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INTRODUCTION

Central serous chorioretinopathy (CSC) is characterized by serous neurosensory retinal detachment and/or retinal pigment epithelial detachment (PED) at the posterior pole.[1] Typically, acute CSC is a self-limited process which spontaneously resolves within 1-4 months.[1] Accordingly, the current recommendation for management of acute CSC is observation and modification of risk factors.[2,3] Treatment is reserved for patients with fluid persisting more than 3 months, or

Correspondence to:
Khalil Ghasemi Falavarjani, MD. Eye Research Center, Rassoul Akram Hospital, Sattarkhan-Niayesh Street, Tehran 14456, Iran.
E-mail: drghasemi@yahoo.com

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signs of chronicity including pigmentary changes and cystoid macular edema (CME).[1]

Conventionally, application of thermal laser photocoagulation for focal extrafoveal leakage has been shown to result in resolution of CSC.[1-3] In recent years, photodynamic therapy (PDT) has been reported to enhance the absorption of subretinal fluid by reducing choroidal vascular hyperpermeability.[1-3] Considering potential complications of conventional PDT including RPE atrophy, retinal pigment epithelium (RPE) rip and choroidal ischemia, a reduction in PDT fluence, verteporfin dose, or a decrease in both parameters has been suggested.[3]

Several studies, mostly small series, have reported promising results for half-dose PDT in CSC.[4-12] However, further evidence is required to establish the safety and efficacy of this protocol.[1] The aim of the present study is to report the outcomes of half-dose PDT in a large series of patients with chronic CSC.

METHODS

In this retrospective study, medical records of all patients who had undergone PDT for chronic CSC from January 2010 to April 2014 were reviewed. The Ethics Committee of Eye Research Center, Iran University of Medical Sciences, Tehran, Iran approved the study and informed consent for PDT had been obtained from the patients.

Inclusion criteria were persistent subretinal fluid for more than 3 months, or symptoms of less than 3 months' duration associated with signs of chronicity such as RPE abnormalities or CME. Patients with confirmed or suspected chorioretinal disorders other than CSC which can produce subretinal exudation, such as choroidal neovascularization, polypoidal choroidal vasculopathy, or inflammatory retinal detachment, were excluded. Moreover, patients who received intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents or underwent laser photocoagulation during the previous 6 months were excluded. At the time of treatment, no patient was on any medication known to affect CSC.

Main outcome measures were resolution of subretinal fluid and best corrected visual acuity (BCVA) which was measured at baseline, and 3, 6 and 12 months after PDT and at the last examination using a Snellen chart and converted to logarithm of minimum angle of resolution (LogMAR) notations for statistical analysis. Evaluation of macular detachment was performed using a spectral domain optical coherence tomography (SD-OCT) machine (Spectralis, Heidelberg Engineering, Heidelberg, Germany) at each visit. At baseline, combined fluorescein angiography (FA) and indocyanine green angiography (ICGA) was performed in all patients.

PDT was performed by one of the two authors (MN and KGF) by administering half the normal dose (3 mg/m^2) of verteporfin (Visudyne; Novartis AG, Basel, Switzerland). Verteporfin was infused over 8 minutes followed by 83 seconds delivery of laser energy at 693 nm 10 minutes after initiating the infusion. Areas of choroidal hyperpermeability at the posterior pole on ICGA were treated.

Statistical analysis were performed using SPSS software version 15 (SPSS Inc. Chicago, IL, USA), and paired *t*-test and correlation tests were used for analysis. *P*-values less than 0.05 were considered significant.

RESULTS

Fifty-three eyes of 51 patients including 7 female and 44 male subjects with mean age of 45.01 ± 8.9 years were studied. The mean duration of symptoms was 12.6 ± 18.01 months. The subjects were followed for a mean period of 19.51 ± 14.04 (range, 3-60) months. All eyes had OCT imaging examinations at 3-month intervals. Clinical examination and OCT images were available in 27 eyes at 6 months and 23 eyes at 12 months of follow up.

Submacular fluid was present in all eyes at baseline examination. In 3 eyes (5.6%), subretinal fluid did not involve the foveal center and PED was present in 11 eyes (20.7%). Subretinal fluid resolved in 51 eyes (96.2%), 12 months after half-dose PDT. In 2 eyes (one patient), subretinal fluid decreased at the 3-month visit; however, it did not resolve completely and an increase in subretinal fluid was detected on OCT examination one year after PDT. Subretinal fluid completely resolved after additional PDT in this patient. One patient with recurrence of subretinal fluid after complete resorption of fluid (14 months after PDT) refused additional treatment. Mean baseline central subfield thickness was 385 ± 113.0 μm which was decreased to 235 ± 39.7, 247 ± 49.7, and 244 ± 49.52 μm three, six and twelve months after PDT respectively (all *P*-values < 0.001).

Mean BCVA was 0.33 ± 0.27 LogMAR before PDT which was significantly improved to 0.11 ± 0.18, 0.11 ± 0.17, 0.17 ± 0.26 and 0.10 ± 0.23 LogMAR three, six and twelve months after PDT, and at the last visit, respectively (all *P*-values < 0.001). Range of BCVA was 20/20 to 20/200 before and 20/16 to 20/200, 20/20 to 20/100, 20/16 to 20/200, and 20/20 to 20/200 at months 3, 6 and 12, and at the last visit after PDT, respectively. At last follow up, BCVA was improved in 46 eyes (86.7%). An increase of ≥2 lines in BCVA occurred in 20 eyes (37.7%). No eye showed a decrease in BCVA.

No significant correlation was found between improvements in BCVA, and patient age and duration of symptoms (*P* = 0.6 and *P* = 0.8, respectively). Statistically significant correlations were observed between improvements in BCVA and baseline BCVA, baseline central subfield thickness and central subfield thickness after absorption of subretinal fluid (*P* < 0.001, *P* = 0.04, and *P* = 0.01, respectively). More BCVA improvement was found in eyes with worse baseline BCVA, higher

baseline central subfield thickness and lower post-PDT central subfield thickness.

No complications attributed to PDT such as RPE tear or choroidal neovascularization were observed during the follow-up period.

DISCUSSION

The exact cause of CSC remains unclear; however, it is believed that abnormal choroidal vessels play a key role in the pathogenesis of CSC.[1] Increased choroidal hyperpermeability as shown by ICGA suggests that treatment targeted to the choroidal vasculature might be useful in eliminating the cause of the disease.[1] PDT induces transient occlusion of abnormal choroidal vessels and alters choroidal permeability.[13] Previous studies have shown beneficial anatomical and visual outcomes with verteporfin PDT for treatment of chronic or recurrent CSC.[1-12] In the largest reported study, members of the Macula Society were surveyed to collect data on PDT treatment for CSC.[14] A total of 265 eyes were treated with normal or half-fluence PDT and subretinal fluid resolved in 81%. Complications were reported in 5.5% including RPE atrophy in 4% and acute severe decrease in vision in 1.5% of patients.

Considering the complications of standard PDT, and regarding the good baseline and potential for visual acuity recovery in CSC patients, modifications in PDT parameters have been suggested. Reduction of the laser radiation dose to half (half-fluence modification) is more popular than reducing the dose of verteporfin (half-dose PDT).[14] Single-session half-fluence PDT (25 J/cm^2) has been reported to result in complete resolution of subretinal fluid in 84-100% of subjects with a recurrence rate of 0-29% in chronic CSC.[1,8,15,16] Corresponding figures after half-dose PDT are 89.2-100% and 0-17.2%.[1,4,8,11] Three authors directly compared the results of half-dose and half-fluence PDT in chronic CSC. Alkin et al[7]compared 36 eyes after low-fluence PDT and 28 eyes after half-dose verteporfin PDT. Complete resolution of subretinal fluid was found in 91.6% and 92.8% of cases in the low-fluence and half-dose PDT groups, respectively. Nicoló et al[8] reported more rapid absorption of fluid and a more lasting effect with half-dose PDT relative to half-fluence PDT. They found complete resolution of subretinal fluid in 26 half-fluence treated eyes (83.9%) and 29 half-dose treated eyes (100%) at 12 months. Recurrence rate was 29% in the half-fluence group and 17.2% in the half-dose group. In contrast to the mentioned reports suggesting better results with half-dose PDT, Kim et al[12] reported no significant differences in visual or anatomical outcomes of 52 patients after either low-fluence or half-dose PDT (26 patients per group). They reported complete photoreceptor recovery at 12 months in 19 (73%) and 14 patients (54%) in the half-fluence and half-dose groups, respectively (P = 0.150).

Fujita et al[11] reported the largest series of patients with chronic CSC treated with half-dose PDT. They reported that 12 months after PDT, 89.2% of 204 eyes (of 204 patients) had complete resolution of serous detachment. Eleven eyes (5.4%) had persistent subretinal fluid throughout the follow-up period and the recurrence rate was 5.9%. In the present study, we found complete resolution of subretinal fluid in 96.2% of eyes 12 months after half-dose PDT. With additional PDT and at final examination, 98.1% of eyes had complete resolution of subretinal fluid. We found an improvement of BCVA in 46 (86.7%) eyes and an increase of ≥2 lines in BCVA in 20 (37.7%) eyes; this is similar to the findings of previous studies reporting an improvement of one line in 50-84% and at least 2 lines in 26-59% of eyes after PDT.[7,9,14] As evident, a discrepancy exists between the rate of fluid resolution and VA improvement which has also been described in other studies.[14,17] Lim et al[14] proposed that this discrepancy may be explained by irreversible damage to photoreceptors or the underlying RPE, or both due to chronicity of subretinal fluid.

Small sample size, retrospective design, and absence of a control group are major limitations of our study. Furthermore, we did not report the correlation between visual acuity and integrity of retinal layers. Despite these limitations, this is one of the largest series reporting promising outcomes with half-dose PDT in patients with chronic CSC. Although resolution of subretinal fluid was observed in the majority of patients, significant improvement in visual acuity may not occur in all eyes.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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