The One-Year Results of Half-Dose Photodynamic Therapy with Verteporfin in Chronic or Recurrent Central Serous Chorioretinopathy

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Objective: *To evaluate the one-year results of half-dose photodynamic therapy with verteporfin in chronic or recurrent central serous chorioretinopathy (CSC).*

Material and Method: *A Retrospective, consecutive case series. Twenty-seven eyes of 27 patients with chronic symptomatic CSC or recurrent CSC underwent photodynamic therapy (PDT) with half-dose (3 mg/m^2) verteporfin. The demographic data such as age, side, gender, spot sizes of laser photodynamic therapy (PDT) were recorded. The primary outcomes were the best correct visual acuity (BCVA), central foveal thickness using the optical coherence tomography (OCT) and complication were recorded as secondary outcome at baseline, month 1,3,6 and 12 post PDT.*

Results: *At 12 months after half-dose PDT, the mean logMAR BCVA improved from 0.32 to 0.18 ($p = 0.001$), the mean central foveal thickness decreased from 375.52 μm to 186.52 μm ($p < 0.001$). The results also showed significant improvement of logMAR BCVA and decreased central foveal thickness after 1 month (0.32 to 0.22, $p = 0.003$ and 375.52 μm to 175.41 μm, $p < 0.001$) and maintained the results until one-year follow-up. Twenty-five eyes (92.59%) showed complete resolution of subretinal fluid at 1 month, 27 patients (100%) showed complete resolution at 3 month and all sustained the complete resolution until the last visit. No serious complications were recorded during and after the treatment.*

Conclusion: *The half-dose PDT in area of fluorescein leakage is one of the effective treatment options for chronic or recurrent CSC, especially in patients who cannot be performed by focal laser photocoagulation. The treatment sustained the good visual results and has no serious complications up to one-year.*

Keywords: *Central serous chorioretinopathy, Half-dose photodynamic therapy, Verteporfin*

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Central serous chorioretinopathy (CSC) is the accumalation of subretinal fluid and the lead to serous neurosensory retinal detachment at the posterior pole. Patients with CSC may experience visual disturbances including micropsia, metamorphopsia, central scotoma, reduced visual acuity, and loss of contrast sensitivity. However, in the majority of patients, CSC is self-limiting and usually resolves within 3-4 months. In cases of chronic or recurrent CSC with persistence serous retinal detachment, patients might develop progressive visual loss due to cystoid macular edema or decompensation of the retinal pigment epithelium (RPE)[1,2].

The use of indocyanine green angiography (ICGA) in CSC patients has improved the authors knowledge in the pathogenesis of CSC and has demonstrated that CSC primarily affects the choroidal circulation, resulting in multifocal areas of choroidal vascular hyperpermeability[3-5].

The management options of CSC were observation in the first 3 months and direct laser thermal photocoagulation for chronic or recurrent CSC. The direct laser thermal photocoagulation had the disadvantage of causing RPE damage produced permanent scotoma, rarely, iatrogenic choroidal neovascularization so that treatments were suggested only in the extrafoveal location.

Photodynamic therapy (PDT) with verteporfin has been considered for treatment of CSC and many studies have demonstrated beneficial visual outcomes in the majority of patients. The mechanism of action of PDT is postulated to be caused by short-term choriocapillaris hypoperfusion and long term choroidal vascular remodeling, leading to reduction in choroidal congestion, vascular hyperpermeability and

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extravascular leakage. However, the use of conventional PDT in treatment of chronic CSC showed some complication such as RPE atrophy and choroidal neovascularization[6,7]. Recently, many studies demonstrated that the such complications caused by PDT may be minimized with the same treatment efficacy by reducing the dose of verteporfin (half-dose PDT) or altering the timing of infusion and laser application[8-10].

The aim of this study is to evaluate the one-year results of half-dose PDT with verteporfin in the treatment of chronic or recurrence CSC.

Material and Method

Study design and patient recruitment

The present study was a retrospective, consecutive case series conducted in the department of ophthalmology, faculty of medicine, Prince of Songkla University, southern Thailand, between June 2010 and March 2011. All investigations adhered to the tenets of the Declaration of Helsinki and the present study was approved by institutional review board and the ethics committee at faculty of medicine, Prince of Songkla University. All patients with chronic symptomatic CSC (duration more than 3 months) or recurrent CSC with permanent visual deficit were included in the present study.

The inclusion criteria were 1) patients with best corrected visual acuity (BCVA) 20/200 or better and follow-up at least 3 months after treatment. 2) Patients with subretinal fluid and/or retinal pigment epithelium detachment involved the foveal area that showed by optical coherence tomography (OCT). 3) Fundus fluorescein angiography (FFA) demonstrated angiographic leakage characteristics of CSC and located at subfoveal or juxtafoveal area that could not performed with focal laser photocoagulation. The patients with extrafoveal leakage were excluded from the present study.

The exclusion criteria were 1) patients who received previous PDT 2) patients with evidence of choroidal neovascular membrane (CNVM), polypoidal choroidal vasculopathy, or other maculopathy assessed by FFA or ICGA 3) patients who received exogenous steroid treatment, patients with systemic diseases such as Cushing's disease, patient with renal diseases and pregnant patients.

Photodynamic therapy

PDT was performed using half-dose of verteporpin (Visudyne®, Norvatis AG, Bulach, Switzerland)-that is 3 mg/m^2 infusion of verteporfin performed over 8 minutes followed by laser treatment (689 nm) at 10 minutes from the commencement of infusion. A total light energy of 50 J/cm^2 for 83 seconds was delivered to the area of leakage as observed in FFA. The spot size was guided by FFA and treated directly to the leakage points. After treatment, protective spectacles were given and patients were instructed to avoid strong light for 2-3 days.

Baseline and follow-up examinations

All patients were assessed at the baseline and followed at month 1, 3, 6 and 12 after PDT. The BCVA was measured with the Early Treatment Diabetic Retinopathy Study (ETDRS) charts and using the logarithm of the minimum angle of resolution (log MAR) visual acuity for analysis. The OCT recording were performed using an OCT machine (Stratus OCT, Carl Zeiss Meditec Inc, Dublin, CA, USA). The six scans of 6 mm centered on the foveal were obtained for measurement of central foveal thickness (CFT). This CFT was measured manually using the retinal thickness mode and was defined as the distance between the inner surface of the RPE and inner surface of neurosensory retina at the fovea. At the baseline, demographic data such as age, side, gender, type and locations of FFA leakage, spot sizes of laser photodynamic therapy were recorded. The BCVA, CFT and complication were recorded at baseline, month 1, 3, 6 and 12 after PDT.

Data analysis

The primary outcomes measures of the study included the serial changes in logMAR BCVA and central CFT from OCT at 0, 1, 3, 6 and 12 months after the treatments.

The serial comparisons of mean logMAR BCVA and CFT were performed using one-way ANOVA with repeated measurement (using sample size = 21). The p-value less than 0.05 were considered statistical significance.

Results

A total of 27 eyes in 27 patients received the safety modified PDT protocol with half-dose verteporfin. The mean age of patients was 43.67 years (range, 33-58 years) and 25 patients (92.6%) were male. The mean duration of symptoms in the patients was 5.50 months (1-24 months). The FFA showed subfoveal leakage in 4 eyes (14.81%) and juxtafoveal leakage in 23 eyes (85.19%).

The mean logMAR BCVA before half-dose PDT was 0.32 (range, 0.00-1.00) and all patients had subretinal fluid involve the foveal. The mean CFT before half-dose PDT was 375.52 μm (range, 159-638 μm). The mean PDT laser spot size was 2,351 μm (range, 1,000-4,500 μm). All demographic data are demonstrated in Table 1.

The numbers of patients which followed-up at 1, 3, 6 and 12 months was 27 (100%), 27 (100%), 23 (85.18%) and 21 cases (77.78%), respectively. All patients received only 1 session of half-dose PDT and none of patients developed adverse events associated with verteporfin such as drip site complications, low back pain or immediate visual loss after PDT.

Visual acuity changes after half-dose PDT

At 1 month after PDT, the mean logMAR BCVA improved significantly from 0.32 to 0.22 (p = 0.003). At 3 months after PDT, the mean logMAR BCVA further improved to 0.18 (p = 0.01). At 6 months and 12 months after PDT, the mean logMAR BCVA was stable at 0.19 and 0.18 (p = 0.005 and 0.001), respectively (Fig. 1). Totally, at 12 months, the level of visual acuity was improved in 18 eyes (85.7%), unchanged in 2 eyes (9.5%) and decreased in 1 eye (4.8%).

Central foveal thickness (CFT) and anatomical changes after half-dose PDT

At 1 month after PDT, the mean CFT from OCT decreased significantly from 375.52 to 175.41 μm (p < 0.001). At 3, 6 and 12 months, the mean CFT was stabilized at 175.85, 184.87 and 186.52 μm, respectively (p < 0.001). The complete resolution of subretinal fluid at 1 month was achieved in 25 eyes (92.59%) and no eye had subretinal fluid at 3 months after the treatment (Fig. 2).

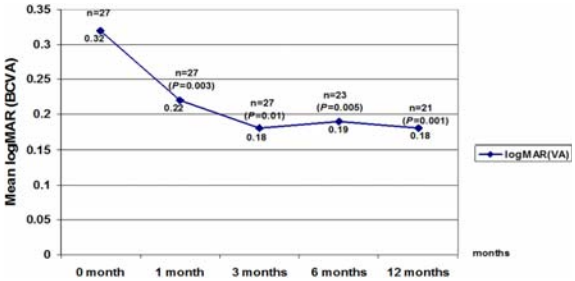
Table 1. The demographic data

Mean Age (years)	43.67 ± 7.27
Sex	
Male (%)	25 (92.59)
Female (%)	2 (7.41)
Duration of symtoms (months)	5.50 ± 5.8
Location of FFA leakage	
Subfoveal leakage	4 (14.81%)
Juxtafoveal leakage	23 (85.19%)
Spot size of PDT (μm)	2,351.85 ± 940.28
BCVA (log MAR)	
At baseline	0.32 ± 0.30
At 12 months post treatment	0.18 ± 0.32
Central foveal thickness (μm)	
At baseline	375.52 ± 122.11
At 12 months post treatment	186.52 ± 42.78
Mean duration of complete resolution (months)	1.15 ± 0.53

FFA = fundus fluorescein angiography, PDT = photodynamic therapy, BCVA = best corrected visual acuity, logMAR = logarithm of minimum angle of resolution, VA = visual acuity, μm = micron

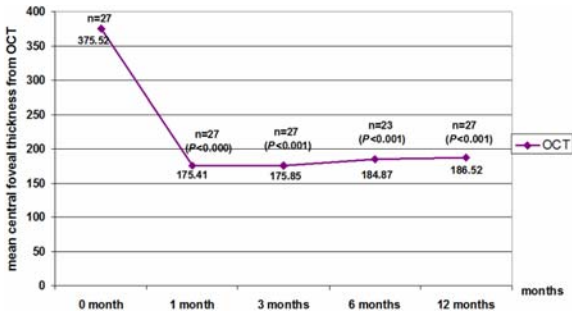
Discussion

The PDT with full-dose verteporfin was demonstrated the good efficacy for treatment of CSC[6,7] but it had many potential adverse events after the treatment. The development of the CNVM after PDT for chronic CSC have reported by Chan et al and Colucciello[7,11]. Moreover, the secondary RPE changes at the site of PDT due to hypoxic damage caused by choriocapillaris occlusion from PDT effect were also reported[6]. For theses awareness, the reduction of verteporfin dosage and the decrease of the interval between the infusion and laser application can



logMAR = logarithm of minimum angle of resolution, BCVA = best corrected visual acuity, VA = visual acuity, p = p-value by one-way ANOVA with repeated measurement

Fig. 1 The serial changes in mean BCVA (logMAR)



OCT = optical coherence tomography, p = p-value by one-way ANOVA with repeated measurement

Fig. 2 The serial changes in central foveal thickness from OCT

enhanced the efficacy and minimizing the side effect of the full-dose PDT. A lower dose of verteporfin might be sufficiency enough to induce choroidal vascular remodeling effect from PDT. The reduction of the drug might also reduce the amount of collateral RPE damage from the treatment. Many current studies demonstrated that use of PDT with half-dose verteporfin for chronic CSC resulted in significant improvement in BCVA and reduction of central foveal thickness following the half dose PDT without serious side effects[8,10].

The present study demonstrated the efficacy of PDT with half-dose verteporfin for chronic CSC and also showed the significant improvement in BCVA and CFT reduction. The treatment effects were showed after 1 month and sustained until the 12 months follow-up. A complete resolution of serous retinal detachment was found in 92.59% after 1 month and all cases after 3 months follow-up. These results suggested that the choriocapillaris was closed after PDT but the subretinal fluid may need up to 3 months period to have a complete resolution. The authors results demonstrated favorably outcomes in term of the rate of complete resolution of subretinal fluid after 3 months comparable with 83.3% reported by Chan in half-dose PDT[10] and 60-83% reported by Ober in full dose PDT[12].

This result suggested that the patients who presented with chronic CSC and had subfoveal or juxtafoveal leakage that cannot safely performed by focal thermal laser could be treated safely by half-dose PDT. The half-dose PDT with verteporfin in this group of patients could significantly improve vision, decrease CFT and have complete resolution of subretinal fluid since early in the first month.

The main limitation of the present study is the lack of a control group using full-dose verteporfin or a placebo group for the comparison. Because there is no head to head comparison, the authors study could not provide any conclusive evidence to answer the question whether chronic or recurrent CSC with subfoveal or juxtafoveal leakage is better than observation or treatment with full-dose verteporfin.

In conclusion, in cases of chronic CSC who showed a clinical favors to treatment and cannot safely performed focal laser treatment, the half-dose PDT is the one of the effective treatment options.

Potential conflicts of interest

None.

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ผลการรักษาผู้ป่วยโรค central serous chorioretinopathy (CSC) ชนิดเรื้อรังหรือเป็นซ้ำด้วยวิธี half-dose photodynamic therapy ในระยะเวลา 1 ปี

พิชัย จิรรัตนโสภา, แมนสิงห์ รัตนสุคนธ์, ปฐมา ภูรยานนทชัย

วัตถุประสงค์: *เพื่อศึกษาผลการรักษาผู้ป่วยโรค central serous chorioretinopathy (CSC) ชนิดเรื้อรังหรือเป็นซ้ำด้วยวิธี half-dose photodynamic therapy ที่ระยะเวลา 1 ปี*

วัสดุและวิธีการ: *การวิจัยย้อนหลังศึกษาผู้ป่วย 27 รายที่ได้รับการวินิจฉัยเป็นโรค central serous chorioretinopathy (CSC) ชนิดเรื้อรังหรือเป็นซ้ำกลับมาใหม่ ที่มีจุดรั่วซึมอยู่ใต้หรือใกล้จุดภาพชัดจากการฉีดสี (fundus fluorescein angiography) และไม่สามารถทำการรักษาด้วยวิธีการยิงเลเซอร์ (focal laser photocoagulation) ผู้ป่วยทั้งหมดได้รับการรักษาด้วยวิธี half-dose photodynamic therapy โดยการศึกษาเก็บข้อมูล ระดับการมองเห็นและความหนาของจุดภาพชัดจากเครื่อง optical coherence tomography ที่ 0,1,3,6 และ 12 เดือนหลังการรักษา รวมถึงบันทึกผลแทรกซ้อนที่อาจจะเกิดขึ้นระหว่างและหลังการรักษา*

ผลการศึกษา: *หลังการักษาเป็นเวลา 12 เดือน พบว่าระดับการมองเห็น (LogMAR BCVA) ดีขึ้นจาก 0.32 เป็น 0.18 ($p = 0.001$), ระดับความหนาของจุดภาพชัดลดลงจาก 375.52 μm เป็น 186.52 μm ($p < 0.001$) โดยพบว่าระดับการมองเห็นดีขึ้น และระดับความหนาของจุดภาพชัดลดลงอย่างมีนัยสำคัญทางสถิติ ($p = 0.003$, $p < 0.001$) ตั้งแต่เดือนแรกหลังการรักษา และคงสภาพผลการรักษาตลอดจนครบหนึ่งปี โดย 25 ตาใน 27 ตา (92.59%) ไม่พบการบวมของจุดภาพชัดที่ 1 เดือน และทุกรายไม่พบการบวมของจุดภาพชัดที่ 3 เดือน นอกจากนี้ยังไม่พบการบวมเป็นซ้ำกลับมาใหม่ตลอด 1 ปีหลังการรักษา รวมทั้งไม่พบผลแทรกซ้อนระหว่างและหลังการรักษา*

สรุป: *การรักษาโรค central serous chorioretinopathy (CSC) ชนิดเรื้อรังหรือเป็นซ้ำกลับมาใหม่ ด้วยวิธี half-dose photodynamic therapy เป็นหนึ่งในการรักษาที่มีประสิทธิภาพ ซึ่งเห็นผลได้ตั้งแต่หนึ่งเดือนหลังการรักษา และพบว่าไม่มีผลแทรกซ้อนที่รุนแรงตลอดหนึ่งปีหลังการรักษา*