Photodynamic Therapy for AMD and Non-AMD Patients: One-Year Results in Thais

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Objective: *To evaluate the effect of photodynamic therapy (PDT) with verteporfin for age-related macular degeneration (AMD) and non-AMD in Thais, and compare with the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) and Verteporfin in Photodynamic Therapy (VIP) study.*
Material and Method: *The authors prospectively evaluated all data of 51 eyes of 51 patients who had undergone PDT and accomplished a 1-year follow up. The assessments were divided into two categories: group 1 included three subsets of AMD, and group 2 was non-AMD. The first group classified into three subgroups: group1A: AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible with recommendation guidelines characteristics, group 1B: AMD with subfoveal CNV and TAP/VIP incompatible, and group 1C: AMD with non-subfoveal CNV. The measurement outcomes comprised of the baseline characteristics, change in visual acuity, and number of treatments.*
Results: *Thirty-eight eyes had CNV-related AMD and 13 eyes were non-AMD. At the 12-month examination, the mean visual acuity change in group 1A, 1B, 1C had increased 0.19 ($p = 0.077$), 0.14 ($p = 0.076$), and 0.24 ($p = 0.003$), respectively. The number of treatments was 1.8 in group 1A, 2.3 in group 1B, and 1.5 in group 1C.*
Conclusion: *PDT is beneficial to Thai patients with AMD at first year, even if they were not compatible with TAP/VIP criteria.*

Keywords: *Photodynamic therapy, Age-related macular degeneration AMD, Non-AMD, Thais*

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Photodynamic therapy (PDT) with verteporfin (Visudyne; Novartis AG, Basel, Switzerland) has been shown to reduce the risk of moderate to severe visual loss in patients with subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration (AMD)[1-5]. It also has benefits in patients with subfoveal CNV due to pathologic myopia or other causes in which the outcome without treatment is likely to be worse than with treatment[6,7]. Based on this information, PDT is considered a standard care for many patients who present with CNV due to AMD and other conditions[8-10]. The similar angiographic and visual effects of PDT were also observed among Caucasian and non-Caucasian patients worldwide[9,10]. The present study reviewed the results of the first 12 months of PDT with verteporfin in Thai patients.

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Material and Method

Fifty-six patients who were prospectively enrolled, and followed up for 12 months, underwent PDT for various etiologies between July 2003 and December 2004 at the Retina unit, Prince of Songkla University, Southern Thailand. Demographic data, diagnosis, and best-corrected visual acuity (BCVA) using Early Treatment of Diabetic Retinopathy Study (EDTRS) chart were collected as baseline. Baseline color photographs and fluorescein angiography (FA) were reviewed by four retina specialists (MR, SV, PH &

DP). The lesion composition was classified according to TAP/VIP criteria, with at least three consensuses of the reviewers.

The subjects were scheduled to assess visual acuity (VA), color photograph, and FA every three months. PDT with verteporfin was recommended if any fluorescein leakage was detected. Interview was conducted to determine adverse events (AE) and visual rehabilitation.

The assessments were divided into two categories: group 1 included three subsets of AMD, and group 2 was non-AMD. The first group was classified into three subgroups. Firstly, group1A: AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible with recommendation guidelines characteristics; 1) the greatest linear dimension (GLD) $\leq$ 5400 □m, and 2) for predominantly classic or minimally classic subfoveal CNV, the BCVA should be 20/40 to 20/200, and 3) for occult with no classic subfoveal CNV, the BCVA should be approximately 20/100 or better. Secondly, group 1B: AMD with subfoveal CNV and TAP/VIP incompatible characteristics. Thirdly, group 1C: AMD with non-subfoveal CNV such as juxtafoveal or extrafoveal CNV. The measurement outcomes comprised of the baseline characteristics, change in visual acuity, and number of treatments. The changes in BCVA were compared between baseline till 12-months follow-up.

The primary outcome was the change in BCVA from baseline till the 12 months follow up period. Paired t-test and Chi-squares tests used where appropriate. All data were expressed as mean and standard deviation (SD). A p-value of less than 0.05 was considered significant difference between groups.

Results

All of fifty-six clients, there were four cases had lost follow up, and one who voluntarily refused the continuous treatment. At last, 51 eyes of 51 patients (91%) had accomplished the 1-year follow up. Thirty-eight eyes (74.5%) had CNV-related AMD and 13 (25.5%) were non-AMD.

The 38 eyes that had CNV-related AMD comprised of 12 eyes in group 1A (31.6%), 18 in group 1B (47.3%), and 8 in group 1C (21.1%). Group 1A included four eyes of predominantly classic CNV, four eyes of minimally classic CNV, and four eyes of occult with no classic CNV. Group 1B included five eyes of predominantly classic CNV, three eyes of minimally classic CNV, and 10 eyes of occult with no classic CNV. The eight eyes of group 1C were graded incompatible on the basis of non-subfoveal CNV.

In group 1A (12 eyes), 11 eyes (91.7%) lost less than 15 letters, eight eyes (66.7%) gained more than 0 letters, and six eyes (50%) gained $\geq$ 15 letters. The mean BCVA at the 12-month visit (20/56 or 0.45 logMAR) was slightly improved compared to the mean baseline BCVA (20/87 or 0.64 logMAR) (increased 0.19 logMAR, p = 0.077). The average total number of treatments in this group was 1.8 (Table 1).

In group 1B (18 eyes), with the average GLD of 4799 □m, eight eyes (44.4%) had GLD beyond 5400 □m and half of them had baseline BCVA worse than 20/200. For the eyes with GLD less than 5400 □m, two eyes (11.1%) had baseline BCVA better than 20/40 and eight eyes (44.4%) had baseline BCVA that was not compatible with TAP/VIP criteria. At the 12-month follow-up, 17 eyes (94.4%) lost less than 15 letters, nine eyes (50%) gained more than 0 letters, and six eyes (33.3%) gained $\geq$ 15 letters (Table 2). The mean BCVA at 12-month visit (20/142 or 0.85 logMAR) was slightly improved compared with baseline (20/195 or 0.99 logMAR) (increased 0.14 logMAR, p = 0.076). The average total number of treatments in this group was 2.3 (Table 1).

Table 1. Baseline characteristics and treatment outcome of AMD eyes at 12-month follow up

Study group (eyes)	Average age (years)	Mean GLD (□m)	Mean baseline BCVA (LogMAR)	Mean 12-month BCVA (LogMAR)	p-value	Average total number of treatments
Group 1A (12 eyes)	67	2797	0.64	0.45	0.077	1.8
Group 1B (18 eyes)	67	4799	0.99	0.85	0.076	2.3
Group 1C (8 eyes)	62	3069	0.69	0.45	0.003	1.5

BCVA = best corrected visual acuity, LogMAR = logarithm of minimal angle of resolution, GLD = greatest linear dimension
Group1A: AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible
Group 1B: AMD with subfoveal CNV and TAP/VIP incompatible
Group 1C: AMD with non-subfoveal CNV

Table 2. The changes of visual acuity in the treatment of AMD eyes

Parameter	Group 1A (n = 12)	Group 1B (n = 18)	Group 1C (n = 8)
Mean VA change (letters ± SD)	8.9 ± 17.0	7.0 ± 16.0	12.6 ± 7.3
VA loss < 15 letters	11 (91.7%)	17 (94.4%)	8 (100%)
VA gain > 0 letter	8 (66.7%)	9 (50%)	8 (100%)
VA gain ≥ 15 letters	6 (50%)	6 (33.3%)	3 (37.5%)
VA 20/200 or worse			
- baseline	2	11	2
- 12-month	1	9	1
VA 20/40 or better			
- baseline	2	3	0
- 12-month	6	4	2

VA = visual acuity, SD = standard deviation
Group 1A: AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible
Group 1B: AMD with subfoveal CNV and TAP/VIP incompatible
Group 1C: AMD with non-subfoveal CNV

Table 3. Baseline characteristics and treatment outcome of non-AMD eyes at 12-month follow up

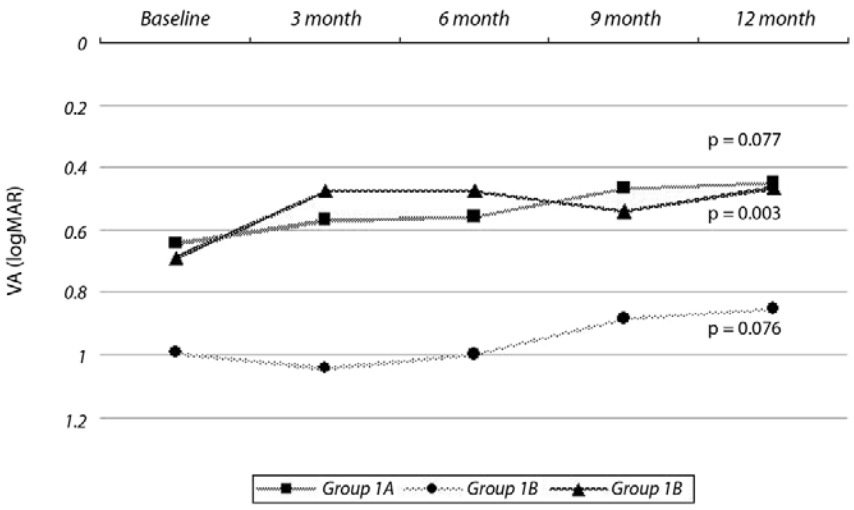
No.	Age (years)	Diagnosis	GLD (□m)	Baseline BCVA treatments	12-month BCVA	No. of visit
1	46	Idiopathic CNV	3000	20/125	20/80	3
2	34	Idiopathic CNV	1625	20/40	20/63-2	3*
3	45	Idiopathic CNV	3031	20/80+2	20/32+1	2
4	45	Idiopathic CNV	3142	20/200	20/32	1
5	45	Idiopathic CNV	2240	20/25	20/25-2	2
6	23	Idiopathic CNV	2979	10/200	20/63	1
7	31	Idiopathic CNV	1479	20/25	20/25-1	2
8	16	CNV in PM	1100	20/200-2	20/25-1	1
9	60	CNV in PM	3865	20/200-1	20/160-1	1
10	44	CSC	2885	20/25+2	20/25+2	1
11	46	CSC	4010	20/50-2	20/50	1
12	56	Choroidal hemangioma	5500	Counting fingers	5/200	2
13	62	Adult vitelliform dystrophy	5583	20/100+2	20/50	1

GLD = greatest linear dimension, □m = micron, BCVA = best corrected visual acuity,
CNV = choroidal neovascularization, PM = pathologic myopia, CSC = central serous chorioretinopathy
* FA showed progression of leakage, patient was scheduled for the next PDT

In group 1C (8 eyes), all eyes were graded incompatible on the basis of non-subfoveal CNV. At the 12-month follow-up, all eyes gained more than 0 letters and 3 eyes (37.5%) gained ≥ 15 letters. The mean BCVA at the 12-month visit (20/56 or 0.45 logMAR) significantly improved compared to baseline (20/98 or 0.69 logMAR) (increased 0.24, p = 0.003). The average total number of treatments in this group was 1.5 (Table 1). The progression of the visual acuity score in each subgroup is summarized in Fig. 1

The 13 eyes of the later group (non-AMD) included seven eyes of idiopathic CNV, two eyes of CNV in pathologic myopia (PM), two eyes of central serous chorioretinopathy (CSC), one case of adult vitelliform dystrophy, and one case of choroidal hemangioma. Baseline characteristics and treatment outcome of non-AMD eyes at 12-months follow up are shown in Table 3.

Acute severe visual acuity decrease after PDT with verteporfin was an uncommon event; the risk did



VA = visual acuity, LogMAR = logarithm of minimal angle of resolution
Group 1A: AMD with subfoveal choroidal neovascularization (CNV) and TAP/VIP compatible
Group 1B: AMD with subfoveal CNV and TAP/VIP incompatible
Group 1C: AMD with non-subfoveal CNV

Fig. 1 Distribution of mean visual acuity score of three subgroups of AMD

not outweigh the benefits of therapy previously reported. When considering verteporfin therapy, patients should be warned of the possibility of this serious adverse event[11]. The present study, two (out of 51) eyes (3.9%) experienced acute severe visual acuity loss that manifested on the day following PDT[12]. The findings revealed the exudative retinal detachment on fundal examination that completely disappeared within one week. Additionally, four eyes (7.8%) had minimal to severe back pain during infusion of verteporfin.

Discussion

From previous studies, various diseases seem to achieve benefit from PDT[1-8,13-15]. In group 1A, the authors included patients who were treated with PDT according to the updated guidelines[8]. At 12-months follow up, 91.7% of eyes in group 1A showed BCVA loss less than 3 lines and 50% gained $\geq$ 3 lines. These results demonstrated better visual results than TAP/VIP studies but were closely related to Japanese Age-Related Macular degeneration (JAT)[11] trial. The JAT trial showed 73% of verteporfin treated eyes had maintained or improved vision (BCVA loss less than 3 lines or improved vision) whereas TAP and VIP studies showed 67% and 49% respectively. Moreover, the mean number of treatments in the present study group was 1.8, which was similar to 1.96 in Chinese eyes[16] but lower than 2.8 from JAT, 3.4 from TAP, and 3.1 from VIP study. For the lesser number of treatments, the possible explanation could be late recognition or late visual awareness of the patients so that the beginning of verteporfin therapy might be in the late stage of the disease, reflecting the lesser number of treatments in the present study. The other explanation of lesser number of treatments and the better visual results was the possibility of idiopathic polypoidal choroidal vasculopathy (IPCV). The authors did not perform indocyanine green angiography (ICGA) in all the cases so the possibility of IPCV mimicking CNV-related AMD cannot be ruled out. With the expected incidence of IPCV in Asian eyes to be approximately 25%[17], the actual percentage of CNV-related AMD eyes with less than 3-line BCVA loss in the present study group might decrease from 91.7% to approximately 70% (68.8%). Even after taking out the possibility of IPCV from the analysis, the present study still showed good visual results that were comparable with the standard studies.

A similar pattern of visual acuity change was observed in eyes with subfoveal CNV from AMD incompatible with TAP/VIP (group1B). Although the baseline characteristics suggested poorer prognosis than group 1A, 94.4% lost less than 3 lines and 33.3%

of eyes still gained ≥ 3 lines at 12-months follow up. The p-value of BCVA change showed slightly significant improvement the same as in group 1A.

For the eye with juxtafoveal or extrafoveal CNV (group 1C), significant visual improvement was observed in the present study (p = 0.003). Blaire et al[18] reported the mean visual acuity change of 0 lines in 19 patients with juxtafoveal CNV. They speculated the progression of CNV beyond subfoveal location could be associated with substantial visual loss. However, no eye in group 1C in the present study developed subfoveal CNV at the 12-month follow up so the BCVA change in this group showed significant improvement as expected.

In the non-AMD group (group 2), many studies showed good visual results in various etiologies. In the present study, the mean improvement in BCVA of idiopathic CNV was 2.8 lines. This visual improvement might not relate to previous reports[19,20] as most of the cases of idiopathic CNV (79%) in the present study were non-subfoveal CNV, and some of them might be IPCV, which showed better results[21]. In addition, the authors have also treated some patients from various etiologies. Nevertheless, although the visual results in this group were excellent, the visual analysis was limited because of the small sample size.

The treatment with PDT was well tolerated in Thai patients. Infusion related-back pain in four patients was transient and occurred only during the infusion of the verteporfin. Acute severe visual loss in two eyes resulted from temporary neurosensory detachment rather than subretinal hemorrhage and disappeared completely after one week.

In conclusion, PDT seems to be a promising treatment strategy in achieving improvement or stabilization of vision in Thais. PDT also appeared to be promising in patients where a lesion was incompatible with TAP/VIP criteria. Further studies and longer follow-up are warranted to assess long-term safety and efficacy of PDT in Thai patients.

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การรักษาผู้ป่วย AMD และ non-AMD ด้วย photodynamic therapy: ผลการรักษา 1 ปีในคนไทย

แมนสิงห์ รัตนสุคนธ์, ศิริรักษ์ วิเศษศิลปานนท์, ภฤศ หาญอุตสาหะ, ดิเรก ผาติกุลศิลา

วัตถุประสงค์: *เพื่อประเมินประสิทธิผลของการรักษาผู้ป่วยโรคจุดภาพชัดเสื่อม (age-related macular degeneration - AMD) และผู้ป่วยที่ไม่เป็นโรคจุดภาพชัดเสื่อม (non-AMD) ด้วยวิธี photodynamic therapy (PDT) ในคนไทย เปรียบเทียบผลการรักษากับการศึกษา treatment of age-related macular degeneration with photodynamic therapy (TAP) และ verteporfin in photodynamic therapy (VIP) study*

วัสดุและวิธีการ: *เก็บรวบรวมข้อมูลผู้ป่วยแบบไปข้างหน้า จากการรักษาตา 51 ข้างด้วยวิธี PDT ในผู้ป่วย 51 คน และสามารถติดตามผลการรักษาได้ครบ 1 ปี การประเมินแบ่งเป็นสองกลุ่ม กลุ่มแรกเป็นผู้ป่วยโรคจุดภาพชัดเสื่อม สามกลุ่มย่อย คือ กลุ่ม 1A เป็นผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี choroidal neovascularization (CNV) ชนิด subfovea และมีลักษณะตรวจพบตรงตามข้อบ่งชี้ในการรักษาด้วย PDT จากการศึกษา TAP/VIP กลุ่ม 1B เป็นผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี CNV ชนิด subfovea แต่มีลักษณะตรวจพบไม่ตรงตามข้อบ่งชี้ กลุ่ม 1C ผู้ป่วยโรคจุดภาพชัดเสื่อมที่มี CNV แบบ non-subfovea ส่วนกลุ่ม 2 เป็นผู้ป่วยที่ไม่เป็นโรคจุดภาพชัดเสื่อม การวัดผลที่ได้รับประกอบด้วยลักษณะตรวจพบก่อนรักษา การเปลี่ยนแปลงระดับการมองเห็น และจำนวนครั้งของการรักษา*

ผลการศึกษา: *จากทั้งหมดมีตา 38 ข้างเป็นโรคจุดภาพชัดเสื่อมและ 13 รายไม่เป็นโรคจุดภาพชัดเสื่อม การตรวจหลังการรักษา 12 เดือน พบว่าระดับการมองเห็นของผู้ป่วยในกลุ่ม 1A, 1B, 1C เพิ่มขึ้น 0.19 ($p = 0.077$), 0.14 ($p = 0.076$) และ 0.24 ($p = 0.003$) ตามลำดับ ส่วนจำนวนครั้งของการรักษาเท่ากับ 1.8 ในกลุ่ม 1A, 2.3 ในกลุ่ม 1B และ 1.5 ในกลุ่ม 1C*

สรุป: *การรักษาผู้ป่วยโรคจุดภาพชัดเสื่อมด้วยวิธี PDT ได้ประโยชน์ในผู้ป่วยคนไทย ให้ผลการรักษาที่น่าพึงพอใจในผู้ป่วย แม้ว่ามีลักษณะตรวจพบไม่ตรงกับเกณฑ์การรักษาจากการศึกษา TAP/VIP*