

Photodynamic therapy to treat choroidal neovascularisation in highly myopic patients: 4 years' outcome

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ABSTRACT

Aims: To report the visual outcome in a series of eyes with myopic choroidal neovascularisation treated by photodynamic therapy (PDT) followed during 48 months.

Methods: Prospective, consecutive, non-randomised interventional case series. Thirty-nine eyes from 36 highly myopic patients treated by PDT were evaluated. Best corrected visual acuity (BCVA) and fluorescein angiography were performed every 3 months. Multiple regression analysis was used to analyse changes in BCVA in relationship with initial BCVA, spherical equivalent, age, diameter of CNV and chorioretinal atrophy.

Results: Mean initial BCVA was 9.0 Early Treatment Diabetic Retinopathy Study lines (SD 4.3). BCVA was 10.4 lines (3.6) at month 12, 9.7 lines (SD 3.9) at month 24, 9.6 lines (SD 3.8) at month 36 and 9.6 lines (SD 4.2) at month 48. BCVA improvement was associated with initial BCVA ($p < 0.002$), lesion diameter ($p < 0.04$) and age ($p < 0.04$) (multiple regression analysis).

Conclusions: Our results suggest a better visual outcome for those eyes with better initial BCVA and larger lesions in younger patients treated by PDT. The poorer results for elderly patients with lower initial BCVA might lead us to consider other therapeutic approaches.

High myopia affects approximately 2% of general population¹ and is a major cause of legal blindness in many developed countries.²

Choroidal neovascularisation (CNV) is the most common vision-threatening complication of high myopia.³ Different therapeutic approaches have been attempted such as thermal laser photocoagulation,⁴ radiotherapy,⁵ surgery^{6,7} and photodynamic therapy with verteporfin (PDT).⁸ The visual outcome of PDT has been reported to be better than the prior therapies or the natural history of this condition.⁹ However, the need for repeated PDT sessions and the appearance of subretinal fibrosis¹⁰ and chorioretinal atrophy¹¹ has prompted the association of other therapies such as the intravitreal injection of steroids.¹²

We report the visual and anatomical outcome of a series of highly myopic patients treated by PDT over 4 years.

PATIENTS AND METHODS

Thirty-six consecutive patients (39 eyes) with subfoveal CNV secondary to high myopia were followed and treated by PDT for at least 4 years at the Retina Unit at the Alicante Institute of Ophthalmology (Spain). Inclusion criteria were: (1) high myopia as defined by refractive error ≥ -6 dioptres (D) and/or axial length longer than

26 mm and characteristic fundus changes; (2) presentation within 6 months of visual acuity loss; (3) fluorescein angiographic documentation of CNV; (4) no previous macular laser; (5) no intraocular surgery in the previous 2 months; (6) best corrected visual acuity (BCVA) $\leq 20/40$; (7) no other ocular disorders, such as angioid streaks or age-related macular degeneration that might cause subfoveal CNV. Pregnant or nursing patients, and patients with diabetic retinopathy, or other causes of visual loss not related to myopic maculopathy were excluded.⁸

The initial evaluation included refraction, BCVA performed with the Early Treatment Diabetic Retinopathy Study (ETDRS) charts (Lighthouse International, New York), slit-lamp examination, tonometry, fundus examination using indirect ophthalmoscopy and fluorescein angiography (FA). This exam was repeated on a 3-month schedule. Verteporfin PDT was performed as described previously.¹³ Patients received further PDT sessions in those cases when fluorescein leakage was identified. PDT was performed not earlier than 3 months after the last session, and not later than 1 week after the last FA.

RESULTS

Thirty-nine eyes (16 right, 23 left) from 36 highly myopic patients (14 male and 22 female) with subfoveal classic CNV treated by PDT completed 4 years follow-up, though some patients occasionally missed one of the visits. The demographics of the patients and the changes in BCVA are described in table 1 and fig 1.

Eighteen eyes gained two to seven lines (46%), 10 eyes (26%) remained stable within one line basal BCVA, and 11 eyes (28%) lost two to six lines by the end of the follow-up period. CNV was completely inactive by the end of month 48 in 38 eyes (97%). Six eyes (15%) needed one PDT session, eight eyes (21%) needed two sessions, five eyes (13%) needed three sessions, 11 eyes (28%) needed four sessions, six eyes (15%) needed five sessions, and three eyes (8%) needed six sessions.

A multiple regression test showed a statistically significant correlation between BCVA gain and initial BCVA ($p < 0.002$) at all time intervals; BCVA gain and lesion diameter ($p < 0.04$) at all time intervals; and BCVA gain and age between months 6 and 24 ($p < 0.04$).

Fundus examination and FA showed a variable degree of chorioretinal atrophy as described by Avila *et al.*¹⁴ Grade 1 atrophy appeared in 12 eyes

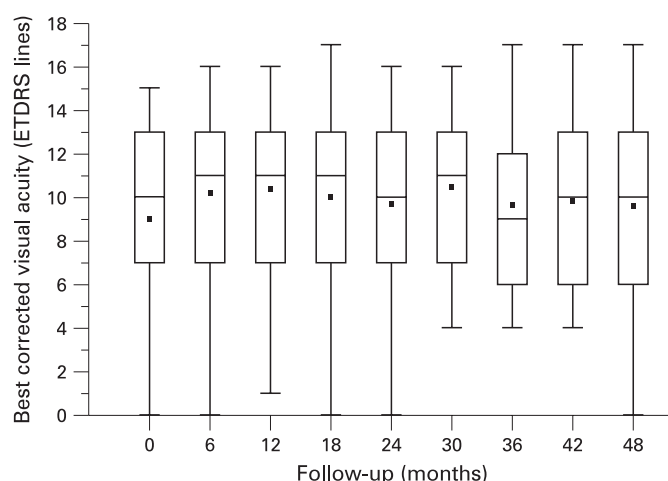


Figure 1 Median and interquartile range values of best corrected visual acuity after photodynamic therapy during a 2-year follow-up. ETDRS, Early Treatment Diabetic Retinopathy Study.

(31%), Grade 2 in eight eyes (20%), Grade 3 in 12 eyes (31%) and Grade 4 in seven eyes (18%).

DISCUSSION

The reports on the natural history of CNV in highly myopic patients show that the long-term visual outcome of myopic CNV is extremely poor due to the development of chorioretinal atrophy around the regressed CNV.¹⁵ These findings encouraged the search for active treatments to prevent long-term visual impairment in patients with myopic CNV. The VIP clinical trial concluded that PDT increased the chances of stabilisation or improvement of visual acuity compared with sham treatment at 1 year.¹³

To our knowledge, this is the longest follow-up reported so far for PDT to treat myopic CNV. We have found visual acuity stabilisation or improvement in 72% of the cases in our series, in agreement with the results reported by other groups for long-term follow-up. Pece *et al* have reported stable or improved vision in 76% of the myopic eyes with juxtafoveal CNV treated by PDT.¹⁶

A better visual prognosis has been previously reported for younger patients and for those with higher spherical equivalent, both as part of the natural history of the condition¹⁷ and after PDT.¹⁶ We have reported similar results in a previous series with shorter follow-up.⁸ In this series with a longer follow-up, the BCVA gain was significantly better for younger patients between months 6 and 24, though the difference was no longer significant for longer follow-up. We have found no correlation between BCVA gain and spherical equivalent, sex, number of PDT sessions or choriocapillaris atrophy (multiple regression analysis).

A better final BCVA among younger patients and among those with better initial BCVA may be associated with a better initial chorioretinal condition such as less scarring and less choriocapillaris atrophy. We may consider that age may play a role inducing choriocapillaris sclerosis and retinal pigment epithelium defects as has been reported for chorioretinal atrophy, which will reduce the chances for improving final BCVA.¹⁸

Our series show BCVA stabilisation or improvement in most of the patients during the first year, though the improvement was not statistically significant after 4 years' follow-up.

Table 1 Demographics and changes in best corrected visual acuity measured in Early Treatment Diabetic Retinopathy Study (ETDRS) lines

	Mean (SD)
Spherical equivalent	-12.9 (6.0)
Age	48.9 (13.0)
Sex (female/male)	22/14
Choroidal neovascularisation diameter	1507 (782)
Total photodynamic therapy sessions	3.3 (1.5)
ETDRS lines baseline (n = 39)	9.0 (4.3)
ETDRS lines 6 months (n = 38)	10.2 (3.6)
ETDRS lines 12 months (n = 37)	10.4 (3.6)
ETDRS lines 18 months (n = 37)	10.0 (3.6)
ETDRS lines 24 months (n = 34)	9.7 (3.9)
ETDRS lines 30 months (n = 33)	10.5 (3.6)
ETDRS lines 36 months (n = 34)	9.6 (3.8)
ETDRS lines 42 months (n = 33)	9.7 (3.8)
ETDRS lines 48 months (n = 39)	9.6 (4.2)
ETDRS lines gain (baseline-12)	p = 0.006 (Student t test for paired data)
ETDRS lines gain (baseline-24)	p = 0.30 (Student t test for paired data)
ETDRS lines gain (baseline-36)	p = 0.97 (Student t test for paired data)
ETDRS lines gain (baseline-48)	p = 0.38 (Student t test for paired data)

We have also found a positive correlation between the number of lines gained and the initial diameter of the lesion. Patients with a low initial BCVA associated with greater diameter lesions may show more vision gain as the lesion becomes inactive than those with smaller lesions in whom a poor initial BCVA may be associated with other causes different from CNV. The progressive decrease in BCVA gain in the long term follow-up may be attributed to the appearance of fibrosis and alterations in the area of the outer photoreceptor segments and RPE.¹⁹

During the past 3 years, the lack of satisfaction after PDT in patients with CNV secondary to high myopia has prompted the association of PDT with intravitreal steroids.^{12–20} These papers reported better results for the subgroup of patients with greater diameter of CNV and worse initial visual acuity. However, the effect of combined therapy was similar to PDT alone on the whole group of patients and on those patients with better initial BCVA and smaller CNVs. These relatively positive results were associated with a considerable risk of increased intraocular pressure and cataracts.

The new antiangiogenic drugs may show a new approach for the treatment of myopic CNV with good results.^{21–22} However, we must bear in mind the risk of repeated intravitreal injections in myopic eyes with a higher risk of retinal detachment due to the more frequent presence of degenerative lesions and peripheral vitreoretinal adhesions. Another point which is still to be considered is the potential risk for teratogenicity among younger patients.

Our results suggest a better visual outcome for those eyes treated by PDT with better initial BCVA and larger lesions, occurring in younger patients after a 4-year follow-up. The poorer results for elderly patients with lower initial BCVA might lead us to consider other therapeutic approaches.

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Competing interests: None.

Ethics approval: The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Patient consent: Written informed consent was obtained prior to the therapy and data gathering.

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