PHOTODYNAMIC THERAPY WITH VERTEPORFIN IN CHOROIDAL NEOVASCULARIZATION AFTER REFRACTIVE SURGERY

TERAPIA FOTODINÁMICA CON VERTEPORFINA EN NEOVASCULARIZACIÓN COROIDEA DESPUÉS DE CIRUGÍA REFRACTIVA

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ABSTRACT

Purpose: To analyze the results obtained with Photodynamic Therapy (PDT) to treat subfoveal and juxtafoveal Choroidal Neovascularization (CNV) in patients with high myopia corrected by Laser-Assisted in situ Keratomileusis (LASIK) or by implanting a Phakic Intraocular Lens (PIOL).

Methods: We analyzed the results from 14 highly myopic eyes corrected by LASIK (seven cases) or by PIOL implantation (seven cases), which later developed CNV and were treated by PDT with verteporfin.

Results: Mean Best Corrected Visual Acuity (BCVA) after refractive surgery was 0.45 SD 0.17 (range, 0.2 to 0.8), with residual spherical equivalent (RSE) -0.5 SD 1.8 D (range, 1 to 5.5 D). After CNV appearance, BCVA was 0.10 SD 0.19 (range, 0.025 to 0.7). CNV was treated in all cases by PDT (mean, 2.0 SD 0.8 treatments). After CNV closure, the mean BCVA improved up to 0.22 SD 0.18 (range, 0.1 to 0.63) (RSE -1.4 SD 1.4 D, range, 0.5 to -4 D). Differences in RSE after refractive surgery

RESUMEN

Propósito: Analizar los resultados obtenidos usando TFD (terapia fotodinámica) con verteporfin como primera elección para tratar la NVC (neovascularización coroidea) subfoveal y yuxtafoveal en pacientes con miopía magna corregida mediante cirugía refractiva (laser-assisted in situ keratomileusis –LASIK– y lentes fáquicas de cámara anterior – LFCA–).

Método: Se estudiaron catorce ojos que presentaban alta miopía a los que se les había realizado LASIK (siete casos) o implante de lente intraocular –LIO– (siete casos), que desarrollaron NVC y fueron tratados con TFD con verteporfin.

Resultados: La media Mejor Agudeza Visual Corregida (MAVC) después de la cirugía fue 0,45 (DE: 0,17; rango: 0,2 a 0,8), con equivalente esférico residual (EER) -0,5 (DE: 1,8D; rango: 1 a 5,5D). La MAVC después de NVC fue 0,10 (DE: 0,19; rango: 0,025 a 0,7). NVC fue tratada en todos los casos por PDT (media, 2,0 DE: 0,8 tratamientos). Después de la cierre de NVC, la media MAVC mejoró hasta 0,22 (DE: 0,18; rango: 0,1 a 0,63) (EER -1,4 DE: 1,4D; rango: 0,5 a -4D).
INTRODUCTION

Choroidal Neovascularization (CNV) is an infrequent but important complication in eyes withMagnus Myopia (MM) (1-4) which can appear after refractive surgery. The appearance of CNV has been described after photorefractive keratectomy (5), after laser-assisted in situ keratomileusis (LASIK) (6) and after anterior chamber phakic lenses (ACPL) (7).

Before the appearance of anti-angiogenic therapy and its good results in preliminary studies (8-11), extra-foveal CNV was treated by means of thermal laser photo-coagulation. Macular translocation (12-14) and photodynamic therapy (PDT) with verteporfin were reserved for treating sub-foveal (15-17) and juxta-foveal CNVs (7) in myopic eyes.

The objective of this article is to analyze the results obtained utilizing PDT with verteporfin as the first choice for treating sub-foveal and juxta-foveal CNS in patients with MM corrected with refractive surgery (LASIK and ACPL).

SUBJECTS, MATERIAL AND METHODS

Fourteen patients with MM (14 eyes) corrected with refractive surgery who had developed sub-foveal and juxta-foveal CNS were examined at the Retina and Vitreous Service of the Ophthalmological Institute of Alicante (12 patients, LASIK or ACPL) and in the Centro Ophthalmological Clinic of Caracas (two patients, LASIK) and included for their study.

Las diferencias en EER después de cirugía refractiva y después de TFD, y las diferencias en MAVC antes y después de TFD no fueron estadísticamente significativas (p=0.82 y p=0.06, respectivamente, aplicada t de Student para datos apareados).

Conclusiones: El empleo de TFD para el tratamiento de la NVC tras la cirugía refractiva permite mantener la MAVC sin inducir cambios en el equivalente esférico.

Key words: Refractive surgery, choroidal neovascularization, photodynamic therapy, LASIK, phakic intraocular lens implantation, pathologic myopia, residual spherical equivalent.

Inclusion criteria

– Refractive error over -6 diopters before refractive surgery and/or axial length over 26 mm.
– Prior refractive surgery (LASIK or ACPL) for correcting high myopia.
– No previous laser treatment over the macula.
– Clinical evidence of sub-foveal and juxtafoveal CNS confirmed with fluorescein angiography (FA).
– Informed consent in writing.

Exclusion criteria

– Clinical signs of Age Related Macular Degeneration (ARMD) such as white drusen, Presumed Ocular Histoplasmosis Syndrome (POHS), as well as other pathologies which may develop CNV in their evolution.
– Pregnancy or breastfeeding.
– Patients who were not apt for PDT.

The mean age was of 36.5 (SD: 10.6 years; range: 24 to 52 years). Ten patients were women and four men. Eight of the treated eyes were right and six left. The mean follow-up after refractive surgery was of 46.1 (SD: 27.2 months; range: 9 to 112 months). The data of these patients are described in Tables I and II.

PDT with verteporfin (Visudyne®, Novartis AG, Bülach, Switzerland) was developed as described above (16,17). The patients received treatment with PDT only if CNV had been proved with Fluorescein angiography (FA), and were made in the period...
between one week after the latest FA with a 3-month interval between sessions. The mean follow-up after the first PDT was of 13.2 months (SD: 7.7 months; range: 5 to 30 months).

The $t$ of Student for paired data was utilized for comparing the differences between the BCVA and the residual spherical equivalent.

### RESULTS

The mean BCVA after surgery was of 0.45 (SD: 0.17; range: 0.2 to 0.8), with mean residual spherical equivalent of -1.5 (SD: 1.8D; range: 1 to 5.5D). The mean time between refractive surgery and the appearance of CNV was of 33 (SD: 24 months; range: 1 to 87). The CNV was sub-foveal in 11 cases and juxta-foveal in 3 (table 11).

CNV appeared in 7 cases after the insertion of ACPL. In five cases angular support phakic lenses were implanted (cases 1-5), one case with phakic lenses fixed in iris (case 7) and one case (# 6) with posterior chamber phakic lens. The CNV appeared in 7 cases after LASIK (cases # 8 - 14).

BCVA was of 0.10 (SD: 0.19; range: 0.025 to 0.7) after CNV (table 2). The differences between BCVA after refractive surgery and the appearance of CNV were statistically significant ($p=0.01$. $t$ of Student for paired data).

After the closure of CNV (three months after the latest PDT, in each case), the mean BCVA improved up to 0.22 (SD: 0.18; range: 0.1 to 0.63).

### Table II

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<th>Patient</th>
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<th>Sex</th>
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<th>rSE</th>
<th>Retinal pathology</th>
<th>Period of study</th>
<th>Refractive surgery</th>
<th>BCVA</th>
<th>Treatment</th>
<th>Final SE</th>
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<td>3</td>
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<tr>
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<td>ACPL **</td>
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<td>0.8</td>
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<td>0.18</td>
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<td>1/87</td>
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<td>0.5/-4</td>
<td>0.63/0.10</td>
<td>9/112</td>
<td>5/30</td>
<td></td>
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</table>

These changes were not statistically significant although for a very small difference (p=0.06. t of Student for paired data).

Four eyes (28.5%) improved over 4 lines, 4 eyes (28.5%) 2 or 3 lines and five eyes (42%) did not exhibit changes (one line or none, gained or lost). Only one eye (7.1%) lost two lines.

From 1 to 4 sessions were required (one session in 4 cases and 4 sessions in one case) with PDT for closing the CNV (mean: 2.0; SD: 0.8 treatments).

The residual spherical equivalent after PDT treatment was of -1.4 (SD: 1.4D; range: 0.5 to 4D). The differences between the residual spherical equivalent after PDT and after refractive surgery were not statistically significant (p=0.82. t of Student for paired data).

DISCUSSION

CNV is one of the major changes of degenerative myopia and is associated with lacquer cracks or streaks (2), which were found in 82 % of eyes with CNV (1). When Bruch’s membrane ruptures, it allows the progression of CNV (1). The prevalence of CNV in high myopia occurs between 4 to 11% (3). Myopia over –6D has been related in the formation of CNV (4), and high myopia is considered to be the main cause of CNV (62) in a study made in young patients (4).

Some publications show the prevalence of CNV in eyes with MM after refractive surgery. Only one case has been published of 5,936 myopic eyes intervened with PRK (5), in 0.10% of 2,955 myopic eyes corrected with LASIK (6) and in 1.70% of 294 myopic eyes corrected with angular support ACPL (7). Only one case has been documented after LASIK in hypermetropic patients (18).

The purpose of our study is to investigate the efficacy and safety of PDT with verteporfin in the treatment of sub-foveal and juxta-foveal CNV in myopic eyes after refractive surgery.

Since the extraction of CNV was discontinued due to its irregular results (19), different solutions were considered when sub-foveal CNV emerged. We could leave the patient without treatment and observe the spontaneous development of the disease. The natural history of CNV in MM eyes after three years is worse than after PDT, although it may be better in patients under 40 years than in those above that age (12). Other authors had previously demonstrated the poor visual acuity associated to the spontaneous evolution of CNV in MM eyes (1,20,21).

Good results have also been published after macular translocation. Fujikado published an improvement of BCVA in 8 out of 11 patients and a worsening in only one of the cases who underwent a macular translocation with 360º retinotomy (13); retina detachment in two cases (one with proliferative vitreo-retinopathy), persistent vitreous hemorrhage and a macular hole in one eye after this procedure.

Limited macular translocation is a simple surgery but Fujii et al (22) has published various complications in at least 34.6%. Another factor to be taken into account is the induction of high astigmatism with scleral shortening in these patients (12), particularly since they had been treated with refractive surgery. Glacet-Bernard et al showed good results in 67% and without changes in 33% of their patients, but they also reported retina detachments, neovascularization in the injection point and CNV recurrence.

VIP 1 showed that PDT with verteporfin can achieve an improved stability index or BCVA improvement in MM patients with CNV (15). In our experience of PDT with verteporfin in myopia magnus patients, good results were observed in terms of BCVA and closure of CNV, with improvements in 61% of patients aged 55 or less, and worsening in 28%. In our studies we did not find any complication associated to PDT (16). The only relevant note is the appearance of sub-retinal fibrosis after PDT in CNV in myopia magnus patients, which does not always involve loss of BCVA (17).

Our study provides the example of 14 eyes with CNV after myopia correction with LASIK or with ACPL implant, treated with PDT with a mean follow-up of 46.1 (SD: 27.2 months; range: 9 to 112 months). BCVA improved after treatment with PDT and the closure of CNV, from 0.10 to 0.22 (p=0.06. t of Student for paired data). Similar results were obtained in an article published by the authors of this paper (16) where the BCVA improvement for patients under 55 years of age (mean age 44.9) were nearly statistically significant (p=0.07. t of Student for paired data).

In the instant study, eight eyes (57.1%) exhibited improvement of over 2 lines and 5 eyes (35.7%) did not show changes (one or no lines gained or lost). One eye (7.1%) lost more than one line.
Another important factor to be considered in these cases is the possible change in the spherical equivalent. These patients submitted to surgery to correct their myopic defect. The residual spherical equivalent after treatment with PDT (-1.4; SD: 1.4D) in our study did not exhibit changes (p=0.82. t of Student for paired data) compared with spherical equivalent after refractive surgery (1.5; SD: 1.8D).

The only different result in this study is the low number of repeated treatments (mean 2.0) compared to 2.6 of our previous study (16) and to 3.4 in the VIP 1 study (15). These two studies included at least one year of follow-up after PDT compared to 13.2; SD: 7.7 months of these patients.

According to our results in terms of BCVA and the absence of complications and changes in the residual spherical equivalent, PDT could be considered as a therapeutic approach for CNV in myopic patients after refractive surgery. However, due to the good results published in preliminary studies about anti-angiogenic treatment of CNV in MM patients, we believe this could be the future treatment for this pathology (8-11). This statement needs to be confirmed in subsequent studies with longer follow-up periods and a larger number of patients.

**REFERENCES**