Myopic Choroidal Neovascularization Membranes Treated With Ranibizumab in Colombian Population

ABSTRACT

Purpose: To describe the characteristics of myopic choroidal neovascular membranes of hispanic subjects treated with a loading dose of Ranibizumab (Lucentis®).

Study design: Non-randomized prospective observational case study.

Methods: Five eyes of 5 patients with naïve CNV secondary to pathological myopia were recruited for this study. Demographics, basal best-corrected visual acuity, grade of myopia, angiographic and tomographic features were obtained at baseline. A loading dose of three monthly Ranibizumab (Lucentis®) injections were given to the recruited subjects. After completion of the loading dose, a complete ophthalmological evaluation, angiography and spectral domain optical coherence tomography (SD-OCT) were obtained subsequently at six and twelve months of follow-up.

Results: The mean age of patients was 45 years. The mean spherical equivalent refractive error was -13.85. At baseline, the mean number of letters was 61.4 and at follow-up to 12 months the mean number of letters was 73.2. The central foveal thickness and subfoveal choroidal thickness decreased in all cases. After loading dose there was no persistent nor recurrent leakage from treated CNV on fluorescein angiography. FAF evidenced an increase in the area of atrophy, with a special circle pattern around the CNV.

Conclusions: This study showed a functional and morphologic improvement at 12 months in five Colombian subjects treated with a loading dose of 3 Ranibizumab monthly injections.

Keywords: Myopic choroidal neovascular membrane, Ranibizumab, Hispanic population.

INTRODUCTION

Pathologic myopia is defined as an excessive elongation of the ocular globe with deformation of the posterior ocular segment, with a subsequent development of a range of retinal and choroidal lesions.1 A demographic study performed in Latin adults aged 40 years and older, reports a prevalence of high myopia of 2.4%.2 Studies indicate that pathologic myopia is the most common cause of choroidal neovascularization (CNV) in young people, and the second most common cause after age related macular degeneration in general population.3 Given this, CNV is a sight-threatening complication occurring in approximately 5.2% to 10.2% of highly myopic eyes.4,5 The formation of CNV results in visual loss, which has profound impact in productivity, quality of life, and career expectations in young people.6 In general, consent exists that intravitreal antiangiogenic drugs are the first line treatment for myopic CNV, showing good functional and anatomic results in most cases.7 Age, baseline best corrected visual acuity, location of myopic CNV, preexisting chorioretinal degenerative changes such as lacquer cracks affecting the foveal, chorioretinal atrophy and previous photodynamic therapy have been demonstrated to correlate with visual outcome after anti-VEGF treatment for myopic CNV.8 Several genetic factors have been studied about the association between VEGF gene polymorphisms and the occurrence and/or anatomic characteristics of choroidal neovascularization in highly myopic eyes.9,10 It is known that polymorphism may be different between populations and there is a lack of studies on myopia and its complications in Latin American population. The objective of this study is to describe the characteristics of myopic choroidal neovascular membranes of hispanic subjects treated with a loading dose of Ranibizumab (Lucentis®).

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Bar Graphs:
- Figure 1. Mean Letters BCVA
- Figure 2. Central Foveal Thickness (microns)
- Figure 3. Subfoveal choroidal thickness (microns)
prospective study was to characterize myopic CNV treated with ranibizumab in a Latin American population.

**MATERIALS AND METHODS**

This is a non-randomized prospective observational case study of 5 eyes of 5 patients with naïve CNV secondary to pathological myopia. Inclusion criteria were patients between 18 and 50 years old, myopia higher than -8.00D in the study eye (or without a prior refractive error ± SD) whose investigator considered that fundus changes are due to myopia, recent onset choroidal neovascular membrane demonstrated by fluorescein angiography in the study eye, and best corrected visual acuity of 20/20 and 1.0 (20/200) Early Treatment Diabetic Retinopathy Study (ETDRS) LogMar chart at 4 meters. Exclusion criteria were media opacity which did not allow adequate clinical, tomographic or angiographic evaluation, presence of other retina pathology that could create confusion in the results, patients previously treated with photodynamic therapy, thermal laser photocoagulation or anti-VEGF agents for myopic CNV, patients not willing or not able to sign informed consent, and women of childbearing age without a safe contraceptive method. Informed consent was obtained from all patients before treatment, after discussing the risks, benefits, and alternative treatment options. The study was performed in adherence to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee.

**RESULTS**

The changes in mean number of letters read (BCVA on ETDRS chart) during the 12-months period are shown in Figure 1. At baseline, the mean number of letters was 61.4 (logMAR 0.50 ± 0.29, Snellen equivalent 20/63). At 4 months, the mean number of letters was 66.6 (logMAR 0.38 ± 0.29, Snellen equivalent 20/48). After 6 months, the mean number of letters was 71 (logMAR 0.28 ± 0.18, Snellen equivalent 20/38) and at follow-up to 12 months the mean number of letters was 73.2 (logMAR 0.24 ± 0.17, Snellen equivalent 20/35). This number of letters gained was similar to the findings in clinical trials.11 The case 4 achieved the highest number of letters gained at final, with a total of 32 letters. The baseline BCVA was the lowest of all (baseline 47.4, and final 79.8 letters).

**Table 1. General Results**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Pre-treatment (mm²)</th>
<th>Post-treatment (mm²)</th>
<th>Increase*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.120</td>
<td>1.710</td>
<td>14.3</td>
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<tr>
<td>2</td>
<td>0.230</td>
<td>0.940</td>
<td>3.4</td>
</tr>
<tr>
<td>3</td>
<td>0.270</td>
<td>0.800</td>
<td>11.4</td>
</tr>
<tr>
<td>4</td>
<td>2.390</td>
<td>2.670</td>
<td>1.06</td>
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<tr>
<td>5</td>
<td>0.430</td>
<td>1.380</td>
<td>3.2</td>
</tr>
<tr>
<td>Mean</td>
<td>0.864</td>
<td>1.420</td>
<td></td>
</tr>
</tbody>
</table>

*Increase times from pre-treatment lesion

**Table 2. Areas of RPE atrophy on fundus auto-fluorescence**

RPE: Retinal Pigment Epithelium

**Picture 1. Fundus auto-fluorescence from subject #2, previous treatment. Black area around CNV site are demarcated (0.220 sq mm)**

**Picture 2. Fundus auto-fluorescence from subject #2, post-treatment. Black area around CNV site are demarcated (0.740 sq mm)**

**Figure 1.** shows the changes in mean number of letters read (BCVA on ETDRS chart) during the 12-months period. The mean ± standard deviation (SD) age of patients was 45.0 ± 3.46 years (range, 42 – 50 years). All patients were hispanics. The mean spherical refractive error ± SD was -13.85 (±5.34). Four eyes had subfoveal CNV and 1 had juxtafoveal (Table 1).

The Ethical Committee of Fundación Oftalmológica Nacional provided ethics approval.
The baseline mean CFT was 354.40 ± 41 microns, during the follow-up was 295.00 ± 77 microns, 267.40 ± 19 microns and 244.60 ± 40 microns at four, six and twelve months respectively (Figure 2). The subjects 1, 2, and 3 were those that showed significant decreased of CFT; these subjects had greater thickness at baseline. Choroidal changes following anti-VEGF therapy have been reported in other studies13,14, in all patients the subfoveal choroidal thickness decreased, with a mean at baseline of 341 ± 60 microns and with a value of 220 ± 53 microns at twelve months (Figure 3). The choroidal neovascular membrane thickness decreased at follow-up in all study subjects, even more in subject 3 the neovascular membrane “disappeared” one month after the loading dose. SD-OCT allows visualization of the external limiting membrane (ELM) and the ellipsoid zone (EZ), according to some authors the EZ correlates with visual acuity14,15. In three patients there was no integrity of the external limiting membrane nor the ellipsoid zone at the baseline. At the end of follow up, only patient 2 had regain anatomic appearance.

The color fundus photographs showed some degree of peripapillary atrophy in all subjects, and this finding did not change during follow-up. A dark rim around the choroidal neovascular membrane was observed in 3 subjects, with similar characteristics. The fundus autofluorescence (FAF) of the eyes with myopic maculopathy is very complex. This is the reason that an increase in the hypoaufotofluorescence area was determined as an increase of areas of RPE atrophy around CNV. Thus, being showed that all patients had areas of RPE atrophy around CNV at baseline (with a mean 0.64 mm2), and at the end of follow up these areas increased in all patients with a mean of 1.42 mm2 (Table 2). The RPE atrophy pattern found on FAF was a circle around the NVC, it was observed in four subjects.

There was only one case in which a lacquer crack was not identified. On fluorescein angiography there were no subjects with persistent leakage from CNV after 1 month of the loading dose and no changes or recurrences were seen until the end of the follow up. There were no systemic nor local adverse events related to intravitreal ranibizumab injection.

DISCUSSION

Several studies, including randomized clinical trials have demonstrated a beneficial effect of anti-VEGF monotherapy in the treatment of myopic CNV. However, few studies include Hispanic patients and not all patients respond to intravitreal anti-VEGF treatment. Even more, visual acuity did not improve despite the resolution of CNV on fluorescence angiography16,17. In this study, there is an improvement on BCVA at twelve months in all five subjects treated with loading dose of Ranibizumab. The patient with the lowest baseline BCVA and highest CNT length had the biggest number of letters gained. The same subject had intraretinal fluid, and during follow up there was no restoration of the integrity of ellipsoid zone nor ELM. The associated poor visual prognosis factors described previously (subfoveal location, age > 40 years and size of the CNV > 400 microns)18,19 were present in four subjects, nevertheless gained a mean of 7 letters at twelve months. These subjects showed a good response to the treatment despite having poor prognostic factors for visual acuity outcomes. Only one subject did not show a clinical significant increase in letters, probably because his visual acuity at baseline was good (20/30, LogMAR 0.18). Previous reports have taken into account the subfoveal choroidal thickness in myopic CNV treated eyes with anti-VEGF, with a significant decrease following therapy, also suggesting its increase as an indicator of CNV reactivation12. These findings are consistent with the present cases, in which a decrease in choroidal thickness was observed in all subjects without signs of reactivation at twelve months. On fluorescein angiography an inactive CNV membrane was observed in all subjects at the end of follow-up. However, longer follow up is needed in patients with myopic CNV since areas of atrophy may develop for progress later on. The findings on FAF has evidenced an increase in the atrophy areas, with a special circle pattern around the CNV, despite this, it was not observed a vision loss in any case during the follow-up period. Regarding this autofluorescence pattern, similar findings were found by Farinha et al20, on Portuguese population, that showed an increase in hypoaufotofluorescence areas around the treated membranes, but in this case associated with poor visual outcome.

A case series was performed due to the low prevalence of pathologic myopia in the local context. However, advantages of this prospective study include follow up, the control over variables such as the strict inclusion of patients under 50 years of age, refractive state and naive myopic choroidal neovascularization.

In conclusion, in this study, intravitreal Ranibizumab has shown to be a well-tolerated and effective treatment for these 5 Hispanic patients with myopic CNV. Visual improvements and anatomic benefits were maintained and extended from baseline to 12 months. Intravitreal Ranibizumab seems to be a good treatment option in Hispanic patients with myopic CNV.