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Case Report

Efficacy of Etamsylate Eye Drops in Wet-Age-Related Macular Degeneration: A Case Report

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Abstract

The principal cause of blindness is age-related macular degeneration which wet form represents 10% of cases. The first line therapy for wet macular degeneration is frequent intravitreal injections of anti-vascular endothelial growth factor which is associated with important secondary effects. We reported previously the efficacy and safety of a single intravitreal injection of etamsylate (a synthetic inhibitor of fibroblast growth factor and vascular endothelial growth factor) in macular degeneration. The present report shows the improvement of visual acuity and retinal anatomical patterns in a patient affected by wet macular degeneration, after 30 days of eye drops instillation.

Keywords: Age-Related Macular Degeneration; Etamsylate; Eye-Drops; Fibroblast Growth Factor; Vascular Endothelial Growth Factor

Abbreviations:

ARMD: Age-Related Macular Degeneration; BCVA: Best-Corrected Visual Acuity; FGF: Fibroblast Growth Factor; FGFR: Fibroblast Growth Factor Receptor; RPE: Retinal Pigment Epithelium; SD-OCT: Spectral-Domain Optical Coherence Tomography; VEGF: Vascular Endothelial Growth Factor

Introduction

Topical ophthalmic instillation is an appearing strategy to deliver drugs to the back of the eye to treat retinal diseases. It has several advantages such as being non-invasive and self-friendly, e.g. allowing self-administration. At present, no topical ophthalmic formulations to treat Age-Related Macular Degeneration (ARMD) and other retinal neurodegeneration illness have reached the market [1].

To date intravitreal injections of anti-Vascular Endothelial Growth Factor (VEGF) drugs is the standard therapy for ARMD however, lately demonstrated as ineffective in reversing the existing neovascularization; moreover, patients could suffer from endophthalmites and retinal detachment due to injections frequency [2].

Drug delivery to the posterior segment of the eye (the retina, choroid, vitreous and optic nerve) is important to potentially treat disorders such as ARMD, diabetic retinopathy, retinal vascular occlusions, posterior uveitis and proliferative vitreous retinopathy. Lacrimal drainage and anatomic barriers can difficult the achievement of therapeutic drug concentrations in the posterior segment of the eye after topical drug administration [3]. However, different animal studies have shown that several drugs can reach the posterior segment of the eye in pharmacological concentrations to achieve a therapeutic effect. For example, eye drop formulation is able to deliver a 60% amount of dexamethasone in the rabbit retina [4]. The aim of our case report study was to analyse the effect of the treatment with etamsylate eye drops in a patient that was diagnosed with wet ARMD.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Case Presentation

A 75-old woman presented with wet-age-related macular degeneration in her left eye which was treated twice a day for 30 days with etamsylate (Dicynone®. Sanofi-Aventis. Paris. France) eye drops. Changes in the macula was the primary outcome and visual acuity was the secondary outcome using Spectral-Domain Optical Coherence Tomography (SD-OCT) and Best-Corrected Visual Acuity (BCVA) by means of Snellen chart (described in decimal scale), respectively.

As depicted in the SD-OCT image before treatment (Fig. 1) the patient presented great macular oedema (775μm in the central macular thickness subfield) and areas with loss of photoreceptors and Retinal Pigment Epithelium (RPE). In contrast, after etamsylate treatment (Fig. 1) normalization of retinal anatomy (central macular thickness was 230μm) including photoreceptors and RPE was achieved. The normalization of retinal structure was associated with a gain of BCVA: 0.10 at baseline versus 0.90 after treatment. No adverse effects were reported during treatment.

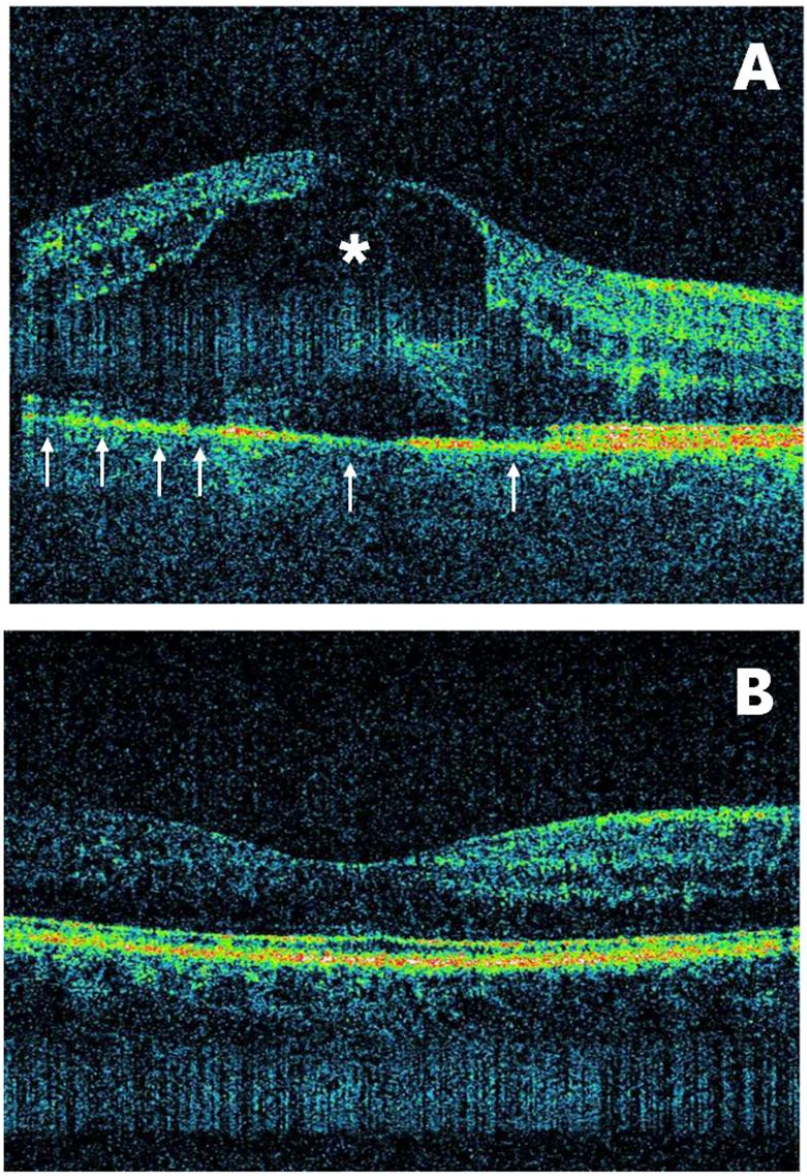

Figure 1: Optical coherence tomograms before [A] and after [B] etamsylate eyedrops. Note in A the loss of photoreceptors (arrows) and RPE in several areas of oedema in the macula (asterix).

Discussion

Intravitreal injections of anti-Vascular Endothelial Growth Factor (VEGF) drugs is increasingly used to treat several neuroretinal degeneration conditions, including ARMD, diabetic retinopathy and retinal vessel occlusion. However, repeated and long-term intravitreal injections that are commonly needed may increase the risk of ocular and systemic complications [5-9]. It is interesting to note that inhibition of Fibroblaslt Growth Factor (FGF) and VEGF in diseases associated with aberrant vascular proliferation, such as ARMD, does not affect normal vascularization [10]. Topical modes of delivery to the posterior segment of the eye are being evaluated by a variety of researchers for their potential usefulness in retinal disease treatment. Topical route of ocular drug administration presents advantages in contrast to intravitreal injections. Indeed, it is more comfortable for the patient because no invasive. Reduction in central macular thickness with topical bronfenac given twice a day in patients with diabetic macular oedema has been reported [11]. Furthermore, topical dorzolamide for the treatment of cystoid macular oedema showed a significant decrease in retinal thickness in 87% of patients [12]. It has been shown recently in animals that topically administered etamsylate remains in several structures of the posterior segment of the eye for a period of time long enough to produce its effects [13]. It has been postulated the importance of FGF and VEGF in inflammatory and angiogenesis-dependent diseases as ARMD, where inflammation and angiogenesis are the main components of the disease progression and FGF and VEGF and its receptors (FGF/FGFRs, VEGF/VEGFRs) are prominently expressed [14,15].

Rationale

Etamsylate, an anti-haemorrhagic drug, interacts with both FGF and VEGF and its receptors, displacing heparin from its binding site, modifying the tridimensional structure of the protein and its receptor recognizing site and consequently dissociating the receptor growth factor signalling process [16,17]. Previously, we have reported the efficacy of intravitreal etamsylate, a synthetic inhibitor of FGF/FGFR axis, in patients with retinal diseases [18-22]. As described for the first time in the present report, etamsylate eyedrops could represent a new non-invasive and safe therapy for treating wet ARMD.

Conclusion

This case report shows the efficacy of etamsylate eye-drops after 30 days of treatment in a patient presenting wet macular degeneration. Etamsylate eyedrops treatment led to normalization of retinal structures and significant gain in visual acuity, which may improve the future management of wet ARMD. Obviously, the potential clinical value of etamsylate eye drops described in the present case report needs to be further investigated in a prospective randomized clinical trial.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Financial Disclosure

None.

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Author's Contribution

All authors read and approved the final manuscript.

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