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Brief report

Intravitreal injection of ziv-aflibercept in the treatment of choroidal and retinal vascular diseases

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Abstract

Purpose: To investigate the short-term outcomes after intravitreal injection of ziv-aflibercept in the treatment of choroidal and retinal vascular diseases.

Methods: Thirty-four eyes of 29 patients with age-related macular degeneration (AMD), diabetic retinopathy, and retinal vein occlusion (RVO) received a single dose intravitreal injection of 0.05 ml ziv-aflibercept (1.25 mg). Visual acuity, spectral domain optical coherence tomography (SD-OCT) activity, and possible side effects were assessed before and at 1 week and 1 month after the intervention.

Results: At 1 month after treatment, mean central macular thickness (CMT) significantly decreased from 531.09 μm to 339.5 μm ($P < 0.001$), and no signs of side effects were observed in any subject. All patients responded to treatment in terms of reduction in CMT. The improvement in visual acuity was statistically non-significant.

Conclusion: Our findings suggest that a single dose intravitreal injection of ziv-aflibercept may have acceptable relative safety and efficacy in the treatment of patients with intraocular vascular disease.

The trial was registered in the Iranian Registry of Clinical Trials (IRCT2015081723651N1)..

Keywords: Ziv-aflibercept; Age-related macular degeneration; Diabetic retinopathy; Anti-vascular endothelial growth factor; Retinal vein occlusion

Introduction

Nowadays, many anti-vascular endothelial growth factor (VEGF) agents are used as the first line in the treatment of intraocular vascular diseases.[1] Until recently, the choice of drugs was limited to bevacizumab (Avastin) and ranibizumab (Lucentis), the former being more popular on account of its lower cost.[2,3] Aflibercept (Eylea) is a new addition to the group, which may offer better efficiency and a longer effect.[4]

Ziv-aflibercept, an anti-VEGF anticancer drug, has the same structure and exerts the same function as aflibercept, but the latter undergoes a different purification process and contains different buffer solutions that are less irritating when injected intravitreally and has a lower osmolarity.[5] However, from a commercial perspective, ziv-aflibercept is a much cheaper recombinant fusion protein. Mansour et al[4] have used evidence from in vitro and in vivo studies[6,7] to address certain concerns in relation to safety in its intraocular use such as osmolality differences and the risk of inducing changes to

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retinal morphology. Regarding the little available information on the safety and efficacy of ziv-aflibercept in patients with intraocular vascular diseases, we performed this study.

Methods

In this prospective interventional case series, patients with age-related macular degeneration (AMD), diabetic macular edema (DME), or retinal vein occlusion (RVO) who had no sign of eye infection and no history of myocardial infarction or cerebrovascular accident were included in this study.

The Ethics Committee of Tehran University of Medical Sciences approved this study; it adhered to the tenets of the Declaration of Helsinki, and a written informed consent was obtained from all participants.

First, 0.05 ml of aqueous humor was extracted through the limbus area with a 29 gauge needle. Then 0.05 ml (1.25 mg) of Ziv-aflibercept (Zaltrap, Sanofi and Regeneron Pharmaceuticals, Inc.) was injected into the intravitreal space through the pars plana using a 31 gauge needle.

In addition to intraocular pressure (IOP) monitoring and an ophthalmic exam, the patients were observed for signs of any progression in lens opacity, intraocular inflammation, and change in retinal structure using the spectral domain optical coherence tomography (SD-OCT) before, 1 week, and 1 month after the injections. In this study, "efficacy" referred to reduction in central macular thickness (CMT). Statistical analysis was performed using paired-test or McNemar's test.

Results

Thirty-four eyes of 29 consecutive patients with a mean age 66.6 ± 11.0 years were enrolled. Five diabetic patients received ziv-aflibercept injections bilaterally. The diagnosis

Table 1
Patient demographics and baseline characteristics.

Characteristic		AMD	RVO	DME
N (full set analysis):		8 eyes in 8 patients	6 eyes in 6 patients	20 eyes in 15 patients
Age (Mean ± SD)		77.4 ± 3.1	66.0 ± 11.7	63.3 ± 10.6
Gender: n (%)	Male	4 (50.0%)	3 (50.0%)	7 (46.7%)
	Female	4 (50.0%)	3 (50.0%)	8 (53.3%)
Prior therapies, n (%)				
Laser therapy: n (%)		1 (12.5%)	1 (16.7%)	13 (65.0%)
Avastin injection: n (%)		6 (75.0%)	1 (16.7%)	16 (80.0%)
Average number of treatments prior to study entry		Mean ± SD: 7.17 ± 3.3 Range: 4–13 injections	6 times	Mean ± SD: 3.7 ± 2.6 Range: 1–12 injections
Time since last injection prior to study enrollment		Median (IQR): 2.0 months (2.25 months) Range: 1–4 months	4 months ago	Median (IQR): 4.5 months (7 months) Range: 1–42 months

N: number, AMD: Age-related macular degeneration, DME: Diabetic macular edema RVO: Retinal vein occlusion, SD: Standard deviation, IQR: Inter quartile range.

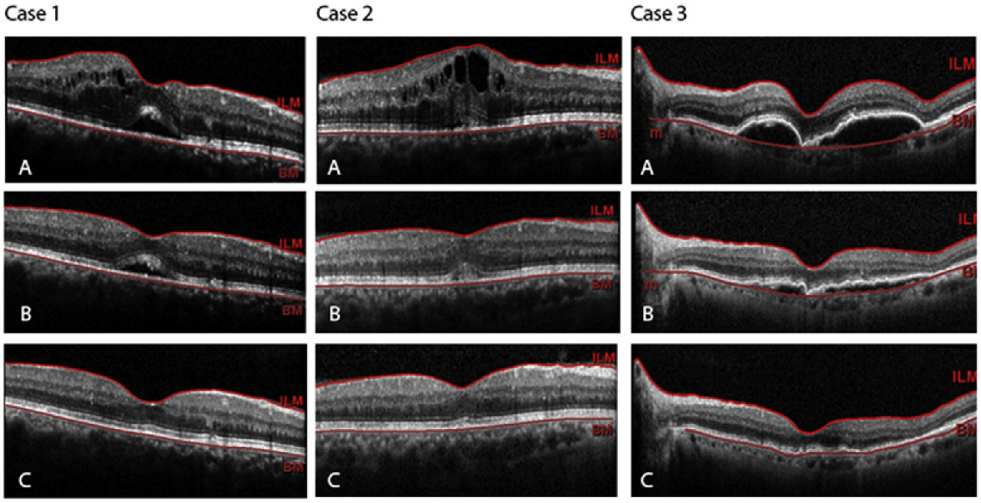

Fig. 1. Spectral-domain optical coherence tomography scans of 3 eyes (Case 1: DME, Case 2: RVO and Case 3: AMD), which underwent intravitreal ziv-aflibercept, at baseline (A), 1 week (B) and at 1-month (C) follow-up, showing disappearance of subretinal fluid (Case 1), intraretinal fluid (Case 1 and Case 2), CME (Case 2), and PED (Case 3). DME: Diabetic macular edema; RVO: Retinal vein occlusion; AMD: Age-related macular degeneration; CME: Cystoid Macular Edema; PED: Pigment epithelial detachment.

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