Original Article

Refractive and Biometric Outcomes Following a Single Dose Intravitreal Bevacizumab Administration

Majid Abrishami [1], MD; Alireza Eslampoor [1], MD; Mohsen Roknizadeh [1], MD; Esmaeil Babaei [*2],MD

1. Eye Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
2 .Ophthalmology Department, Geriatric Ophthalmology Research Center, Shahid Sadoughi University of Medical Sciences ,Yazd, Iran.

Corresponding Author: Esmaeil Babaei
E-mail: esmaeil.babaei@ahoo.com

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Abstract

Purpose: To evaluate the effect of intravitreal bevacizumab monotherapy on refractive and biometric parameters among patients with central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO) or clinically significant macular edema (CSME).

Patients and Methods: This prospective study included patients aged between 35-50 years who received a single dose intravitreal injection of bevacizumab in Khatam-Al-Anbia eye hospital, Mashhad University of Medical Sciences, Mashhad, Iran, from 2015 to 2017. Dry and cycloplegic refraction, visual function, accommodative amplitude, keratometry results, axial length, anterior chamber depth, lens thickness, vitreous length and central corneal thickness, before and 1 and 3 months after injection were evaluated and compared.

Results: Twenty seven patients (fifteen females and twelve males) entered the study with the mean age of 45.18 ± 2.68 years. The mean best corrected visual acuity (BCVA) of patients improved significantly (P = 0.006) three months post injection compared to before injection. No statistically significant difference was observed between the refractive parameters (dry and cycloplegic refraction), accommodative amplitude, biometric parameters including keratometry, axial length, and lens thickness, before and 1 or 3 months after injection.

Conclusion: Based on our findings bevacizumab monotherapy improved the mean BCVA among patients with CRVO, BRVO, or CSME, but had no significant effect on refractive and biometric parameters of the treated eyes up to 3 months after injection.

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Introduction

Vascular endothelial growth factor (VEGF) is an angiogenesis activator that can lead to formation of new blood vessels, lymphangiogenesis and changing vascular permeability. VEGF inhibitors can be an effective option for management of several kinds of vitreoretinal diseases including age related macular degeneration (AMD), choroidal neovascularization (CNV), diabetic macular edema (DME) and retinal vein occlusion (RVO) by decreasing the angiogenesis and vessels permeability [1-5].

Bevacizumab is a full-length monoclonal antibody to VEGF which is approved for the treatment of metastatic colorectal cancer, and is also used for treatment of some ocular diseases as an intravitreal injection [6]. Although many studies have reported good treatment success without any local or systemic side effect following intravitreal bevacizumab injection in variety of ocular diseases [7], but there are some concerns about some possible ocular side effects, namely the refractive and biometric outcomes. There are not sufficient human studies to evaluate these parameters in English literature.

The purpose of the present study was to evaluate the effect of a single dose of intravitreal bevacizumab injection on the refractive and biometric properties of the eye such as dry and cycloplegic refraction, accommodative amplitude, keratometry, axial length, anterior chamber depth, lens thickness, vitreous length and central corneal thickness in patients with central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO) and clinically significant macular edema (CSME).

Patients and Methods

This prospective study included twenty-seven participants with CRVO, BRVO or CSME aged between 35-50 years who received a single dose intravitreal injection of bevacizumab in Khatam-Al-Anbia eye hospital, Mashhad University of Medical Sciences, Mashhad, Iran, from 2015 to 2017. The study protocol was approved by our institutional ethics committee and all participants gave written consent before entering the study. Patients with other retinal diseases, previous intravitreal injection, any ocular surgery, or best corrected visual acuity (BCVA) of less than 40/100 were excluded.

A single intravitreal dose (1.25 mg/0.1 ml) of bevacizumab (Avastin, Genentech, Inc., South San Francisco, CA) was injected 3.5 mm posterior to the limbus in the upper temporal quadrant using a 30-gauge needle under strict aseptic techniques following instillation of 3 drops of 5 % Betadine on the conjunctiva. Patients were monitored for inflammation the day after intravitreal injection.

BCVA was measured according to standardized refraction protocol using a Snellen chart at 6 m and was converted to LogMAR unit for analysis. Objective refraction and keratometry measurements were performed using a Topcon KR-8000 (Topcon, Tokyo, Japan) auto refractometer. Cycloplegic refraction was measured 30 minutes after three times instilling of one drop of tropicamide with five minute intervals. Accommodative amplitude was measured using a ruler and negative lens.

Axial length and vitreous length using IOLMaster (Carl Zeiss Meditec, Inc. Dublin, California, USA), and anterior chamber depth, lens thickness and central corneal thickness using ultrasound biomicroscopy (Zeiss-Humphrey Instruments, Inc. San Leandro, CA, USA) were also measured and compared between before injection and 1 month and 3 months after injection. Data were recorded in special forms and analyzed using SPSS

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software version 18 (IBM, Armonk, NY, USA). P values less than 0.05 were considered statistically significant. For each parameter, the differences from baseline to each time point after injection (1, and 3 months) were compared.

Results

In this study 27 eyes of 27 patients were included and all of them were given a single dose of intravitreal bevacizumab. Twelve patients (46.4 %) were male and 15 patients (53.6 %) were female. The mean age of patients was 45.18 ± 2.68 years. Six patients (22.2 %) had CRVO, 3 patients (11.1 %) had BRVO and 18 patients (66.7 %) had CSME. The baseline characteristics of the patients entering the study are displayed in table 1.

At 3 months following intravitreal bevacizumab injection monotherapy the mean LogMAR BCVA improved significantly from 0.23 ± 0.11 to 0.20 ± 0.11 (P = 0.006). Repeated measures ANOVA test and its nonparametric equivalent Friedman test, showed that there was no significant difference between the mean refractive parameters of the eyes before and after injection. Also, there was no statistically significant difference between the mean of accommodative amplitude before and 1 and 3 months after injection. Finally, there were no statistically significant differences in the mean values of the other biometric parameters such as keratometry, axial length, anterior chamber depth, lens thickness, central corneal thickness, and vitreous length before and 1 and 3 months after injection.

The results of the comparison between measured parameters at baseline and at months 1 and 3 after injection are shown in table 2.

Discussion

Anti-VEGF therapy has been used frequently in treatment of a variety of ocular diseases including AMD, CNV, DME and RVO 1-5. There are some previous reports indicating that anti-VEGF agents might lead to improvement of vision 8-10 among these patients; but its short term and long term effects on refractive and biometric findings has not been thoroughly evaluated.

Table1: Baseline demographics of 27 patients treated with a single dose of intravitreal bevacizumab entering the study

Description	Total	Male	Female	P value
Number	28 (100 %)	13 (46.4 %)	15 (53.6 %)	-
Age (y)	45.18 ± 2.68	45 ± 2.91	45.33 ± 2.55	0.75*
BCVA (LogMAR)	0.23 ± 0.11	0.23 ± 0.11	0.22 ± 0.10	0.89*
Ocular diseases				
CRVO	6 eyes (21.4 %)	3 (50 %)	3 (50 %)	
BRVO	3 eyes (10.7 %)	1 (33.3 %)	2 (66.7 %)	0.884**
CSME	19 eyes (67.9 %)	9 (47.4 %)	10 (52.6 %)	

* Based on Independent Samples T Test

* Based on Chi-Square Test

CRVO: central retinal vein occlusion; BRVO: branch retinal vein occlusion; CSME: clinically significant macular edema; LogMAR: logarithm of the minimum angle of resolution

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Table 2: Corneal and biometric parameters in the eyes injected with bevacizumab before and 1 and 3 months after injection

Description	Preinjection	Month 1	Month 3	P-value*
K1(D)	44.35 ±1.85	44.34 ± 1.84	44.40 ± 1.85	0.78
K2 (D)	45.32 ± 2.18	45.38 ± 2.24	45.41 ± 2.27	0.118
AL (mm)	23.45 - 22.90 (23.16)	23.46 - 22.87 (23.19)	23.51 - 22.81 (23.16)	0.714
ACD (mm)	2.72 ± 0.04	2.74 ± 0.04	2.74 ± 0.41	0.664
Lens thickness (micron)	4.20 ± 0.44	4.21 ± 0.40	4.20 ± 0.41	0.829
CCT (micron)	516.32 ± 32.13	517.32 ± 32.03	517.71 ± 32.28	0.305
Vitreus length (mm)	15.63 ± 0.77	15.59 ± 0.77	15.63 ± 0.76	0.626
BCVA (LogMAR)	0.23 ± 0.11	0.22 ± 0.10	0.20 ± 0.11	0.006
Accommodative Amplitude	2.12 ± 0.77	2.15 ± 0.79	2.08 ± 0.77	0.089

* Based on Paired Samples T test

K: keratometry; AL: axial length; ACD: anterior chamber depth; CCT: central corneal thickness; BCVA: best corrected visual acuity

In the present study we observed no statistically significant difference between the refractive parameters (dry and cycloplegic refraction), accommodative amplitude, biometric parameters including keratometry, axial length, and lens thickness, before and 1 or 3 months after a single dose of bevacizumab injection. Similar to our findings Axer-Siegel et al., 11 in an animal study including rabbit eyes found no significant differences in refractive and biometric parameters in eyes injected with intravitreal bevacizumab and the control group. Also Chatziralli et al., 12 evaluated the refractive changes following intravitreal ranibizumab injection in 35 patients with diabetic macular edema. Their results showed no significant difference in the mean refractive error before and following the injection of bevacizumab in patients with DME.

Our study showed that among patients treated with a single dose of bevacizumab the mean BCVA significantly improved 3 months after injection in comparison to before injection. Similar to our findings Deák et al., 13 in their study, which included 20 patients receiving bevacizumab for treatment of DME, reported a statistically significant improvement in BCVA after treatment.

This study had some limitations including a relatively low sample size, short duration of follow-up and only evaluating the patients before and after injection without including a control group.

Conclusion

Based on our findings bevacizumab monotherapy improved the mean BCVA among patients with CRVO, BRVO, or CSME, but had no significant effect on refractive and biometric parameters of the treated eyes up to 3 months after injection.

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Authors ORCIDs

Majid Abrishami:
https://orcid.org/0000-0002-4696-3350
Esmaeil Babaei:
https://orcid.org/0000-0001-8490-3589

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present study.

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