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Short-Term Effect on Intraocular Pressure after Intravitreal Aflibercept Injection for Diabetic Macular Edema

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Abstract

Purpose: *There is limited data available on the short-term effect of intravitreal aflibercept injection on intraocular pressure (IOP) for diabetic macular edema (DME). We performed a prospective, observational clinical study to evaluate short-term IOP changes after aflibercept injection in eyes with DME.*

Methods: *Patients with diabetes mellitus type II and associated DME were recruited at King Abdulaziz Medical City, Saudi Arabia, between December 2015 and October 2016. All eyes were injected with 2 mg(0.05ml) of intravitreal aflibercept. Inclusion criteria were patients with DME, patients eligible for aflibercept injection, patients aged 18 years or more. Exclusion criteria were patients with a history of anti-VEGF injection, argon laser photocoagulation, glaucoma, antiglaucoma medications, uveitis, or steroid. We measured IOP using Tono-Pen (Tono-Pen XL, Reichert Inc., Depew, NY, USA) immediately before injection, at 5, 15, 30, 45, 60 min and 1 day after injection. We compared short-term IOP changes before and after aflibercept injections using paired t-test for statistical analysis.*

Results: *A total of 14 eyes from 14 DME patients (7 female and 7 male) with a mean age of 62.43±10.68 years fulfilled the inclusion criteria. Our findings showed that the mean IOP readings recorded before injection, at 5, 15, 30, 45, 60 min and 1 day after injection were 19.71±1.90, 32.07±13.68 mmHg (p=0.005), 23.43±6.38 mmHg(p=0.043), 20.86±5.07 mmHg(p=0.476),19.50±3.11 mmHg(p=0.803),19.21±3.17 mmHg(p=0.583) and 17.71±1.59(p= 0.011) respectively. Comparing the mean IOP before and after intravitreal aflibercept injection, it was significantly higher at 5 and 15 min after injection. However, the mean IOP returned to normal pre-injection level at 60 min (p=0.583). Three eyes (21.43%) had persistent increased IOP one day after intravitreal aflibercept injection. Comparing pre and post injection mean IOP at 5, 15 min and 1 day in terms of gender effect, the mean IOP changes were not statistically significant (p=0.591, 0.473, 0.345; respectively).*

Conclusions: *Our study confirmed that intravitreal aflibercept injection is safe with respect to short-term IOP changes in patients with DME. A significant short-term rise of IOP occurred within 15 minutes after injection then it returned to normal in most patients. The effect of gender on the mean IOP before and after aflibercept injection was not statistically significant.*

Keywords: ***Aflibercept, intraocular pressure, intravitreal injection.***

1. Introduction

The discovery of intravitreal injections that target vascular endothelial growth factor (VEGF) has revolutionized the management of the ocular neovascular diseases. Aflibercept (Eylea™, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA, and Bayer Pharma AG, Berlin, Germany) can effectively reduce intraocular level of VEGF and vascular permeability related to diabetic macular edema (DME) by downregulating VEGF-A, VEGF-B, and placental growth factor, which can cause pathologic angiogenesis. Aflibercept is a soluble human fusion protein, formed by fusion of the third domain of human VEGF receptor 2 and the second domain of human VEGF receptor 1 to the Fc domain of human IgG1 [1].

Intravitreal injection of aflibercept is predicted to elevate intraocular pressure (IOP) secondary to increased vitreous volume in a similar way to how other anti-VEGF agents elevate IOP, such as ranibizumab [2]. There is limited data available on the short-term effect of intravitreal aflibercept injection on IOP for DME. We performed a prospective, observational clinical study to evaluate short-term IOP changes after aflibercept injection in eyes with DME. To our knowledge, this is the first paper associated with the issue after reviewing the literature.

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2. Methods

Study Design

We investigated 14 eyes of 14 patients with Diabetes Mellitus (DM) type II and associated DME recruited at the Division of Ophthalmology, King Abdulaziz Medical City, Eastern Region, Saudi Arabia, from December 2015 through October 2016. Seven patients were men and seven patients were women, averaging 62.43±10.68 years of age (mean ± standard deviation). We conducted this prospective, observational clinical study in accordance with the Declaration of Helsinki and received approval from the institutional review committees of King Abdullah International Medical Research Center. Signed informed consent was obtained from all study subjects. Exclusion criteria compromised patients with a history of any ocular surgery, anti-VEGF intravitreal injection, argon laser photocoagulation, glaucoma, uveitis, or steroid use, ophthalmic disorders except mild refractive errors and cataract, and a history of taking anti-glaucoma medications.

All patients underwent a complete ophthalmic examination, including best-corrected visual acuity, slit-lamp examination, tonometry, fundus biomicroscopy, fluorescein angiography (FA), optical coherence tomography (Topcon Corporation, Japan). All patients underwent intravitreal injection with 2mg (0.05 ml) of aflibercept. Patients were uniformly sterilely prepped, which included instillation of topical antibiotic and anesthetic drops, insertion of a lid speculum, and a 5% povidone-iodine flush, followed by a rinse with balanced salt solution. Using a cotton-tipped applicator soaked with a topical anesthetic, the superotemporal area of sclera to be injected was anesthetized. After marking the injection site on the sclera with a caliper measuring 3.5 mm from the limbus, the conjunctiva was displaced slightly with a sterile cotton-tipped applicator just before entering the eye with a needle. All the injections were performed using tunneled injection without a reflux by the same surgeon (T.A.), that is, all the injected volume of aflibercept was kept in the vitreous. After injection, the injection site was occluded temporarily and was massaged with a sterile cotton-tipped applicator as the needle was withdrawn from the eye. IOP was measured using Tono-Pen (Tono-Pen XL, Reichert Inc., Depew, NY, USA) immediately before injection, at 5, 15, 30, 45, 60 min and 1 day after injection.

Statistical Analysis

We compared short-term IOP changes before and after aflibercept injections using paired t-test for statistical analysis. Data were represented as mean ± standard deviation (SD). All statistical analyses were performed using SPSS Version 13.0 statistical analysis software and p values less than 0.05 were considered statistically significant.

3. Results

This study included 14 DME patients. There were 7 (50.00%) males and 7(50.00%) females with a mean age of 62.43 ± 10.68 years fulfilled the inclusion criteria .The lens status of these patients were 10(71.4%) patients with Phakic and 4(28.4%) patients with Pseudophakic. The patients IOP were measured and recorded preoperative , at 5,15,30,45,60 min and 1day after the injection were 19.71 ± 1.90 mmHg, 32.07 ± 13.68 mmHg (p=0.005), 23.43 ± 6.38 mmHg(p=0.043), 20.86 ± 5.07 mmHg(p=0.476), 19.50 ± 3.11 mmHg(p=0.803), 19.21 ± 3.17 mmHg(p=0.583), 17.71 ± 1.59 mmHg(p=0.011) respectively as shown in **(Table 1)**.

Table 1: Sociodemographic and clinical characteristics of patients (n =14)

Characteristics	N (%)
Gender	
Males	7 (50.00)
Females	7 (50.00)
Lens status	
Phakic	10 (71.4)
Pseudophakic	4 (28.4)
Age mean	62.43 ± 10.68
Preoperative IOP	19.71 ± 1.90
5 minutes IOP	32.07 ± 13.68
15 minutes IOP	23.43 ± 6.38
30 minutes IOP	20.86 ± 5.07
45 minutes IOP	19.50 ± 3.11
*60 minutes IOP	19.21 ± 3.17
One day post-operative	17.71 ± 1.59
Patients remained with increased IOP one day post-operatively	3 (21.43)

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After intravitreal injection of aflibercept at 5 minutes, the result shows a significantly higher IOP than preoperative measurements (p=0.005), at 15 minutes IOP show a significantly higher than preoperative IOP (p=0.043), and One day postoperative IOP is significantly lower than preoperative IOP (p=0.011).

Comparing the mean IOP before and after intravitreal aflibercept injection, it was significantly higher at 5 and 15 min after injection. However, the mean IOP returned to the normal pre-injection level at 60 min (p=0.583) .In the result, there were 3eyes (21.43%) had persistent increased IOP one day after intravitreal injection as shown in **(Table 2)**.

Table 2: Paired t-test comparing preoperative and post-operative IOP (n =14)

Characteristics	t-test	p-value
Preoperative IOP versus 5 minutes IOP	3.374	0.005
Preoperative IOP and 15 minutes IOP	2.239	0.043
Preoperative IOP and 30 minutes IOP	0.734	0.476
Preoperative IOP and 45 minutes IOP	0.255	0.803
Preoperative IOP and 60 minutes IOP	0.563	0.583
Preoperative IOP and one day postoperative	2.944	0.011

In comparison, there is no statistically significant effect of gender on the pre and post injection mean IOP at 5,15 minutes, and 1 day (p=0.591, 0.473, 0.345; respectively) .Also the result show no statistically significant effect between the lens status and pre and post injection mean IOP at 5,15 minutes, and 1 day (p=0.691, 0.980, 0.447; respectively) as shown on (Table 3)

Table 3: Independent t-test comparing preoperative and post-operative IOP with patients characteristics (n =14)

Characteristics	t-test	p-value
Gender		
Preoperative IOP versus 5 minutes IOP	0.551	0.591
Preoperative IOP and 15 minutes IOP	0.741	0.473
Preoperative IOP and one day postoperative	1.009	0.345
Lens status		
Preoperative IOP versus 5 minutes IOP	0.407	0.691
Preoperative IOP and 15 minutes IOP	0.025	0.980
Preoperative IOP and one day postoperative	0.786	0.447

4. Discussion

The discovery of intravitreal injections that target vascular endothelial growth factor (VEGF) has revolutionized the management of the ocular neovascular diseases. Aflibercept can effectively reduce the intraocular level of VEGF and vascular permeability related to diabetic macular edema (DME) [1].

Intravitreal injection of aflibercept is predicted to elevate intraocular pressure (IOP) secondary to increased vitreous volume in a similar way to how other anti-VEGF agents elevate IOP, such as ranibizumab [2]. There is limited data available on the short-term effect of intravitreal aflibercept injection on IOP for DME.

To our knowledge, there is no publication demonstrating the impact of intravitreal injection of aflibercept on IOP in patients with DME. In the present study, aflibercept injection was safe with regard to short-term IOP changes in patients with DME.

5. Conclusions

Our study confirmed that intravitreal aflibercept injection is safe with respect to short-term IOP changes in patients with DME. A significant short-term rise of IOP occurred within 15 minutes after injection then it returned to normal in most patients. The effect of gender on the mean IOP before and after aflibercept injection was not statistically significant.

Study Limitations

The limitations of our study were short follow-up period and lack of control group. A large randomized study can further confirm the safety of aflibercept injection in patients with DME.

In summary, intravitreal aflibercept demonstrated transient IOP elevation, which came back to normal within 15 minutes after intravitreal injection without using ocular hypotensive medications. No serious systemic or ocular adverse events were reported.

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Competing Interests

The authors have no proprietary or commercial interest in any materials discussed in this paper. The authors declare no financial support or conflict of interests.

References

[1] Fauser, S, Schwabecker V, and Muether PS. Suppression of intraocular vascular endothelial growth factor during aflibercept treatment of age-related macular degeneration. Am J Ophthalmol. 2014; 158(3):532–536.
[2] Sharei V, Höhn F, Köhler T, Hattenbach LO, Mirshahi A. Course of intraocular pressure after intravitreal injection of 0.05 mL ranibizumab (Lucentis). Eur J Ophthalmol. 2010; 20:174–179.
[3] Stamper R. A History of Intraocular Pressure and its Measurment. Optom Vis Sci 2011; 88(1):E16-28.
[4] Bhan A, Browning AC, Shah S, et al. Effect of corneal thickness on intraocular pressure measurments with the pmeumotonometer, Goldmann applanation tonometer, and Tono-Pen. Invest Ophthalmol Vis Sci 2002; 43(5):1389-92.
[5] Gupta V, Sony P, Agarwal HC, et al. Inter-instrument agreement and influence of central corneal thickness on measurements with goldmann, Pneumotonometer and noncontact tonometer in glaucomatous eyes. Indian J Ophthalmol 2006; 43(5):1389-92
[6] Kirby A, Gebski V, Keech AC. Determining the sample size in a clinical trial. Med J Aust.2002; 177:256-7.
[7] Larsan S, Osnes M, Eidsaunet W, Sandvik L. Factors influencing the sample size, exemplified by studies on gastroduodenal tolerability of drugs. Scand J Gastroenterol. 1985; 20:395-400.
[8] Prakesh B, Babu SR,Sureshkumar K. Response of Ayurvedic therapy in the treatment of migraine without aura. Int J Ayurveda Research.2010; 1:29-35.

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